Summary

Clinical Descriptions

- The two main eating disorders are anorexia nervosa and bulimia nervosa. Binge eating disorder is being studied for possible inclusion in the DSM-V. The symptoms of anorexia nervosa include refusal to maintain normal body weight, an intense fear of being fat, a distorted sense of body shape, and, in women, amenorrhea. Anorexia typically begins in the mid-teens, is 10 times more frequent in women than in men, and is comorbid with several other disorders, notably depression. Its course is not favorable, and it can be life threatening. The symptoms of bulimia nervosa include episodes of binge eating followed by purging, fear of being fat, and a distorted body image. Like anorexia, bulimia begins in adolescence, is much more frequent in women than in men, and is comorbid with other diagnoses, such as depression. Prognosis is somewhat more favorable than for anorexia.

Etiology

- Research in the eating disorders has examined genetics and brain mechanisms. Evidence is consistent with a possible genetic diathesis. Endogenous opioids and serotonin, both of which play a role in mediating hunger and satiety, have been examined in eating disorders. Low levels of both these brain chemicals have been found in people with eating disorders, but evidence that these cause eating disorders is limited. Dopamine is also involved with eating, but its role in eating disorders is less well studied.
- On a psychological level, several factors play important roles. Psychodynamic theories of eating disorders emphasize parent–child relationships and personality characteristics. Research on characteristics of families with an eating-disordered child have yielded different data depending on how the data were collected. Reports of people with eating disorders show high levels of conflict, but actual observations of the families do not find them especially troubled. Studies of personality have found that people with eating disorders are high in neuroticism and perfectionism and low in self-esteem. Many women with eating disorders report being abused as children, but early abuse does not appear to be a specific risk factor for eating disorders.
- Cognitive behavioral theories of eating disorders propose that fear of being fat and body-image distortion make weight loss a powerful reinforcer. Among people with bulimia nervosa, negative affect and stress precipitate binges that create anxiety, which is then relieved by purging.
- As sociocultural standards changed to favor a thinner shape as the ideal for women, the frequency of eating disorders increased. The objectification of women's bodies also exerts pressure for women to see themselves through a sociocultural lens. The prevalence of eating disorders is higher in industrialized countries, where the cultural pressure to be thin is strongest. White women tend to have greater body dissatisfaction and general eating disturbances than African American women, though the prevalence rates for actual eating disorders are not markedly different between these two ethnic groups.

Treatment

- The main neurobiological treatment of eating disorders is the use of antidepressants. Although somewhat effective, dropout rates from drug-treatment programs are high and relapse is common when people stop taking the medication. Treatment of anorexia often requires hospitalization to reduce the medical complications of the disorder. Providing reinforcers for weight gain has been somewhat successful, but no treatment has yet been shown to produce long-term maintenance of weight gain.
- Cognitive behavioral treatment for bulimia focuses on questioning society's standards for physical attractiveness, challenging beliefs that encourage severe food restriction, and developing normal eating patterns. Outcomes are promising, both in the short and long term.
- Prevention programs show promise, particularly those programs that include girls age 15 or older, involve more than one session, and are interactive rather than didactic (i.e., lecture format). Outcomes appear promising up to 3 years after the prevention programs are instituted.

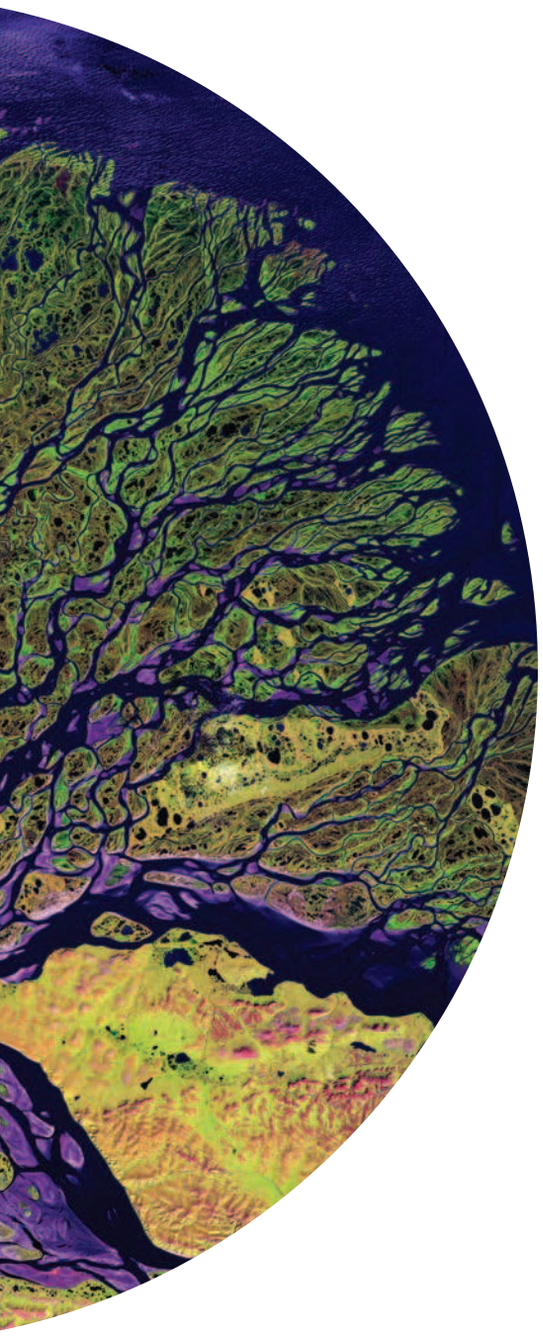
Answers to Check Your Knowledge Questions

9.1 1. c; 2. d; 3. d
9.2 1. F; 2. T; 3. F; 4. F; 5. T
9.3 1. cognitive behavior therapy; 2. hospitalization, medications, family therapy; 3. dissonance reduction, healthy weight.

Key Terms

anorexia nervosa
binge eating disorder
body mass index (BMI)
bulimia nervosa
obese

10 Substance-Related Disorders



LEARNING GOALS

1. Be able to differentiate between substance dependence and abuse.
2. Be able to describe the epidemiology and symptoms of drug and alcohol abuse and dependence.
3. Be able to understand the major etiological factors for substance-related disorders, including genetic factors, neurobiological factors, mood and expectancy effects, and sociocultural factors.
4. Be able to describe the approaches to treating substance-related disorders, including psychological treatments, medications, and drug substitution treatments.
5. Be able to delineate the major approaches to prevention of substance-related disorders.

PEOPLE HAVE USED VARIOUS substances in the hope of reducing physical pain or altering states of consciousness for centuries. Around the world, almost all people use one or more substances that affect the central nervous system, relieving physical and mental anguish or producing euphoria. Despite the often devastating consequences of taking such substances into the body, their initial effects are usually pleasing, a factor that is perhaps at the root of **substance-related disorders**.

Clinical Descriptions, Prevalence, and Effects of Substance-Related Disorders

The United States is a drug culture. Americans use drugs to wake up (coffee or tea), to stay alert throughout the day (cigarettes, soft drinks), to relax (alcohol), and to reduce pain (aspirin). The widespread availability and frequent use of various drugs sets the stage for the potential abuse of drugs, the topic of this chapter.

In 2006, over 20 million people over the age of 12 in the United States reported having used an illicit drug [Substance Abuse and Mental Health Services Administration (SAMHSA), 2007]. In addition, 125 million Americans over the age of 12 reported alcohol use of some kind, and 57 million Americans reported at least one episode of binge drinking (defined as having five or more drinks) in the last 30 days (SAMHSA, 2007). Over 15 million people abused prescription drugs such as pain medication in 2003, more than double the number that did so in 1992 (National Center on Addiction and Substance Abuse, 2005). Recent data on the frequency of use of several drugs, legal and illegal, are presented in Table 10.1. These figures do not represent the frequency of abuse or dependence but simply provide an indication of the pervasiveness of drug use in the United States.

Table 10.1 Percentage of U.S. Population Reporting Drug Use in Past Month (2006)

Substance	Percentage Reporting Use
Alcohol	50.9
Cigarettes	29.6
Marijuana	6.0
Nonmedical psychotherapeutics	2.8
Cocaine	1.0
Hallucinogens	0.4
Inhalants	0.2

Source: Substance Abuse and Mental Health Services Administration (2007).

Drug use by adolescents is considerable, but the percentage of adolescents (ages 12–17) who used any illicit drug decreased between 2002 and 2006 from 11.6 to 9.8 percent (SAMHSA, 2007). In 2006, 16.6 percent of youths reported using alcohol.

The pathological use of substances falls into two categories: substance abuse and substance dependence. **Substance dependence**, also referred to as **addiction**, is characterized by DSM-IV-TR as the presence of many problems related to taking the substance. These include using more of the substance than intended, trying unsuccessfully to stop, having physical or psychological problems made worse by the drug, and experiencing problems at work or with friends.

Substance dependence typically involves either tolerance or withdrawal. **Tolerance** is indicated by either (1) larger doses of the substance being needed to produce the desired effect or (2) the effects of the drug becoming markedly less if the usual amount is taken. **Withdrawal** refers to the negative physical and psychological effects that develop when a person stops taking the substance or reduces the amount. Substance withdrawal symptoms can include muscle pains and twitching, sweats, vomiting, diarrhea, and insomnia. Some investigators argue that withdrawal should be mandatory for the diagnosis of substance dependence (Langenbucher et al., 2000). In general, being dependent on a drug is associated with more severe problems (Schuckit et al., 1998).

For the less serious diagnosis of **substance abuse,** the person must experience problems such as failure to meet obligations at work or within the family. Use of the substance may also expose the person to physical dangers, as in driving while drunk. Social relationships may be strained, and legal problems may be frequent.

In 2006, over 22 million people in the United States met the diagnostic criteria for substance abuse or dependence. This figure represents over 9 percent of the U.S. population—not a trivial number. Of this large number of people, most (nearly 15 million) met criteria for alcohol abuse or dependence. Close to 4 million met the criteria for drug abuse or dependence, and over 3 million met the criteria for both drug and alcohol problems (SAMHSA, 2007).

Drug and alcohol dependence are among the most stigmatized of disorders. Terms such as "*addict*" or "*alcoholic*" are tossed about carelessly, as if these words capture the essence of people, not the disorder that they suffer from. Historically, drug and alcohol problems have been viewed as moral lapses rather than as conditions in need of treatment. Unfortunately, such attitudes persist today. Yet there is convincing evidence that becoming dependent on drugs or alcohol is not, in fact, only a matter of personal choice. True, people make decisions about whether or not to try alcohol or drugs, but the ways in which these decisions and the substances involved interact with an individual's neurobiology, social setting, culture, and other environmental factors all conspire to create dependence. Such factors put some people at higher risk for substance dependence than others; it is a mistake to consider substance-related disorders as somehow solely the result of moral failing or personal choice. But it is also a mistake to consider those dependent on drugs or alcohol as being without recourse to change the course of their disorder. Treatment and behavioral change can work in this sphere in much the same way they can work for diseases such as diabetes, where people can change the course of their disease with insulin and diet control.

We turn now to an overview of the major substance-related disorders, those involving alcohol, nicotine, marijuana, opiates, stimulants, and hallucinogens.

DSM-IV-TR Criteria for Substance Dependence

Three or more of the following:

- Tolerance
- Withdrawal
- Substance taken for a longer time or in greater amounts than intended
- Desire or efforts to reduce or control use
- Much time spent trying to obtain the substance
- Social, recreational, or occupational activities given up or reduced
- Continued use despite knowing problems caused by substance

DSM-IV-TR Criteria for Substance Abuse

Maladaptive use of a substance shown by 1 of the following:

- Failure to meet obligations
- Repeated use in situations where it is physically dangerous
- Repeated substance-related legal problems
- Continued use despite problems caused by the substance

Clinical Case: Alice

Alice was 54 years old and living alone when her family finally persuaded her to check into an alcohol rehabilitation clinic. She had taken a bad fall while drunk, and it may have been this event that finally got her to admit that something was wrong. Her drinking had been out of control for several years. She began each day with a drink, continued through the morning, and was totally intoxicated by the afternoon. She seldom had any memory for events after noon of any day. Since early adulthood she had drunk regularly, but rarely during the day and never to the point of drunkenness. The sudden death of her husband in an automobile accident two years earlier had triggered a quick increase in her drinking, and within 6 months she had slipped into a pattern of severe alcohol dependence. She had little desire to go out of her house and had cut back on social activities with family and friends. Repeated efforts by her family to get her to curtail her intake of alcohol had only led to angry confrontations.

Alcohol Abuse and Dependence

The term "*alcoholic*" is familiar to most people, yet it does not have a precise meaning. DSM-IV-TR distinguishes between alcohol dependence and alcohol abuse. Unfortunately, some researchers have only measured abuse without distinguishing dependence. People who meet DSM-IV-TR criteria for alcohol abuse experience negative social and occupational effects from the drug. However, they do not show tolerance, withdrawal, or a compulsive pattern of abuse.

People who are dependent on alcohol generally have more severe symptoms, such as tolerance or withdrawal, than do people who only abuse alcohol without being dependent (Schuckit et al., 1998). The effects of the abrupt withdrawal of alcohol in a chronic, heavy user may be rather dramatic because the body has become accustomed to alcohol. Specifically, a person may feel anxious, depressed, weak, restless, and unable to sleep. He or she may have muscle tremors, especially of the fingers, face, eyelids, lips, and tongue, and pulse, blood pressure, and temperature may be elevated.

In relatively rare cases, a person who has been drinking heavily for a number of years may also experience **delirium tremens (DTs)** when the level of alcohol in the blood drops suddenly. The person becomes delirious as well as tremulous and has hallucinations that are primarily visual but may be tactile as well. Unpleasant and very active creatures—snakes, cockroaches, spiders, and the like—may appear to be crawling up the wall or over the person's body or to be filling the room. Feverish, disoriented, and terrified, the person may claw frantically at his or her skin to get rid of the creatures.

An etching showing the vivid portrayal of delirium tremens in a scene in a play. (Culver Pictures, Inc.)

Although changes in the liver enzymes that metabolize alcohol can account to a small extent for tolerance, research suggests that the central nervous system is responsible as well. Some research suggests that tolerance results from changes in the number or sensitivity of GABA or glutamate receptors (Tsai et al., 1998). Withdrawal may result because some neural pathways increase their activation to compensate for alcohol's inhibitory effects in the brain.

Both alcohol abuse and dependence are often part of **polydrug abuse**, abusing more than one drug at a time. It is estimated, for example, that 80 to 85 percent of people who abuse alcohol are smokers. This very high comorbidity may occur because alcohol and nicotine are cross-tolerant; that is, nicotine can induce tolerance for the rewarding effects of alcohol and vice versa. Thus, consumption of both drugs may be increased to maintain their rewarding effects (Rose et al., 2004).

Most people who meet criteria for alcohol abuse do not go on to develop alcohol dependence. For example, one prospective study found that only 3.5 percent of

persons meeting DSM-IV-TR criteria for alcohol abuse had developed alcohol dependence 5 years later, a number not significantly greater than the 2.5 percent of the population who developed alcohol dependence for the first time over the same 5-year period (Schuckit et al., 2001).

Polydrug abuse involves the abuse of multiple drugs. Alcohol and nicotine are a frequent combination, although most people who smoke and drink in social situations do not abuse substances. (Timothy Shonnard/Stone/Getty Images.)

Prevalence and Cost of Alcohol Abuse and Dependence

In a recent U.S. epidemiological study based on the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), lifetime prevalence rates for alcohol dependence defined by DSM-IV criteria were greater than 12 percent, and lifetime prevalence rates for alcohol abuse were over 17 percent (Hasin et al., 2007).

Alcohol use is especially frequent among college-age adults. This is true for binge drinking, defined as having five drinks in a short period of time (e.g., within an hour), and heavy-use drinking, defined as having five drinks on the same occasion five or more times in a 30-day period. Among both male and female college students, binge and heavy-use prevalence rates are 43.5 and 17.6 percent, respectively (SAMHSA, 2004). Binge drinking even occurs with high frequency among high school students. Generally speaking, the prevalence of binge drinking is highest among people aged 18 to 25, with a peak prevalence at age 22 (SAMHSA, 2007).

Binge drinking can have serious consequences. Estimates suggest that as many as 1,400 college students die from alcohol-related incidents (e.g., driving under the influence, toxicity) each year. An additional 600,000 are assaulted by other students who have been drinking, and as many as 70,000 students are sexually assaulted [National Institute on Alcohol Abuse and Alcoholism (NIAAA), 2002].

The prevalence of alcohol problems differs by ethnicity and education level as well. White adolescents and adults are more likely to abuse alcohol than African American adolescents and adults. Binge and heavy-use drinking is lowest among Asian Americans (SAMHSA, 2007). Alcohol dependence is most prevalent among Native Americans and Hispanic and least prevalent among Asian Americans and African Americans (Smith et al., 2006).

Alcohol abuse and dependence are comorbid with several personality disorders, mood disorders, schizophrenia, and anxiety disorders as well as with other drug use (Kessler et al., 1997; Morgenstern et al., 1997; Skinstad & Swain, 2001). According to the Substance Abuse and Mental Health Services Administration (2004), 21.3 percent of people suffering from alcohol or drug dependence or abuse also have at least one other mental disorder.

Expenditures on health care for people dependent on alcohol have been estimated to be over $26 billion annually (NIAAA, 2001). Alcohol-related traffic fatalities are a serious problem, and the highest-risk drivers are young men. Through vigorous law enforcement efforts and educational campaigns such as those waged by MADD (Mothers Against Drunk Driving), the situation has improved. Alcohol-related traffic fatalities declined 5 percent between 1993 and 2003, and another 2.4 percent between 2003 and 2004. Still, there were 16,694 deaths from drinking-related driving in 2004, representing nearly 4 out of every 10 traffic fatalities that year. [National Highway Transportation & Safety Administration (NHTSA), 2003, 2005]. More men than women died in alcohol-related fatalities in 2003, and the highest percentage of fatalities with blood alcohol contents of greater than .08 (the legal limit in many states) was among adults aged 21–24 (NHTSA, 2003; SAMHSA, 2004).

Alcohol is often implicated in vehicular accidents. The driver of this New York subway train, which derailed, killing 5 and injuring over 100 people, was intoxicated. (Corbis Images.)

Blood Alcohol Concentration Calculator									
# OF DRINKS CONSUMED/SEX		WEIGHT							
		100	120	140	160	180	200	220	240
1	Male	.04	.04	.03	.03	.02	.02	.02	.02
	Female	.05	.04	.04	.03	.03	.03	.02	.02
2	Male	.09	.07	.06	.05	.05	.04	.04	.04
	Female	.10	.08	.07	.06	.06	.05	.05	.04
3	Male	.13	.11	.09	.08	.07	.07	.06	.05
	Female	.15	.13	.11	.10	.08	.08	.07	.06
4	Male	.17	.15	.13	.11	.10	.09	.08	.07
	Female	.20	.17	.15	.13	.11	.10	.09	.09
5	Male	.22	.18	.16	.14	.12	.11	.10	.09
	Female	.25	.21	.18	.16	.14	.13	.12	.11
6	Male	.26	.22	.19	.16	.15	.13	.12	.11
	Female	.30	.26	.22	.19	.17	.15	.14	.13
7	Male	.30	.25	.22	.19	.17	.15	.14	.13
	Female	.36	.30	.26	.22	.20	.18	.16	.15
8	Male	.35	.29	.25	.22	.19	.17	.16	.15
	Female	.41	.33	.29	.26	.23	.20	.18	.16
9	Male	.39	.35	.28	.25	.22	.20	.18	.16
	Female	.46	38	.33	.29	.26	.23	.21	.19
10	Male	.39	.35	.28	.25	.22	.20	.18	.16
	Female	.51	.42	.36	.32	.28	.25	.23	.21
11	Male	.48	.40	.34	.30	.26	.24	.22	.20
	Female	.56	.46	.40	.35	.31	.27	.25	.23
12	Male	.53	.43	.37	.32	.29	.26	.24	.21
	Female	.61	.50	.43	.37	.33	.30	.28	.25
13	Male	.57	.47	.40	.35	.31	.29	.26	.23
	Female	.66	.55	.47	.40	.36	.32	.30	.27
14	Male	.62	.50	.43	.37	.34	.31	.28	.25
	Female	.71	.59	.51	.43	.39	.35	.32	.29
15	Male	.66	.54	.47	.40	.36	.34	.30	.27
	Female	.76	.63	.55	.46	.42	.37	.35	.32

Figure 10.1 Blood alcohol concentration calculator. Note that values are just estimates. An actual BAC will vary depending on metabolism and amount of food in the stomach.

Short-Term Effects of Alcohol How does alcohol produce its short-term effects? After being swallowed and reaching the stomach, alcohol begins to be metabolized by enzymes. Most of it goes into the small intestine, and from there is absorbed into the blood. It is then broken down, primarily in the liver, which can metabolize about 1 ounce of 100-proof (50 percent alcohol) liquor per hour. Quantities in excess of this amount remain in the bloodstream. Whereas absorption of alcohol can be very quick, removal is always slow.

Although Figure 10.1 shows mean blood alcohol levels based on a person's weight and amount of alcohol consumption, the effects of alcohol vary with its concentration in the bloodstream. Levels in the bloodstream depend on the amount ingested in a particular period of time, the presence of food in the stomach (food retains the alcohol and reduces its absorption rate), the weight and body fat of the person drinking, and the efficiency of the liver. Two ounces of alcohol will thus have a different effect on a 180-pound man who has just eaten than on a 110-pound woman with an empty stomach. However, women achieve higher blood alcohol concentrations even after adjustment for differences in body weight, perhaps due to differences in body water content between men and women.

Alcohol produces its effects through its interactions with several neural systems in the brain. It stimulates GABA receptors, which may account for its ability to reduce tension. (GABA is a major inhibitory neurotransmitter; the benzodiazepines, such as Xanax, have an effect on GABA receptors similar to that of alcohol.) Alcohol also increases levels of serotonin and dopamine, and this may be the source of its ability to produce pleasurable effects. Finally, alcohol inhibits glutamate receptors, which may cause the cognitive effects of alcohol intoxication, such as slowed thinking and memory loss.

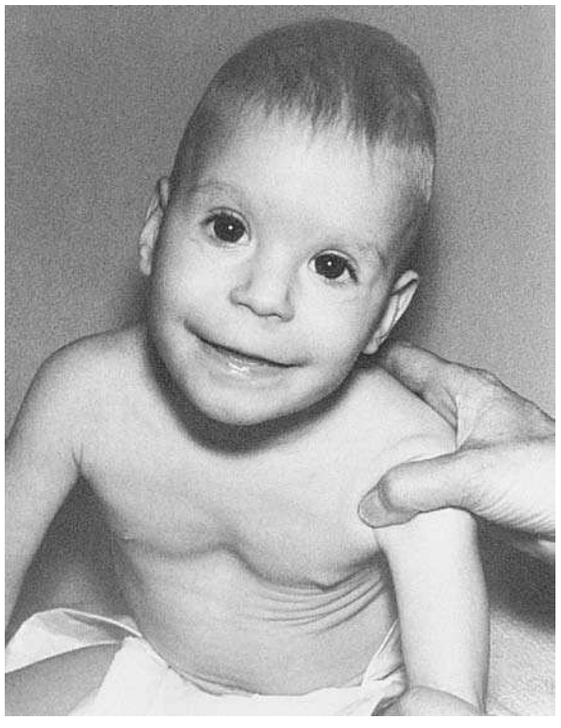
A novel study examined the effects of alcohol on both the brain and behavior. Participants were given different doses of alcohol while in an fMRI scanner performing a simulated driving test (Calhoun, Pekar, & Pearlson, 2004). The low dose (.04 blood alcohol content) led to just a small impairment in motor functioning, but the high dose (.08 blood alcohol content) led to more significant motor impairment that interfered with driving ability. Furthermore, the effects of the alcohol in the brain were in areas associated with monitoring errors and making decisions (the anterior cingulate and orbitofrontal cortex), which suggested to the researchers that people at the legal limit of alcohol may make poor decisions about driving and not realize they are making mistakes.

Long-Term Effects of Prolonged Alcohol Abuse Almost every tissue and organ of the body is adversely affected by prolonged consumption of alcohol. For example, alcohol provides so many calories—a pint of 80-proof spirits supplies about half a day's caloric requirements—that drinkers often reduce their intake of food. But the calories provided by alcohol are empty; they do not supply the nutrients essential for health, and the result can be severe malnutrition. Alcohol also contributes directly to malnutrition by impairing the digestion of food and absorption

of vitamins. In older people who have chronically abused alcohol, a deficiency of B-complex vitamins can cause amnestic syndrome, a severe loss of memory for both recent and long-past events. These memory gaps are often filled in by reporting imaginary events (confabulation).

Prolonged alcohol use plus reduction in the intake of proteins contributes to the development of cirrhosis of the liver, a disease in which some liver cells become engorged with fat and protein, impeding their function; some cells die, triggering an inflammatory process, and when scar tissue develops, blood flow is obstructed. Taken together, chronic liver disease and cirrhosis rank 12th among causes of death in the United States, with 27,257 deaths in 2002 (Kochanek et al., 2004).

Other common changes to the body due to drinking include damage to the endocrine glands and pancreas, heart failure, erectile dysfunction, hypertension, stroke, and capillary hemorrhages, which are responsible for the swelling and redness in the face, and especially the nose, of people who chronically abuse alcohol. Chronic heavy drinking is associated with damage to many areas of the brain, many of which are implicated in memory functions.



Heavy drinking during pregnancy can cause fetal alcohol syndrome. Children with this disorder can have facial abnormalities and mental retardation. (Courtesy of James W. Hanson.)

Heavy alcohol consumption by a woman during pregnancy is the leading known cause of mental retardation among children. The growth of the fetus is slowed, and cranial, facial, and limb anomalies can be produced, a condition known as **fetal alcohol syndrome (FAS)**. Even moderate drinking can produce undesirable, if less severe, effects on the fetus, leading the National Institute on Alcohol Abuse and Alcoholism to counsel total abstention during pregnancy as the safest course. Research with children who did not have FAS but whose mothers drank moderately (i.e., about one drink per day) during the first trimester revealed that these children had impairments in learning and memory (Willford et al., 2004) and exhibited growth deficits (such as smaller head size and lower height and weight) at age 14 (Day et al., 2004). Newer research is beginning to solve the puzzle of why some fetuses exposed to alcohol will not develop any problems, whereas others will have profound problems. For example, by 6 months of age, infants exposed to alcohol prenatally may exhibit problems in attention that can then contribute to the development of other cognitive problems later in childhood (Kable & Coles, 2004). The news is not all bad. Animal research has shown that some of the problems associated with prenatal alcohol exposure, such as deficits in learning and memory, can be turned around (Klintsova et al., 2002). In addition, research suggests that growth deficits associated with prenatal alcohol exposure can be mitigated if children are raised in a more stable and healthy environment, indicating that the biological effects of early alcohol exposure are sensitive to environmental conditions (Day & Richardson, 2004).

Although it is appropriate and accurate to pay attention to the negative effects of alcohol, other evidence points to the positive health benefits for some people. Light drinking, especially of red wine, has been related to lower risk for coronary heart disease and stroke (Sacco et al., 1999; Theobald et al., 2000). If alcohol does have a beneficial effect, it could be either physiological (e.g., acetate, a metabolite of alcohol, increases coronary blood flow) or psychological (a less-driven lifestyle and diminished hostility). Some hypothesize that consumption of low to moderate amounts of red wine may lower cholesterol levels. Indirect evidence for this hypothesis has recently been found in an animal study, where researchers discovered that pigment substances in red wine called polyphenols interfered with the synthesis of a peptide called endothelin-1, which is believed to contribute to atherosclerosis (Corder et al., 2001).

Check Your Knowledge 10.1 (Answers are at the end of the chapter.)

True or false?

1. The diagnosis of substance dependence requires both tolerance and withdrawal.
2. Research suggests that nicotine can enhance the rewarding properties of alcohol.
3. Even moderate drinking by pregnant women can cause learning and attention problems in their children.

California's Tobacco Education Media Campaign parodies tobacco ads to illustrate health risks associated with smoking and to attack pro-tobacco influences. (Courtesy of California Department of Health Services.)

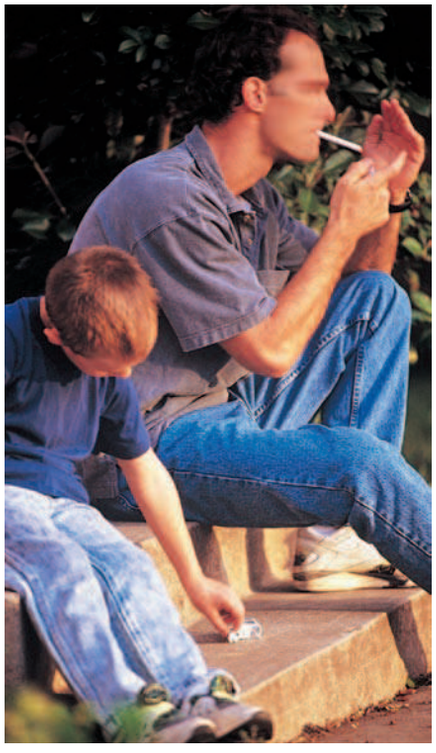
Nicotine and Cigarette Smoking

Not long after Columbus's first commerce with Native Americans, sailors and merchants began to imitate the Native Americans' smoking of rolled leaves of tobacco, with the result that they, too, began to crave it. When not smoked, tobacco was—and is—chewed or ground into small pieces and inhaled as snuff. **Nicotine** is the addicting agent of tobacco. The neural pathways that become activated stimulate the dopamine neurons in the mesolimbic area that seem to be involved in producing the reinforcing effects of most drugs (Stein et al., 1998).

Prevalence and Health Consequences of Smoking The threat to health posed by smoking has been documented convincingly by the Surgeon General of the United States in a series of reports since 1964. It is estimated that more than 440,000 American tobacco users die prematurely each year [U.S. Department of Health and Human Sources (USDHHS) 2004)]. Cigarette smoking is responsible in some way for one of every six deaths in the United States, killing more than 1,100 people each day. It remains the single most preventable cause of premature death in the United States as well as in other parts of the world. Lung cancer kills more people than any other cancer, and cigarette smoking is probably the cause of as many as 87 percent of lung cancers.

Among the other medical problems associated with, and almost certainly caused or exacerbated by, long-term cigarette smoking are emphysema; cancers of the larynx and of the esophagus, pancreas, bladder, cervix, and stomach; complications during pregnancy; sudden infant death syndrome; periodontitis; and a number of cardiovascular disorders (USDHHS, 2004). The most probable harmful components in the smoke from burning tobacco are nicotine, carbon monoxide, and tar, which consist primarily of certain hydrocarbons, many of which are known carcinogens (Jaffe, 1985).

In 2006, nearly 73 million people in the United States used a tobacco product (cigarette, cigar, smokeless tobacco, pipe), and over 3 million youths between the ages of 12 and 17 reported using a tobacco product in the past month. Smoking is more prevalent among white and Hispanic adolescents than among African American or Asian American adolescents. In general, smoking is more prevalent among men than women. However, prevalence among girls and boys between the ages of 12 and 17 is the same (SAMSHA, 2007). The Surgeon General's report in 2004 estimated that the costs of smoking in the United States exceeded $157 billion a year, with half of that reflecting medical costs and the other half reflecting costs of lost productivity.



Parental smoking greatly increases the chances that children will begin to smoke. (Peter Poulides/Stone/Getty Images.)

Research demonstrates the significance of ethnicity in nicotine addiction as well as the intricate interplay among behavioral, social, and biological factors (Leischow, Ranger-Moore, & Lawrence, 2000). It has been known for years that African American cigarette smokers are less likely to quit and are more likely, if they continue to smoke, to get lung cancer. Why? It turns out that they retain nicotine in their blood longer than do whites, that is, they metabolize it more slowly (Mustonen et al. 2005). Another reason has to do with the type of cigarette smoked. African Americans are more likely to smoke menthol cigarettes, and research shows that people who smoke menthol inhale more deeply and hold the smoke in for longer, thus providing more opportunity for deleterious effects (Celebucki et al., 2005).

Research has found that Chinese Americans metabolize less nicotine from cigarettes than either white or Latino smokers (Benowitz et al., 2002). In general, lung cancer rates are lower among Asians than whites or Latinos. The relatively lower metabolism of nicotine among Chinese Americans may help explain why lung cancer rates are lower in this group.

Health Consequences of Secondhand Smoke As we have known for many years, the health hazards of smoking are not restricted to those who smoke. The smoke coming from the burning end of a cigarette, so-called **secondhand smoke**, or environmental tobacco smoke (ETS), contains higher concentrations of ammonia, carbon monoxide, nicotine, and tar than does the smoke actually inhaled by the smoker. Environmental tobacco smoke is blamed for close to 40,000 deaths a year in the United States. In 1993 the Environmental Protection Agency classified ETS as a hazard

Children of mothers who smoke are at increased risk for respiratory infections, bronchitis, and inner ear infections. (Jennie Woodcock, Reflections Photolibrary/Corbis Images.)

The Surgeon General's report from 2006 noted that no amount of secondhand smoke is safe. (Courtesy The U.S. Department of Health and Human Services.)

on a par with asbestos and radon. In 2006, the Surgeon General issued a report detailing the health hazards of secondhand smoke. The National Institute of Health has classified ETS as a known carcinogen, indicating that evidence has established a cause–effect relationship between ETS and cancer. Effects of ETS include the following:

- Nonsmokers can suffer lung damage, possibly permanent, from extended exposure to cigarette smoke. Those living with smokers are at greatest risk. Precancerous lung abnormalities have been observed in those living with smokers, and nonsmokers are at greater risk for developing cardiovascular disease and lung cancer. In addition, some nonsmokers have allergic reactions to the smoke from burning tobacco.
- Babies of women exposed to secondhand smoke during pregnancy are more likely to be born prematurely, to have lower birth weights, and to have birth defects.
- Children of smokers are more likely to have upper respiratory infections, asthma, bronchitis, and inner ear infections than are their peers whose parents do not smoke. Secondhand smoke can cause sudden infant death syndrome (SIDS).

The Surgeon General has stated that the best form of prevention for exposure to secondhand smoke is to promote smoke-free environments as there is really no safe level of exposure to secondhand smoke (USDHHS, 2006). In recent years, various local governments have passed ordinances regulating cigarette smoking in public places and work settings. Smoking is banned in many supermarkets, buses, hospitals, and government buildings and on all domestic U.S. airline flights. Restaurants must often post signs indicating whether they have an area for nonsmokers, and in many states, such as California, New York, Delaware, Connecticut, Massachusetts, Rhode Island, and Maine, smoking is banned altogether in restaurants. Indeed, smoking is banned in nearly all public places in these seven states, and it is likely that more states will adopt similar regulations.

Marijuana

Marijuana consists of the dried and crushed leaves and flowering tops of the hemp plant, *Cannabis sativa*. It is most often smoked, but it may be chewed, prepared as a tea, or eaten in baked goods. **Hashish**, much stronger than marijuana, is produced by removing and drying the resin exudate of the tops of cannabis plants.

Originally the hemp plant was extensively cultivated in the United States not for smoking but for its fibers, which were used in the manufacture of cloth and rope. By the nineteenth century, the medicinal properties of cannabis resin had been noted, and it was marketed by several drug companies as a treatment for rheumatism, gout, depression, cholera, and neuralgia.

Recreational use of hashish in a fashionable apartment in New York City in the nineteenth century. An 1876 issue of the *Illustrated Police News* carried this picture with the title "Secret Dissipation of New York Belles: Interior of a Hasheesh Hell on Fifth Avenue." (Culver Pictures, Inc.)

It was also smoked for pleasure, though this was little seen in the United States until 1920. At that time, the passage of the Eighteenth Amendment prohibiting the sale of alcohol prompted some people to begin smoking marijuana brought across the border from Mexico. Unfavorable reports in the press attributing crimes to marijuana use led to the enactment of a federal law against the sale of the drug in 1937. Today marijuana use is illegal in most countries.

Prevalence of Marijuana Use Marijuana is the most frequently used illicit drug. In 2006, nearly 15 million people over the age of 12 reported using marijuana (SAMHSA, 2007). See Figure 10.2 for data on usage from 2002 to 2006. The prevalence is higher among men than women, with nearly twice as many men than women reporting use in the past month in 2006 (SAMHSA, 2007). Marijuana abuse and dependence is more common among Native Americans and European-Americans, and less common among African Americans, Hispanics, and Asian Americans (Stinson et al., 2006). Marijuana use is generally greater in the United States, Australia, and New Zealand than in the European Union, Africa, Asia, South America, and Canada (Rey, Martin, & Krabman, 2004).

Effects of Marijuana As with most other drugs, marijuana use has its risks. Generally, the more we learn about a drug, the less benign it turns out to be, and marijuana is no exception (see Focus on Discovery 10.1).

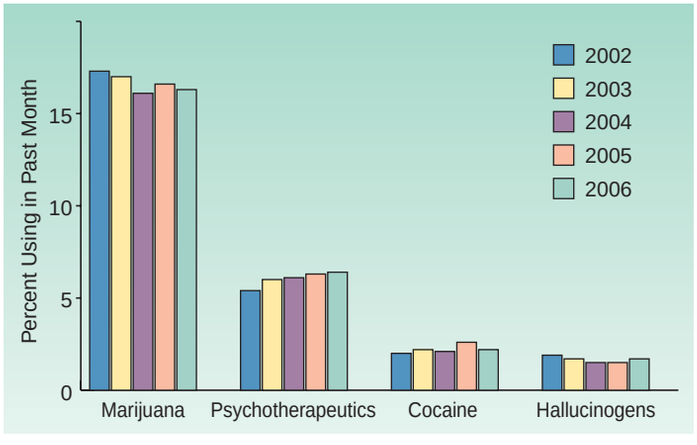


Figure 10.2 Trends in young adults' use of marijuana in the previous month.

Psychological Effects The intoxicating effects of marijuana, like those of most drugs, depend in part on its potency and the size of the dose. Smokers of marijuana find it makes them feel relaxed and sociable. Large doses have been reported to bring rapid shifts in emotion, to dull attention, to fragment thoughts, to impair memory, and to give the sense that time is moving more slowly. Extremely heavy doses have sometimes been found to induce hallucinations and other effects similar to those of LSD, including extreme panic, sometimes arising from the belief that a frightening experience will never end. Dosage can be difficult to regulate because it may take up to half an hour after smoking marijuana for its effects to appear; many users thus get much higher than intended.

The major active chemical in marijuana is delta-9-tetrahydrocannabinol (THC). The amount of THC in marijuana is variable, but marijuana is more potent now than it was two decades ago (Zimmer & Morgan, 1995). In addition, users smoke more in a session now than in the past (e.g., a "blunt" contains more cannabis than a joint).

An abundance of scientific evidence indicates that marijuana can interfere with a wide range of cognitive functions. Of special significance are findings that show loss of short-term memory. One prospective study assessed IQ scores at multiple time points among users between the ages of 17 and 23 and found a decline of about 4 points in current users (Fried et al., 2002).

Several studies have demonstrated that being high on marijuana impairs complex psychomotor skills necessary for driving. Poor performance after smoking one or two marijuana cigarettes containing 2 percent THC can persist for up to eight hours after a person believes he or she is no longer high, creating the danger that people will drive when they are not functioning adequately.

Does chronic use of marijuana affect intellectual functioning even when the person is not using the drug? Unfortunately, there are not many well-controlled studies that have been conducted to address this question. Collectively, current evidence suggests that long-term users may exhibit a slight impairment in learning and memory, but there is not strong evidence to suggest such impairments persist after discontinuation of use (Rey et al., 2004).

Physical Consequences The short-term effects of marijuana include bloodshot and itchy eyes, dry mouth and throat, increased appetite, reduced pressure within the eye, and somewhat raised blood pressure.

We know that the long-term use of marijuana seriously impairs lung structure and function (Grinspoon & Bakalar, 1995). Even though marijuana users smoke far fewer cigarettes than do tobacco smokers, most inhale marijuana smoke more deeply and retain it in their lungs for

FOCUS ON DISCOVERY 10.1

Is Marijuana a Gateway Drug?

The so-called stepping-stone, or gateway, theory of marijuana use has been around for a long time. According to this view, marijuana is dangerous not only in itself but also because it is a first step for young people on the path to becoming addicted to other drugs, such as heroin.

Studies have established several specific dangers from using marijuana, as described in the text. But is marijuana a gateway to more serious substance abuse or dependence? First of all, there is little evidence to suggest that this theory applies to African Americans. Furthermore, about 40 percent of regular marijuana users do not go on to use such drugs as heroin and cocaine (Stephens, Roffman, & Simpson, 1993). So if by *gateway* we mean that escalation to a more serious drug is inevitable, then marijuana is not a gateway drug. However, we do know that many, but far from all, who abuse heroin and cocaine began their drug experimentation with marijuana. And at least in the United States and New Zealand, users of marijuana are more likely than nonusers to experiment later with heroin and cocaine (Fergusson & Horwood, 2000; Kandel, 2002; Miller & Volk, 1996).

Most people who use marijuana do not go on to use heroin, but many heroin users do begin their drug use with marijuana. (Mauritius/SuperStock, Inc.)

Thus, even though marijuana use often precedes other drug use, it does not appear to *cause* later drug use, as the term *gateway* implies. Rather, it may be that marijuana is the first drug to be tried because it is more socially acceptable than other drugs.

much longer periods of time. Since marijuana has some of the same carcinogens found in tobacco, its harmful effects are greater than would be expected were only the absolute number of cigarettes or pipefuls considered. For example, one marijuana cigarette smoked in the typical way is the equivalent of five tobacco cigarettes in carbon monoxide intake, four in tar intake, and ten in terms of damage to cells lining the airways (Sussman et al., 1996).

How does marijuana affect the brain? In the early 1990s, researchers identified two cannabinoid brain receptors, called CB1 and CB2 (Matsuda et al., 1990; Munro, et al., 1993). CB1 receptors are found throughout the body and the brain, with a particularly high number in the hippocampus, an important region of the brain for learning and memory. Based on accumulating evidence, researchers have concluded that the well-documented short-term memory problems associated with marijuana use are linked to the effects of marijuana on these receptors in the hippocampus (e.g., Sullivan, 2000).

In addition, a PET study found that smoking marijuana was associated with increased blood flow to regions in the brain often associated with emotion, including the amygdala and the anterior cingulate. Decreased blood flow was observed in regions of the temporal lobe that have been associated with auditory attention, and participants in this study who were high on marijuana performed poorly on a listening task (O'Leary et al., 2000). These findings might help explain some of the psychological effects associated with marijuana use, including changes in emotion and attentional capabilities.

Is marijuana addictive? Contrary to widespread earlier belief, it may be. Controlled observations have confirmed that habitual use of marijuana does produce tolerance (Compton, Dewey, & Martin, 1990). Whether long-term users experience withdrawal when accustomed amounts of marijuana are not available is less clear, though surveys and laboratory studies conducted in the past 10 years suggest that withdrawal symptoms, such as restlessness, anxiety, tension, stomach pains, and insomnia do occur (Rey et al., 2004).

Therapeutic Effects Ironically, therapeutic uses of marijuana came to light just as the negative effects of regular and heavy usage of the drug were being uncovered. In the 1970s several double-blind studies showed that THC and related drugs could reduce the nausea and loss of appetite that accompany chemotherapy for some people with cancer (e.g., Salan, Zinberg, & Frei, 1975). Later findings confirmed this result (Grinspoon & Bakalar, 1995). Marijuana often appears to reduce nausea when other antinausea agents fail. Marijuana is also a treatment for the discomfort of AIDS (Sussman et al., 1996).

Demonstrators in New York advocate the legalization of marijuana for medical purposes. (Spencer Platt/Liaison Agency, Inc./Getty Images.)

The potential benefits of smoking marijuana were confirmed in reports by a panel of experts to the National Institutes of Health (NIH; Ad Hoc Advisory Group of Experts, 1998) and a committee of the Institute of Medicine, a branch of the National Academy of Sciences (Institute of Medicine, 1999). These reports suggested that these benefits be taken more seriously by medical researchers and clinicians. The NIH agreed to fund research on the subject, including research on whether the benefits from taking THC in pill form are comparable to what people report from smoking marijuana. (Most people report more beneficial effects from smoking than from swallowing THC in capsule form; this may be due to other compounds than THC in marijuana leaves that are separate from THC.) The Institute of Medicine report recommended that people with "debilitating symptoms" or terminal illnesses be allowed to smoke marijuana under close medical supervision for up to 6 months; the rationale for smoking was based on the just-mentioned findings that THC swallowed by mouth does not provide the same relief. But the Institute of Medicine report also emphasized the dangers of smoking per se and urged the development of alternative delivery systems, such as inhalers.

The recommendations of medical experts represent sharp disagreement with the federal government. California passed Proposition 215 in 1996, a law that makes it legal for physicians to recommend marijuana to help people with AIDS and other seriously ill people cope with pain and relieve nausea from medications used in treating their illnesses. Federal authorities took issue with the California law, and the U.S. Supreme Court ruled in May 2001 that federal law prohibits the dispensing of marijuana for those medical purposes. Interestingly, this ruling did not expressly forbid the *use* of the drug to alleviate pain and nausea. In June 2005, the Supreme Court ruled that the federal government could prohibit the use of marijuana for medical purposes even though the voters in California had approved it. California is not the only state to approve the use of marijuana for medical purposes—11 other states have approved laws similar to California's—so this ruling will likely extend beyond California. State officials in these 12 states will not prosecute people for using medical marijuana even though federal officials may do so. It seems likely that the debate on this issue will continue for years to come.

Quick Summary

Alcohol and drug use is common in the United States. The DSM-IV-TR lists substance dependence, which typically includes either tolerance or withdrawal, and substance abuse as two major categories of substance-related disorders.

Withdrawal from alcohol can involve hallucinations and delirium tremens. People who abuse or are dependent on alcohol may use other drugs, particularly nicotine. Alcohol dependence can have quite a variable course. Alcohol use is particularly high among college students; men are more likely to drink alcohol than women, and differences in use, abuse, and dependence by ethnicity have been observed. Even light or moderate drinking during pregnancy can be associated with later problems in learning for the child.

Smoking remains prevalent, though it has been on the decline. Cigarette smoking causes a number of illnesses, including several cancers, heart disease, and other lung diseases. Although more men smoke than women, the rates are the same among adolescent boys and girls. The ill effects of tobacco are greater for African Americans. Secondhand smoke, also called environmental tobacco smoke, is also linked to a number of serious health problems.

Marijuana makes people feel relaxed and sociable, but it can also interfere with attention, memory, and thinking. In addition, it has been linked to lung-related problems. It remains among the most prevalently used drugs, particularly among younger people. Men use it more than women. Users can develop tolerance to marijuana; it is less clear whether withdrawal symptoms occur after users stop smoking it. Marijuana also has therapeutic benefits, particularly for those suffering from the side effects of chemotherapy and for people with AIDS.

Check Your Knowledge 10.2

Fill in the blanks.

1. List three types of cancer that are caused by smoking.
2. Marijuana can have _____ effects on learning and memory; it is less clear if there are _____ effects.
3. List three of the therapeutic benefits of marijuana.

Opiates

The **opiates**, which fall under the broader category of *sedatives*, include opium and its derivatives morphine, heroin, and codeine. Synthetic barbiturates and minor tranquilizers (benzodiazepines used in the treatment of anxiety), such as secobarbital (Seconal) and diazepam (Valium), are also considered sedatives.

The opiates are a group of addictive sedatives that in moderate doses relieve pain and induce sleep. Foremost among them is **opium**, originally the principal drug of illegal international traffic; it was known to the people of the Sumerian civilization, dating as far back as 7000 B.C. They gave the poppy that supplied this drug the name opium, meaning "the plant of joy."

In 1806 the alkaloid **morphine**, named after Morpheus, the Greek god of dreams, was separated from raw opium. This bitter-tasting powder proved to be a powerful sedative and pain reliever. Before its addictive properties were noted, it was commonly used in medicines. In the middle of the nineteenth century, when the hypodermic needle was introduced in the United States, morphine began to be injected directly into the veins to relieve pain.

Concerned about administering a drug that could disturb the lives of people, scientists began studying morphine. In 1874 they found that morphine could be converted into another powerful pain-relieving drug, which they named **heroin**. Used initially as a cure for morphine addiction, heroin was substituted for morphine in cough syrups and other patent medicines. So many maladies were treated with heroin that it came to be known as G.O.M., or "God's own medicine" (Brecher, 1972). However, heroin proved to be even more addictive and more potent than morphine. Today, heroin is most often injected, though it can also be smoked, snorted, or taken orally.

More recently, opiates legally prescribed as pain medications, including **hydrocodone** and **oxycodone,** have become drugs of abuse [National Drug Intelligence Center (NDIC), 2001]. Hydrocodone is most often combined with other drugs, such as acetaminophen (the active agent in Tylenol) to create prescription pain medicines such as Vicodin, Zydone, or Lortab. Oxycodone is found in medicines such as Percodan, Tylox, and OxyContin. Vicodin is one of the most commonly abused drugs containing hydrocodone, and OxyContin is one of the most commonly abused drugs containing oxycodone.

An opium poppy. Opium is harvested by slitting the seed capsule, which allows the raw opium to seep out. (Dr. Jeremy Burgess/Photo Researchers.)

Prevalence of Opiate Abuse and Dependence There are enormous difficulties in gathering data, but the considered opinion is that there are more than a million people addicted to heroin in the United States, with an estimated 300,000 users in 2006 alone (SAMHSA, 2007).

Heroin used to be confined to poor neighborhoods and urban environments. In the early 1990s, it became popular among middle- and upper-middle-class college students and young professionals. From 1995 to 2002, rates of use among adults 18 to 25 increased from 0.8 percent to

Clinical Case: James

James was a 27-year-old man who had been addicted to heroin for 7 years. He first tried heroin during his time in the Marine Corps. Unable to control his habit, he was dishonorably discharged from the Marines a year later. He lived with his family for a short time, but after stealing money and valuables to support his habit, he was asked to leave the house. He then began living on the street, panhandling for money to support his habit. He also donated blood platelets when he was physically able. Over the years, James lost a tremendous amount of weight and became quite malnourished. He was over 6 feet tall, but he weighed only 150 pounds. Food wasn't a priority on most days, though he was usually able to gather a meal of scraps from the local diner. James tried to get into several rehabilitation programs, but they required that he remain free of heroin for at least a week before he could be admitted. James was able to resist for a day or two, but then withdrawal symptoms would begin, making it too painful to continue without the drug. A friend from the streets, formerly addicted to heroin, had recently helped James get to a methadone clinic. James tried methadone for a few weeks but was unable to tolerate the long waits outside the clinic each morning and the shame of being stared at by people passing on their way to work. Still, having been free of heroin for over a week, James gained admittance to a residential treatment program. One of the physicians at the program prescribed a newly approved medication called Suboxone that eased the discomfort of heroin withdrawal while also replacing the cravings for heroin. James no longer needed to go to the methadone clinic, and he was getting job training at the treatment program. He was hopeful that he would shake his habit for good.

Heroin was synthesized from opium in 1874 and was soon being added to a variety of medicines that could be purchased without prescription. This ad shows a teething remedy containing heroin. It probably worked. (National Library of Medicine/Photo Researchers.)

1.6 percent. In Baltimore, Boston, and Newark, heroin accounted for between 62 and 82 percent of drug-related hospital admissions in 2003. Deaths attributable to heroin in Baltimore, Chicago, Detroit, and Philadelphia ranged from 275 to nearly 500 in 2003 [Community Epidemiology Work Group (CEWG), 2003].

From 1990 to 1997, reports of hydrocodone abuse increased by 173 percent in the United States, and between 2002 and 2003, use of hydrocodone among people age 12 and older increased from 4.5 million to 5.7 million. Reports of oxycodone abuse increased 43 percent in just 1 year, from 1997 to 1998 (SAMHSA, 2004). Prescriptions for OxyContin, a drug containing oxycodone, jumped 1,800 percent between 1996 and 2000 [Drug Enforcement Administration (DEA), 2001]. The rates of abuse of these drugs have remained relatively stable since 2002 (SAMHSA, 2007).

The illicit supply seems to come largely from prescriptions that are forged, stolen, or diverted to dealers on the black market. As prescribed, OxyContin comes in a pill format with polymer coating. Unfortunately, the pills can easily be dissolved into a form that can then be injected or snorted. The legitimate sales price of a 40-milligram OxyContin pill ranges from $0.50 to $1.00, but pills sell on the street for $25.00 to $40.00 each. Abuse of OxyContin appears to be more prevalent in rural areas, but it is rapidly spreading to large metropolitan areas (DEA, 2001; Meier, 2003). OxyContin's effects are quite similar to those of heroin, so health professionals are concerned that people dependent on OxyContin who can no longer afford its hefty street price will turn to heroin, which is less expensive. As shown in Figure 10.3, visits to hospital emergency rooms after overdoses of hydrocodone and oxycodone have been steadily increasing since 1994, with nearly 48,000 such visits in 2002 (Ball & Lehder Roberts, 2004).

Psychological and Physical Effects Opiates produce euphoria, drowsiness, and sometimes a lack of coordination. Heroin and OxyContin also produce a "rush," a feeling of warm, suffusing ecstasy immediately after an intravenous injection. The user sheds worries and fears and has great self-confidence for 4 to 6 hours. However, the user then experiences a severe letdown, bordering on stupor.

Opiates produce their effects by stimulating neural receptors of the body's own opioid system (the body naturally produces opioids, called endorphins and enkephalins). Heroin, for example, is converted into morphine in the brain and then binds to opioid receptors, which are located throughout the brain. Some evidence suggests that a link between these receptors and the dopamine system is responsible for opiates' pleasurable effects. However, evidence from animal studies suggests that opiates may achieve their pleasurable effects via their action in the area of the brain called the nucleus accumbens, perhaps independently from the dopamine system (Koob et al., 1999).

Opiates are clearly addicting, for users develop tolerance and show withdrawal symptoms. Withdrawal from heroin may begin within 8 hours of the last injection, at least after high tolerance has built up. During the next few hours after withdrawal begins, the person typically

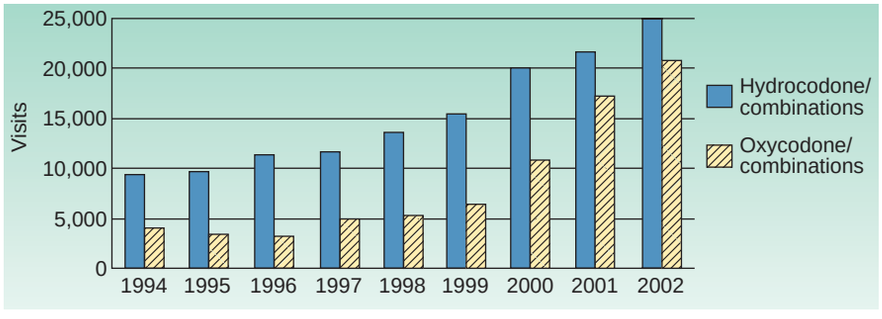


Figure 10.3 Emergency room visits after overdoses of hydrocodone and oxycodone have increased dramatically in less than 10 years. From Office of Applied Studies, SAMHSA, Drug Abuse Warning Network, 2002 (03/2003 update).

experiences muscle pain, sneezes, and sweating; becomes tearful; and yawns a great deal. The symptoms resemble those of influenza. Within 36 hours, the withdrawal symptoms become more severe. There may be uncontrollable muscle twitching, cramps, chills alternating with excessive flushing and sweating, and a rise in heart rate and blood pressure. The person is unable to sleep, vomits, and has diarrhea. These symptoms typically persist for about 72 hours and then diminish gradually over a 5 to 10-day period.

People who abuse opiates face serious problems. In a 29-year follow-up of 500 people addicted to heroin, about 28 percent had died by age 40; half of these deaths were from homicide, suicide, or accident, and one-third were from overdose (Hser, Anglin, & Powers, 1993). The social consequences of using an illegal drug are also serious. The drug and obtaining it become the center of the person's existence, governing all activities and social relationships. The high cost of drugs—users must often spend upwards of $200 per day for opiates—often drives users into acquiring money through illegal activities, such as theft, prostitution, or selling drugs.

An additional problem associated with intravenous drug use is exposure, through sharing needles, to infectious agents such as the human immunodeficiency virus (HIV), which causes AIDS. Notably, there is good consensus among scientists that the free distribution of needles and syringes reduces needle sharing and the spread of infectious agents associated with intravenous drug use (Gibson, 2001; Yoast et al., 2001). Contrary to popular political rhetoric, such programs in combination with methadone treatment (discussed later in this chapter) do not lead to an increase in either initial or continued use of drugs. In 2004, California adopted a law that allows pharmacists to sell up to 10 syringes without a prescription.

Synthetic Sedatives

Barbiturates were first synthesized in 1903 as aids for sleeping and relaxation. Since then, hundreds of different barbiturates have been synthesized. These drugs were initially prescribed frequently, but in the 1940s a campaign was mounted against them because they were discovered to be addictive. Physicians then began to prescribe barbiturates less frequently. From 1975 to the early 1990s, use steadily declined, but it now appears to be on the rise (Johnston, O'Malley, & Bachman, 2001). Other types of synthetic sedatives are also part of this upward trend. Benzodiazepines, such as Valium, are commonly used and abused.

Synthetic sedatives relax the muscles, reduce anxiety, and in small doses produce a mildly euphoric state. Like alcohol, they are thought to produce these psychological effects by stimulating the GABA system. With excessive doses, however, speech becomes slurred and gait unsteady. Judgment, concentration, and ability to work may be extremely impaired. The user loses emotional control and may become irritable and combative before falling into a deep sleep. Very large doses can be fatal because the diaphragm muscles relax to such an extent that a person suffocates. Many users accidentally kill themselves by drinking alcohol, which magnifies the effects of sedatives. Not surprisingly, prolonged excessive use can damage the brain.

Increased tolerance follows prolonged use of synthetic sedatives. The withdrawal reactions after abrupt termination are particularly severe and long lasting and can cause sudden death. The delirium, convulsions, and other symptoms resemble the symptoms that follow abrupt withdrawal from alcohol.

Stimulants

Stimulants act on the brain and the sympathetic nervous system to increase alertness and motor activity. Amphetamines are synthetic stimulants; cocaine is a natural stimulant extracted from the coca leaf. Focus on Discovery 10.2 discusses a less risky and more prevalent stimulant, caffeine.

Amphetamines

The first **amphetamine**, benzedrine, was synthesized in 1927, and other amphetamines were synthesized soon after. Almost as soon as benzedrine became commercially available in the early 1930s as an inhalant to relieve stuffy noses, the public discovered its stimulating effects, and physicians soon began to prescribe it and the other amphetamines to control mild depression and appetite. During World War II, soldiers on both sides were supplied with amphetamines to ward off fatigue.

Amphetamines such as benzedrine, dexedrine, and methedrine produce their effects by causing the release of norepinephrine and dopamine and blocking the reuptake of these neurotransmitters. Amphetamines are taken orally or intravenously and can be addicting. Wakefulness

FOCUS ON DISCOVERY 10.2

Our Tastiest Addiction—Caffeine

What may be the world's most popular drug is seldom viewed as a drug at all, and yet it has strong effects, produces tolerance in people, and even subjects habitual users to withdrawal (Hughes et al., 1991). Users and nonusers joke about it, and most readers of this book have probably had some this very day. We are, of course, referring to **caffeine**, a substance found in coffee, tea, cocoa, cola and other soft drinks, some cold remedies, and some diet pills.

Two cups of coffee, containing between 150 and 300 milligrams of caffeine, affect most people within half an hour. Metabolism, body temperature, and blood pressure all increase; urine production goes up, as most of us will attest; there may be hand tremors, appetite can diminish, and, most familiar of all, sleepiness is warded off. Panic disorder can be exacerbated by caffeine, not surprising in light of the heightened sympathetic nervous system arousal occasioned by the drug. Extremely large doses of caffeine can cause headache, diarrhea, nervousness, severe agitation, even convulsions and death. Death, though, is virtually impossible unless the person grossly overuses tablets containing caffeine, because the drug is excreted by the kidneys without any appreciable accumulation.

The caffeine found in coffee, tea, and soft drinks is probably the world's favorite drug. (Sepp Seitz/Woodfin Camp & Associates.)

Although it has long been recognized that drinkers of very large amounts of regular (caffeinated) coffee daily can experience withdrawal symptoms when consumption ceases, people who drink no more than two cups of regular coffee a day can suffer from clinically significant headaches, fatigue, and anxiety if caffeine is withdrawn from their daily diet (Silverman et al., 1992), and these symptoms can interfere with social and occupational functioning. These findings are disturbing because more than three-quarters of Americans consume a little more than two cups of regular coffee a day (Roan, 1992). And although parents usually deny their children access to coffee and tea, they often do allow them to imbibe caffeine-laden soft drinks, hot chocolate, and cocoa, and to eat chocolate candy and chocolate and coffee ice cream. Thus, our addiction to caffeine can begin to develop as early as 6 months of age, the form of it changing as we move from childhood to adulthood.

is heightened, intestinal functions are inhibited, and appetite is reduced—hence their use in dieting. The heart rate quickens, and blood vessels in the skin and mucous membranes constrict. The person becomes alert, euphoric, and outgoing and is possessed with seemingly boundless energy and self-confidence. Larger doses can make a person nervous, agitated, and confused; other symptoms include palpitations, headaches, dizziness, and sleeplessness. Sometimes heavy users become extremely suspicious and hostile, to the extent that they can be dangerous to others. Large doses taken over a period of time can induce a state quite similar to paranoid schizophrenia.

Tolerance to amphetamines develops rapidly, so more and more of the drug is required to produce the stimulating effect. One study demonstrated tolerance after just 6 days of repeated use (Comer et al., 2001). As tolerance increases, some users may stop taking pills and start injecting methedrine, the strongest of the amphetamines, directly into the veins. Users may give themselves repeated injections of the drug and maintain intense and euphoric activity for a few days, without eating or sleeping, after which, exhausted and depressed, they sleep, or crash, for several days. Then the cycle starts again. After several repetitions of this pattern, the physical and social functioning of the person deteriorates considerably. Behavior becomes erratic and hostile, and users may become dangerous to themselves and others.

Clinical Case: Anton

Anton, a 37-year-old man, had just been arrested for a parole violation, stealing a package of string cheese from a convenience store. He was also found to be under the influence of methamphetamine. Two months earlier, he had been released from prison after serving time for petty theft and for purchasing methamphetamine. He was determined to remain out of prison, but his cravings for meth were so intense that he was unable to abide by the terms of his parole. He had been using meth since he was 26 years old, and he had been arrested numerous times for drug-related offenses, including prostitution (to get money to support his habit).

Methamphetamine Abuse of an amphetamine derivative called **methamphetamine** skyrocketed in the 1990s. Some estimates indicate that as many as 4.7 million people in the United States have tried methamphetamine at some point (Anglin et al., 2000). In 2006, over 700,000 people used methamphetamine (SAMHSA, 2007).

Men tend to abuse methamphetamine more often than women in contrast with abuse of other amphetamines, where few gender differences occur. Among adolescents, however, abuse by both males and females has almost doubled since 1992 (Oetting et al., 2000). White males are most likely to abuse meth, but studies suggest that use among Hispanic Americans and Native Americans is on the rise (Oetting et al., 2000).

Like other amphetamines, methamphetamine can be taken orally or intravenously. It can also be taken intranasally (i.e., by snorting). In a clear crystal form, the drug is often referred to as "crystal meth" or "ice." Craving for methamphetamine is particularly strong, often lasting several years after use of the drug is discontinued. Craving is also a reliable predictor of later use (Hartz, Fredrick-Osborne, & Galloway, 2001).

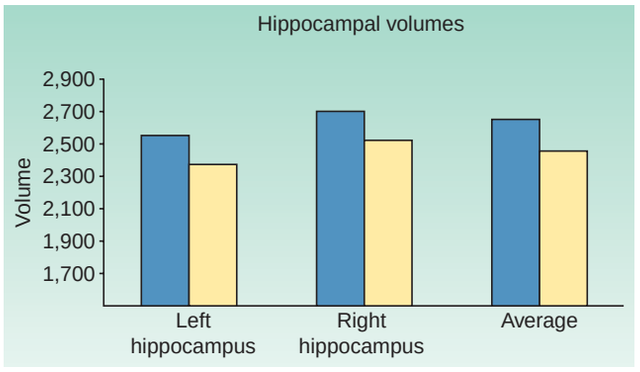


Figure 10.4 Results from an fMRI study showing that those who abused methamphetamine (yellow bars) had smaller hippocampal volume (size) than those in the control group (blue bars) who did not abuse methamphetamine. Adapted from Thompson et al. (2004).

Several studies done with animals have indicated that chronic use of methamphetamine causes damage to the brain, affecting both the dopamine system and the serotonin system (Frost & Cadet, 2000). Neuroimaging studies have found similar effects in the human brain, particularly in the dopamine system. For example, one study of chronic meth users who met DSM diagnostic criteria for dependence found a number of users with damage to the hippocampus (see Figure 10.4). The volume of the hippocampus was smaller among chronic meth users, and this correlated with poorer performance on a memory test (Thompson et al., 2004). Another study reported that people who abused methamphetamine but who were currently clean of the substance, some for as long as 11 months, had a significant reduction in a dopamine transporter gene (a transporter gene is a gene that either lets a drug enter a cell or prevents a drug from entering a cell) (Volkow et al., 2001). In fact, in 3 of the 15 people studied, the reduction in dopamine reuptake was similar to that seen in the less severe stages of Parkinson's disease. Moreover, those with a history of methamphetamine abuse performed more slowly than a comparison group on several motor tasks, a finding similar to that seen with people with Parkinson's disease.

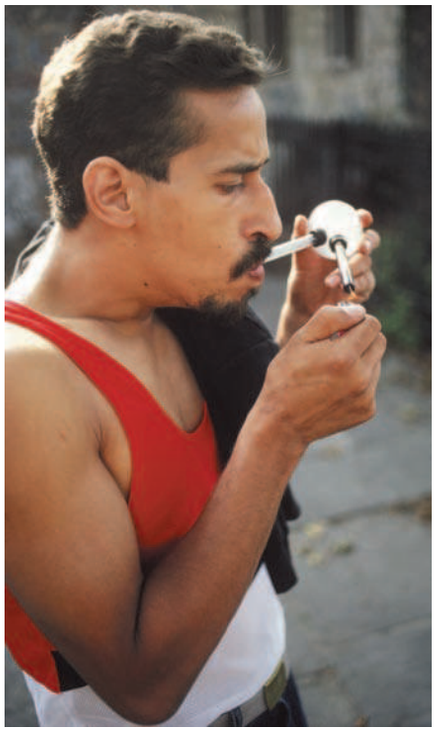
In a different study, men who were in treatment for methamphetamine dependence participated in a laboratory task of decision making while having their brains scanned with fMRI (Paulus, Tapert, & Schuckit, 2005). The researchers found that lower activation in several brain areas (dorsolateral prefrontal cortex, insula, and areas of the temporal and parietal lobes) during the decision-making task predicted relapse in methamphetamine abuse 1 year after treatment. It seems obvious that poor decision making might put one at higher risk for relapse. What this study also showed was that the brain areas that contribute to sound decision making are disrupted in some people who are dependent on methamphetamine. What is less clear is whether the methamphetamine damaged these areas or whether these areas were damaged before methamphetamine use began.

A caveat should be noted here. One difficulty with conducting these types of studies is finding participants who use only the drug of interest (in this case, methamphetamine) so that any observed effects can be linked to that drug and not others. However, it is difficult to find meth users who have not at some point used other substances, particularly alcohol and nicotine. For example, in one of the studies described above, the meth users did not differ from the control group in alcohol consumption, but they did smoke more (Thompson et al., 2004). Nevertheless, it seems clear that the deleterious effects of methamphetamine are many and serious.

Chemicals for manufacturing methamphetamine, such as ephedrine, are readily available, though laws such as the Methamphetamine Control Act of 1996 have been passed to try to cut off the supply. When supplies of ephedrine became low, pseudoephedrine, a common substance in many over-the-counter decongestants, was substituted, but these substances are now also better regulated. Some chemicals used to make methamphetamine are highly volatile and dangerous to breathe, causing damage ranging from eye irritation and nausea to coma and death.

A coca plant. The leaves contain about 1 percent cocaine. (Dr. Morley Read/Photo Researchers.)

Cocaine The alkaloid **cocaine** was first extracted from the leaves of the coca shrub in the mid-1800s and has been used since then as a local anesthetic. In the mid-1980s a new form of cocaine, called **crack**, appeared on the streets. Crack comes in a rock-crystal form that is then



Crack use is highest in urban areas. (Wesley Bocxe/Photo Researchers, Inc.)

heated, melted, and smoked. The name *crack* comes from the crackling sound the rock makes when being heated. The presence of crack brought about an increase in the number of users of cocaine and in casualties. Because it was available in small, relatively inexpensive doses ($10 for about 100 milligrams versus $100 per gram of cocaine), younger and less affluent buyers began to experiment with the drug and to become addicted (Kozel & Adams, 1986). Crack is now most often used in poorer urban areas.

Cocaine use in general soared in the 1970s and 1980s, increasing by more than 260 percent between 1974 and 1985. Men use cocaine and crack more often than women do. Although the use of cocaine dramatically decreased in the late 1980s and early 1990s, it began to rise again in the mid-1990s, particularly among high school and college students and young adults in general. Indeed, from 2000 to 2002, there were about a million new users per year. Among users, 25 percent met DSM criteria for cocaine dependence in 2003 (SAMHSA, 2004). In 2006, 2.4 million people over the age of 12 reported using cocaine, and 700,000 reported using crack (SAMHSA, 2007). In short, cocaine and crack remain significant drugs of abuse.

Cocaine has other effects, in addition to reducing pain. It acts rapidly on the brain, blocking the reuptake of dopamine in mesolimbic areas. Cocaine yields pleasurable states because dopamine left in the synapse facilitates neural transmission. Self-reports of pleasure induced by cocaine are strongly related to the extent to which cocaine has blocked dopamine reuptake (Volkow et al., 1997). Cocaine can increase sexual desire and produce feelings of self-confidence, well-being, and indefatigability. An overdose may bring on chills, nausea, and insomnia, as well as strong paranoid feelings and terrifying hallucinations of insects crawling beneath the skin. Chronic use can lead to heightened irritability, impaired social relationships, paranoid thinking, and disturbances in eating and sleeping. Some, but not all, users develop tolerance to cocaine, requiring a large dose to achieve the same effect. Other users may become more sensitive to cocaine's effects, which are believed to be a contributing factor in deaths after a fairly small dosage. Stopping cocaine use appears to cause severe withdrawal symptoms.

Cocaine is a vasoconstrictor, causing the blood vessels to narrow. As users take larger and larger doses of the purer forms of cocaine now available, they are more often rushed to emergency rooms and may die of an overdose, often from a heart attack [National Institute on Drug Abuse (NIDA), 2004a]. Cocaine also increases a person's risk for stroke and causes cognitive impairments, such as difficulty paying attention and remembering. Because of its strong vasoconstricting properties, cocaine poses special dangers in pregnancy, for the blood supply to the developing fetus may be compromised.

Cocaine can be sniffed (snorted), smoked in pipes or cigarettes, swallowed, or even injected into the veins; some heroin users mix the two drugs. In the 1970s cocaine users in the United States began to separate, or free, a component of cocaine by heating it with ether. When purified by this chemical process, the cocaine base—or freebase—produces very powerful effects because it is absorbed so rapidly. Like most drugs, the faster it is absorbed, the quicker and more intense the high. Freebase is usually smoked in a water pipe or sprinkled on a tobacco or marijuana cigarette. It is rapidly absorbed into the lungs and carried to the brain in a few seconds, where it induces an intense 2-minute high, followed by restlessness and discomfort.

Cocaine can be smoked, swallowed, injected, or snorted as shown here. (Mark Antman/The Image Works.)

Hallucinogens, Ecstasy, and PCP

LSD and Other Hallucinogens In 1938 the Swiss chemist Albert Hofmann manufactured a few milligrams of *d*-lysergic acid diethylamide into a drug know today as **LSD**. The term *psychedelic*, from the Greek words for "soul" and "to make manifest," was applied to emphasize the subjectively experienced expansion of consciousness reported by users of LSD and often referred to by them as a "trip." The term in current use for LSD and other drugs with similar effects is **hallucinogen**, which refers to the main effects of such drugs, hallucinations. Unlike the hallucinations in schizophrenia, however, these are usually recognized by the person as being caused by the drug.

The use of LSD and other hallucinogens peaked in the 1960s; by the 1980s, only 1 or 2 percent of people could be classified as regular users. In 2006, there were about 100,000 users (SAMHSA, 2007) down from 1 million in 2002 (SAMHSA, 2004). There is no evidence of withdrawal symptoms during abstinence, but tolerance appears to develop rapidly (McKim, 1991). Among youths between the ages of 12 and 17, African Americans are less likely to use hallucinogens than whites, Asian Americans, or Hispanics [Office of Applied Studies (OAS), 2002].

In addition to hallucinations, LSD can alter a person's sense of time (it seems to go slowly). A person using LSD may have sharp mood swings but can also experience an expanded consciousness such that he or she seems to appreciate sights and sounds like never before.

The effects of hallucinogens depend on a number of psychological variables in addition to the dose itself. A person's set—that is, attitudes, expectancies, and motivations with regard to taking drugs—is widely held to be an important determinant of his or her reactions to hallucinogens. The context in which the drug is experienced is also important.

Many users experience intense anxiety after taking LSD, in part because the perceptual experiences and hallucinations can provoke fears that they are "going crazy." For some, these anxieties unfold into full-blown panic attacks. The anxiety usually subsides as the drug is metabolized. A minority of people, however, go into a psychotic state that can require hospitalization and extended treatment.

Mescaline, obtained from the peyote cactus, is used in certain religious rites of Native American people of the American Southwest and northern Mexico. (Kal Muller/Woodfin Camp & Associates.)

Flashbacks (also referred to as hallucinogen persisting perception disorder, or HPPD) are visual recurrences of psychedelic experiences after the physiological effects of the drug have worn off. They occur in some people who have used LSD, most frequently in times of stress, illness, or fatigue. Flashbacks seem to have a force of their own; they may come to haunt people weeks and months after they have taken the drug and are very upsetting for those who experience them.

Other hallucinogens include mescaline and psilocybin, whose effects are thought to be due to stimulating serotonin receptors. **Mescaline**, an alkaloid and the active ingredient of peyote, was isolated in 1896 from small, disklike growths of the top of the peyote cactus. The drug has been used for centuries in the religious rites of Native American people living in the U.S. Southwest and northern Mexico. **Psilocybin** is a crystalline powder that Hofmann isolated from the mushroom *Psilocybe mexicana* in 1958.

Ecstasy and PCP A newer hallucinogen-like substance, **Ecstasy**, became illegal in 1985. Ecstasy includes both MDA (methylenedioxyamphetamine) and MDMA (methylenedioxymethamphetamine). **MDMA** was first synthesized in the early 1900s, and it was used as an appetite suppressant for World War I soldiers. Chemical precursors to MDMA are found in several commonly used spices, such as nutmeg, dill, saffron, and sassafras. Not until the 1970s were the psychoactive properties of MDMA reported in the scientific literature. **MDA** was first synthesized in 1910, but it was not until the 1960s that its psychedelic properties came to the attention of the drug-using, consciousness-expanding generation of the times.

Ecstasy contains compounds from both the hallucinogen and amphetamine families, but its effects are sufficiently different from either that some have suggested putting it in its own category, called the "entactogens" (Morgan, 2000). Today it remains popular on college campuses and in clubs. Focus on Discovery 10.3 discusses the use and effects of another club drug, nitrous oxide. Across all ages, Ecstasy use seems to have peaked in 2001, with 1.8 million users. From 2002 to 2003, the number of users age 12 and over decreased from 676,000

Clinical Case: Tamara

Tamara tried Ecstasy (X) for the first time when she was a freshman in college. She went to her first rave, and a friend gave her a pill she thought was a Sweet Tart. Within a short period of time, she began to feel almost magical, as if she was seeing everything around her in a new light. She felt incredibly close to her friends and even to men and women she had just met. Hugging and close dancing were intensely pleasurable, in a completely new way. A few days after the party, she asked her friend about the "Sweet Tart" and found out how she could obtain more. But the next time she tried X, she was unable to achieve the same pleasurable feelings. Instead, she felt more subdued, even anxious. After several more times using X, she noticed that despite her enthusiasm and even craving for the effects, she found instead that she felt a little depressed and anxious, even several days after taking the drug.

FOCUS ON DISCOVERY 10.3

Nitrous Oxide—Not a Laughing Matter

Nitrous oxide is a colorless gas that has been available since the nineteenth century. Within seconds, it induces lightheadedness and a state of euphoria in most people; for some, important insights seem to flood the mind. Many people find otherwise mundane events and thoughts irresistibly funny, hence the nickname *laughing gas*.

Many people have received nitrous oxide at a dentist's office to facilitate relaxation and otherwise make a potentially uncomfortable and intimidating dental procedure more palatable. A major advantage of nitrous oxide over other analgesics and relaxants is that a person can return to a normal waking state within minutes of breathing enriched oxygen or normal air.

Nitrous oxide fits in the broader category of inhalants and has been used recreationally since it first became available, although it has been illegal for many years in most states except as administered by appropriate health professionals. As with the other drugs examined in this chapter, illegality has not prevented unsupervised use. It is one of the most prevalently used inhalants among teens (sniffing glue, gasoline, and paint are more prevalent), with rates of use as high as 22 percent among those who use inhalants (Wu, Pilowsky, & Schlenger, 2004). Sometimes called "hippie crack" or "whippets," nitrous oxide balloons are often combined with the use of Ecstasy and other drugs at parties with bright laser lights and loud dance music (i.e., at raves).

Nitrous oxide is no laughing matter. (BananaStock/SUPERSTOCK.)

to 470,000. Despite this general decline, use among Hispanics does not appear to be declining (SAMHSA, 2004).

Ecstasy acts primarily by contributing to both the release and the subsequent reuptake of serotonin (Huether, Zhou, & Ruther, 1997; Liechti et al., 2000; Morgan, 2000). It was believed at one time that the use of Ecstasy was relatively harmless, but accumulating scientific evidence suggests that it may have neurotoxic effects on the serotonin system (De Souza, Battaglia, & Insel, 1990; Gerra et al., 2000). It is difficult to say if these toxic effects are directly due to drug use, since no studies in humans to date have assessed serotonin functioning both before and after Ecstasy use. Studies with animals, however, have shown that a single dose of Ecstasy causes serotonin depletion and that prolonged use can damage serotonin axons and nerve terminals (Harkin et al., 2001; Morgan, 2000).

Users report that Ecstasy enhances intimacy and insight, improves interpersonal relationships, elevates mood and self-confidence, and promotes aesthetic awareness. It can also cause muscle tension, rapid eye movements, jaw clenching, nausea, faintness, chills or sweating, anxiety, depression, depersonalization, and confusion. Some evidence suggests that the subjective and physiological effects of Ecstasy, both pleasurable and adverse, may be stronger for women than men (Liechti et al., 2000).

Ecstasy is a popular party drug but, like many drugs, is not free of ill effects. (Lynne Sobol/Montes De Oca & Associates.)

PCP, phencyclidine, often called *angel dust*, is another drug that is not easy to classify. Developed as a tranquilizer for horses and other large animals, it generally causes serious negative reactions, including severe paranoia and violence. Coma and death are also possible. PCP affects multiple neurotransmitters in the brain, and chronic use is associated with a variety of neuropsychological deficits. People who abuse PCP are likely to have used other drugs either before or concurrently with PCP, so it is difficult to sort out whether neuropsychological impairments are due solely to PCP, to other drugs, or to the combination. Use of PCP increased in the early to mid-1990s but was believed to be on the decline in the late 1990s. However, between 2000 and 2002, the number of arrests, emergency room visits, and treatment admissions linked to PCP increased in urban areas such as Chicago, Dallas, Los Angeles, Philadelphia, Phoenix, and Washington, D.C. (NIDA, 2004c).

Quick Summary

Opiates include heroin and other pain medications like hydrocodone and oxycodone. Abuse of prescription pain medications has risen dramatically, and overdoses are common. Initial effects of opiates include euphoria; later, users experience a letdown. Death by overdose from opiates is a severe problem. Other problems include exposure to HIV and other infectious agents through the use of shared needles. Synthetic sedatives are prescribed less than they used to be. They relax the muscles, reduce anxiety, and can produce a mildly euphoric state. Large doses can be fatal. Withdrawal is severe for opiates and synthetic sedatives.

Amphetamines are stimulants that produce wakefulness, alertness, and euphoria. Men and women use these equally. Tolerance develops quickly. Methamphetamine is a synthesized amphetamine, and use has increased dramatically since the 1990s. Men use it more than women and whites more than other ethnic groups. Methamphetamine can damage the brain, including the hippocampus. Cocaine and crack remain serious problems. Cocaine can increase sexual desire, feelings of well-being, and alertness, but chronic use is associated with problems in relationships, paranoia, and trouble sleeping, among other things. The faster crack or cocaine is absorbed, the more quickly and intensely the person becomes high.

LSD was a popular hallucinogen in the 1960s and 1970s, often billed as a mind-expanding drug. The mind-expanding drug of the 1990s became Ecstasy. Although these drugs do not typically elicit withdrawal symptoms, tolerance can develop. There is some indication that Ecstasy use may be on the decline, but not among all ethnic groups. PCP remains a problem in urban areas. This drug can cause severe paranoia and violence.

Check Your Knowledge 10.3

True or false?

1. Withdrawal from heroin begins slowly, days after use has been discontinued.
2. The use of OxyContin began in urban areas but quickly spread to rural areas.
3. Methamphetamine is a less potent form of amphetamine, less likely to be associated with brain impairment.
4. Ecstasy contains compounds associated with hallucinogens and amphetamines.

Etiology of Substance-Related Disorders

Becoming substance dependent is generally a developmental process. The person must first have a positive attitude toward the substance, then begin to experiment with using it, then begin using it regularly, then use it heavily, and finally abuse or become dependent on it (see Figure 10.5). The general idea is that after prolonged heavy use, some people become ensnared by the biological effects of tolerance and withdrawal.

It appears that the factors that contribute to substance dependence may depend on the point in the process that is being considered. For example, developing a positive attitude toward smoking and beginning to experiment with tobacco are strongly related to smoking by other family members (Robinson et al., 1997). In contrast, becoming a regular smoker is more strongly related to smoking by peers and being able to acquire cigarettes readily (Robinson et al., 1997; Wang et al., 1997).

More generally, adopting a developmental approach to understanding the etiology of substance-related disorders requires the study of persons across time, beginning at the earliest sign of substance use. Studies of the trajectories of substance-related problems among adolescents are becoming more frequent, and the findings suggest, not surprisingly, that different adolescents follow different trajectories (Jackson, Sher, & Wood, 2000; Wills et al., 1999). For example, one study identified two typical trajectories toward alcohol abuse in adolescence: (1) a group that began drinking early in

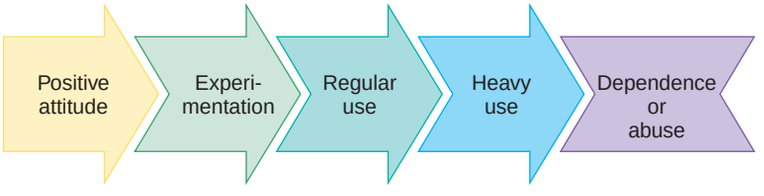


Figure 10.5 The process of becoming dependent on a drug.

adolescence and continued to increase their drinking throughout high school and (2) a group that started drinking a lesser amount in early adolescence and increased drinking at two peak points, one in middle school and another later in high school. Boys were more likely to follow the trajectory of the first group; girls were more likely to follow the trajectory of the second group, with even steeper trajectories in drinking than the boys (Li, Duncan, & Hops, 2001).

Other views incorporate what we know about the developing brain, particularly in adolescence. A review of the literature points to the fact that the area of the brain linked to judgment and decision making, novelty seeking, and impulse control—that is, the frontal cortex—is still developing at the time when adolescents are beginning to experiment with drugs and alcohol (Chambers, Taylor, & Potenza, 2003). The neural systems believed to be important for reward, including dopaminergic, serotonergic, and glutamatergic pathways, all pass through the developing frontal cortex.

Although applicable in many cases, a developmental approach does not account for all cases of substance abuse or dependence. For example, there are documented cases in which heavy use of tobacco or heroin did not result in dependence. Furthermore, we must remember that we are not talking about an inevitable progression through stages. Some people have periods of heavy use of a substance—for example, alcohol—and then return to moderate use. In the following sections, we discuss genetic, neurobiological, psychological, and sociocultural factors associated with substance-related disorders. Keep in mind that these factors are likely to be differently related to different substances. Genetic factors, for example, may play some role in alcohol dependence but be less important in hallucinogen abuse.

Genetic Factors

Much research has addressed the possibility that there is a genetic predisposition for drug and alcohol abuse and dependence. Several studies have shown that relatives and children of problem drinkers have higher-than-expected rates of alcohol abuse or dependence (e.g., Chassin et al., 1999). Furthermore, family studies show that the relatives of those who abuse substances are at increased risk for abusing many substances, not just the one that was the basis for selecting the proband (Bierut et al., 1998; Merilkangas et al., 1998). Stronger evidence for a genetic diathesis comes from twin studies, which have revealed greater concordance in identical twins than in fraternal twins for alcohol abuse by men (McGue, Pickens, & Svikis, 1992), smoking (True et al., 1999), heavy use or abuse of marijuana (Kendler & Prescott, 1998), and drug abuse in general (Tsuang et al., 1998). Behavioral genetics studies indicate that the genetic and shared environmental risk factors (see Chapter 2) for illicit drug abuse and dependence may be rather nonspecific (Karkowski, et al., 2000; Kendler, Jacobsen, et al., 2003). That is, genetic and shared environmental risk factors appear to be the same no matter what the drug (marijuana, cocaine, opiates, hallucinogens, sedatives, stimulants). This appears to be true for both men and women (Kendler, Prescott, et al., 2003).

The ability to tolerate large quantities of alcohol may be an inherited diathesis for alcohol abuse or dependence. That is, to become a dependent on alcohol, a person has to be able to drink a lot. Some ethnic groups, such as Asians, may have a low rate of alcohol abuse because of physiological intolerance, which is caused by an inherited deficiency in an enzyme involved in alcohol metabolism. About three-quarters of Asians experience unpleasant effects like flushing (blood flow to the face) from small quantities of alcohol, which may protect them from alcohol abuse or dependence. Research has also emerged on the mechanism through which genetics plays a role in smoking. Like most drugs, nicotine appears to stimulate dopamine release and inhibit its reuptake, and people who are more sensitive to these effects of nicotine are more likely to become regular smokers (Pomerleau et al., 1993). Research has examined a link between a gene that regulates the reuptake of dopamine and smoking. One form of this gene has been related to being less likely to begin smoking (Lerman et al., 1999) and being more likely to have quit (Sabo et al., 1999). Research has also found that genes contribute to the body's ability to metabolize nicotine, with some people able to do this quickly and others more slowly. Slower nicotine metabolism means that nicotine stays in the brain longer. A longitudinal study of seventh graders showed that those adolescents who had genes linked with slower nicotine metabolism were more likely to become dependent on it 5 years later (O'Loughlin et al., 2005).

Other evidence has found that people with a defect in a gene called CYP2A6, which is associated with the metabolism of nicotine, smoke fewer cigarettes and are less likely to become dependent on nicotine (Rao et al., 2000). This is an interesting example of a gene defect serving a protective function. It will be important to replicate this finding with other samples.

Neurobiological Factors

You may have noticed that in our discussions of specific drugs, the neurotransmitter dopamine has almost always been mentioned. This is not surprising given that dopamine pathways in the brain are importantly linked to pleasure and reward. Drug use typically results in rewarding or pleasurable feelings, and it is via the dopamine system that these feelings are produced. In short, people take drugs to feel good. Research with both humans and animals shows that nearly all drugs, including alcohol, stimulate the dopamine systems in the brain (see Figure 10.6), particularly the mesolimbic pathway (Camí & Farré, 2003; Koob, 2008). Researchers have wondered, then, if problems in the dopamine pathways in the brain might somehow account for why certain people become dependent on drugs. Some evidence suggests that people dependent on drugs or alcohol have a deficiency in the dopamine receptor DRD2 (Noble, 2003).

People take drugs not only to feel good. They also take them to feel less bad. This is particularly true once a person becomes dependent on a substance, such as alcohol, methamphetamine, or heroin, whose withdrawal symptoms are excruciatingly unpleasant. In other words, people take drugs to avoid the bad feelings associated with withdrawal. A substantial body of research with animals supports this motivation for drug-taking behavior (Koob & Le Moal, 2008), and this research helps to explain why relapse is so common.

Investigators have proposed a neurobiological theory, referred to as an *incentive-sensitization theory*, that considers both the craving for drugs (what they term "wanting") and the pleasure that comes with taking the drug (what they term "liking") (Robinson & Berridge, 1993, 2003). In their view, the dopamine system linked to reward, or liking, becomes supersensitive not just to the direct effects of drugs but also to the cues associated with drugs (e.g., needles, spoons, rolling paper). This sensitivity to cues induces craving, or wanting, and people go to extreme lengths to seek out and obtain drugs. Over time, the liking of drugs decreases, but the wanting remains very intense. These investigators argue that the transition from liking to powerful wanting, accomplished by the drug's effects on brain pathways involving dopamine, is what maintains the addiction.

Many researchers study the neurobiology of wanting or craving. A number of laboratory studies have shown that cues for a particular drug can elicit responses not altogether unlike

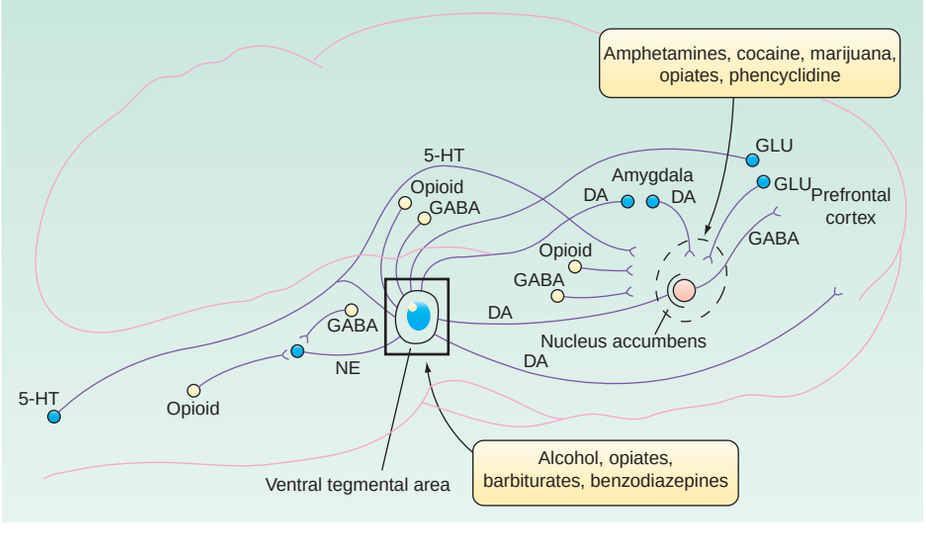


Figure 10.6 Reward pathways in the brain that are affected by different drugs. DA = dopamine; GABA = gamma-aminobutyric acid; GLU = glutamate; 5-HT = serotonin. Adapted from Cami & Farré (2003).

those associated with actual use of the drug. For example, those who were dependent on cocaine showed changes in physiological arousal, cravings, "high" feelings, and more negative emotions in response to cues of cocaine, which consisted of audio- and videotapes of people preparing to inject or snort cocaine, than did people not dependent on cocaine (e.g., Robbins et al., 2000). Brain imaging studies have shown that cues for a drug, such as a needle or a cigarette, activate the reward and pleasure areas of the brain implicated in drug use.

Of course, neurobiological, genetic, and environmental factors do not operate in isolation. The most comprehensive explanations for substance-related disorders will be those that consider how environmental factors enable genetic or neurobiological factors to have their effects. Research with animals shows this quite clearly. For example, studies of mice that were separated from their mothers at birth (a very stressful occurrence, even for mice!) responded to injections of amphetamine or cocaine later in life very differently from mice that had not been separated but had experienced stress early in life (a lot of handling by humans). The investigators showed that these two types of early stress differently impacted the way in which the dopamine system developed in these animals, which then contributed to their drug responses (Meaney, Brake, & Gratton, 2002).

Psychological Factors

In this section, we look at three types of psychological factors that may contribute to the etiology of substance-related disorders. First, we consider the effects of drugs (particularly alcohol and nicotine) on mood; we examine the situations in which a tension-reducing effect occurs and the role of cognition in this process. Second, we consider people's expectancies about the effects of substances on behavior, including beliefs about the prevalence with which a drug is used and about the health risks associated with using that drug. Third, we consider personality traits that may make it more likely for some people to use drugs heavily.

Mood Alteration It is generally assumed that one of the main psychological motives for using drugs is to alter mood—that is, drug use is reinforced because it enhances positive moods or diminishes negative ones. For example, most people believe that an increase in tension (e.g., because of a bad day at the office) leads to increased alcohol consumption. It has also been argued that stress might causes increases in smoking, at least the initiation of smoking and relapse after quitting smoking (Kassel, Stroud, & Paronis, 2003; Shiffman & Waters, 2004).

Longitudinal studies of stress and consumption have provided some support for this idea. For example, a longitudinal study of adolescent smokers found that increases in negative affect and negative life events were associated with increases in smoking (Wills, Sandy, & Yaeger, 2002). Other studies found that life stress precedes alcohol-related relapses (e.g., Brown et al., 1990). But other longitudinal research did not find that alcohol consumption increased after reports of greater life stress (Brennan, Schutte, & Moos, 1999). Because so many third variables may relate to stress and substance consumption, most would agree that laboratory experimental studies are important in this area. Findings from those studies are complex and suggest that if tension reduction works, it only does so in certain contexts for certain people. In addition, substances can reduce more than just tension. For example, research has found that alcohol lessens negative emotions, but it also lessens positive emotions in response to anxiety-provoking situations (Curtin et al., 1998; Stritzke, Patrick, & Lang, 1995).

Studies of the tension-reducing properties of nicotine have also yielded mixed findings, with some studies showing that nicotine reduces tension and others not finding this effect (Kassel et al., 2003). The reasons for the mixed findings may have to do with a failure to consider the stages of smoking. That is, tension reduction and negative affect seem to play more of a role in the initiation of smoking than in the maintenance of smoking or in relapse after treatment (Kassel et al., 2003). Furthermore, it may not be nicotine that is associated with a reduction in negative affect, but rather the sensory aspects of smoking (i.e., inhaling). An experimental study randomly assigned smokers to have cigarettes with or without nicotine (indistinguishable by participants) after inducing a negative or positive mood (Perkins et al., 2008). The researchers also manipulated smokers' expectancies. That is, some smokers expected and received a cigarette with nicotine, others expected nicotine but didn't get it, others expected no nicotine and didn't get it, and

others expected no nicotine but received it anyway. Smoking reduced negative affect after both mood inductions, but this was true for smokers regardless of what they expected and actually received to smoke (i.e., a cigarette with or without nicotine). Instead, the effects of inhaling, whether there was nicotine or not, had the greatest association with reducing negative affect.

Subsequent research to examine the reasons for these inconsistent results has focused on the situation in which alcohol or nicotine is consumed—specifically, a situation in which distraction is present. Findings indicate that alcohol may reduce tension by altering cognition and perception (Curtin et al., 1998; Steele & Josephs, 1988, 1990). Alcohol impairs cognitive processing and narrows attention to the most immediately available cues, resulting in "alcohol myopia" (Steele & Josephs, 1990). In other words, the intoxicated person has less cognitive capacity and tends to use that capacity to focus on an immediate distraction, if available, rather than on tension-producing thoughts, with a resultant decrease in anxiety. Experimental studies have also shown that cognitive distraction can also reduce aggressive behavior in people who are intoxicated (Giancola & Corman, 2007).

The benefits of distraction have also been documented for nicotine. Specifically, smokers who smoked in the presence of a distracting activity had a reduction in anxiety, whereas smokers who smoked without a distracting activity did not experience a reduction in anxiety (Kassel & Shiffman, 1997; Kassel & Unrod, 2000). However, alcohol and nicotine may increase tension when no distractions are present. For example, a person drinking alone may focus all his or her limited cognitive capacity on unpleasant thoughts, begin brooding, and become increasingly tense and anxious, a situation reflected in the expression "crying in one's beer."

In sum, the few available experimental studies suggest that there are important limits to when and how substances may reduce tension. Much more experimental research is needed (Kassel et al., 2003).

Tension reduction is only one aspect of the possible effects of drugs on mood. Some people may use drugs to reduce negative affect, whereas others may use drugs to increase positive affect when they are bored (Cooper et al., 1995). In this case, increased drug use results from a high need for stimulation combined with expectancies that drugs will promote increased positive affect. These patterns have been confirmed among people who abuse alcohol and cocaine (Cooper et al., 1995; Hussong et al., 2001).

Expectancies about Alcohol and Drug Effects If it is true that alcohol does not reduce stress when consumed after the fact, why do so many people who drink believe that it helps them unwind? Expectation may play a role here—that is, people may drink after stress not because it actually reduces tension but because they expect it to do so. In support of this idea, studies have shown that people who expect alcohol to reduce stress and anxiety are those likely to be frequent users (Rather et al., 1992; Sher et al., 1991; Tran, Haaga, & Chambless, 1997). Furthermore, drinking amount and positive expectancies about alcohol appear to influence each other. The expectation that drinking will reduce anxiety increases drinking, which in turn makes the positive expectancies even stronger (Smith et al., 1995).

Other research has shown that expectancies about a drug's effects—for example, the beliefs that a drug will stimulate aggression and increase sexual responsiveness—predict increased drug use in general (Stacy, Newcomb, & Bentler, 1991). Similarly, people who believe (falsely) that alcohol will make them seem more socially skilled are likely to drink more heavily than those who accurately perceive that alcohol can interfere with social interactions. In now-classic experiments demonstrating the power of expectancies, participants who believe they are consuming a quantity of alcohol when they are actually consuming an alcohol-free beverage subsequently become more aggressive (Lang et al., 1975). Alcohol consumption is associated with increased aggression, but expectancies about alcohol's effects can also play a role (Bushman & Cooper, 1990; Ito, Miller, & Pollack, 1996).Thus, as we have seen in other contexts, cognitions can have a powerful effect on behavior. Research also suggests a reciprocal relationship between expectancies and alcohol use: positive expectancies predict alcohol use, and alcohol use helps to maintain and strengthen positive expectancies (e.g., Sher et al., 1996).

The extent to which a person believes a drug is harmful and the perceived prevalence of use by others are also factors related to use. In general, the greater the perceived risk of a drug, the less likely it will be used. For example, in 2003, marijuana use among adolescents who perceived

great risk was 1.8 percent, whereas use among youths who perceived no, little, or moderate risk was 11.2 percent (SAMHSA, 2004). Similarly, many smokers do not believe that they are at increased risk for cancer or cardiovascular disease (Ayanian & Cleary, 1999). Furthermore, alcohol and tobacco are used more frequently among people who overestimate the frequency with which these substances are used by others (Jackson, 1997).

Personality Factors Personality factors may help to explain why certain people are more likely to abuse or become dependent on drugs and alcohol. Personality factors that appear to be important in predicting the later onset of substance-related disorders include high levels of negative affect, sometimes called *negative emotionality*; a persistent desire for arousal along with increased positive affect; and constraint, which refers to cautious behavior, harm avoidance, and conservative moral standards. One longitudinal study found that 18-year-old adolescents who were low in constraint but high in negative emotionality were more likely to develop a substance-related disorder as young adults (Krueger, 1999).

Another longitudinal, prospective study investigated whether personality factors could predict the onset of substance-related disorders in over 1,000 male and female adolescents at age 17 and then again at age 20 (Elkins et al., 2006). Low constraint and high negative emotionality predicted the onset of alcohol, nicotine, and illicit drug abuse and dependence for both men and women.

In another study, kindergarten children were rated by their teachers on several personality traits and were followed up several years later (Killen et al., 1997). Anxiety (e.g., worries about things, fear of new situations) and novelty seeking (e.g., being restless, fidgety) predicted the onset of getting drunk, using drugs, and smoking. Prospective, longitudinal studies do not support depression and anxiety as predictors of whether people initiate smoking (Kassel et al., 2003).

Sociocultural Factors

Sociocultural factors play a widely varying role in substance abuse and dependence. People's interest in and access to drugs are influenced by peers, parents, the media, and cultural norms about acceptable behavior.

At the broadest level, for example, we can look at great cross-national variation in substance consumption. Some research suggests that there are commonalities in substance use across countries. For example, a cross-national study of alcohol and drug use among high school students in 36 countries found that alcohol was the most common substance used across countries, despite great variation in the proportions of students who consumed alcohol, ranging from 32 percent in Zimbabwe to 99 percent in Wales (Smart & Ogburne, 2000). In all but two of the countries studied, marijuana was the next most commonly used drug. In those countries where marijuana was used most often (with more than 15 percent of high school students having ever used marijuana), there were also higher rates of use of amphetamines, Ecstasy, and cocaine.

Alcohol dependence is more prevalent in countries in which alcohol use is heavy, such as major wine-producing countries. Everyone is drinking wine in this French bar. (Eric Brissaud/Liaison Agency, Inc./Getty Images.)

Despite the commonalities across countries, other research documents striking cross-national differences in alcohol consumption. For example, the highest consumption rates have typically been found in wine-drinking societies, such as France, Spain, and Italy, where drinking alcohol regularly is widely accepted (deLint, 1978). Cultural attitudes and patterns of drinking thus influence the likelihood of drinking heavily and therefore of abusing alcohol. One finding that seems quite similar across different cultures is that men consume more alcohol than women. An analysis conducted by the International Research Group on Gender and Alcohol found that men drank more than women in Australia, Canada, the Czech Republic, Estonia, Finland, Israel, the Netherlands, Russia, Sweden, and the United States. Despite this consistency in gender differences, there was a large disparity across countries in the extent to which men drank more than women. For example, men drank

three times more than women in Israel but only one and a half times more than women in the Netherlands (Wilsnack et al., 2000). These findings suggest that cultural prescriptions about drinking by men and women are important to consider.

Ready availability of the substance is also a factor. For example, in wine-drinking societies, wine is present in many settings, even in university cafeterias. Also, rates of alcohol abuse are high among bartenders and liquor store owners, people for whom alcohol is readily available (Fillmore & Caetano, 1980). In 2003, drug use among youths who had been approached by drug dealers was 35 percent, compared to just under 7 percent among youths who had not been approached (SAMHSA, 2004). With regard to smoking, if cigarettes are perceived as being easy to get and affordable, the rate of smoking increases (Robinson et al., 1997). This is one of the reasons states raise taxes on alcohol and cigarettes so frequently. Of course, this tactic disproportionately affects the poor, which is not only unfair but does not necessarily target all who would benefit from substances being less available.

Family factors are important as well. For example, exposure to alcohol use by parents increases children's likelihood of drinking (Hawkins et al., 1997). Unhappy marriages predicted the onset of alcohol abuse or dependence in a study of nearly 2,000 married couples (Whisman et al., 2006). Acculturation into American society may interact with family factors for people of other cultural and ethnic backgrounds. For example, a study of middle school Hispanic students in New York found that children who spoke English with their parents were more likely to smoke marijuana than children who spoke Spanish (Epstein, Botvin, & Diaz, 2001). Psychiatric, marital, or legal problems in the family are also related to drug abuse, and a lack of emotional support from parents is linked to increased use of cigarettes, marijuana, and alcohol (Cadoret et al., 1995; Wills, DuHamel, & Vaccaro, 1995). Finally, longitudinal studies have shown that a lack of parental monitoring leads to increased association with drug-abusing peers and subsequent higher use of drugs (Chassin et al., 1996; Thomas et al., 2000).

The social setting in which a person operates can also affect substance abuse. For example, studies of smokers in daily life show that they are more likely to smoke with other smokers than with nonsmokers. In addition, smoking was more likely to occur in or outside bars restaurants, or at home, rather than in the workplace or in others' homes (Shiffman et al., 2002, 2004). Another study showed that having friends who smoke predicts smoking (Killen et al., 1997). In longitudinal studies, peer-group identification in the seventh grade predicted smoking in the eighth grade (Sussman et al., 1994) and increased drug use over a 3-year period (Chassin et al., 1996). Peer influences are also important in promoting alcohol and marijuana use (Hussong et al., 2001; Stice, Barrera, & Chassin, 1998; Wills & Cleary, 1999).

These findings support the idea that social networks influence a person's drug or alcohol behavior. However, other evidence indicates that people who are inclined to abuse substances may actually select social networks that conform to their own drinking or drug use patterns. Thus, we have two broad explanations for how the social environment is related to substance abuse: a social influence model and a social selection model. A longitudinal study of over 1,200 adults designed to test which model best accounted for drinking behavior found support for both models (Bullers, Cooper, & Russell, 2001). A person's social network predicted individual drinking, but individual drinking also predicted subsequent social network drinking. In fact, the social selection effects were stronger, indicating that people often choose social networks with drinking patterns similar to their own. No doubt the selected networks then support or reinforce their drinking.

Advertising is one way that expectancies develop. (Bill Aron/PhotoEdit.)

Another variable to be considered is the media. Television commercials associate beer with athletic-looking males, bikini-clad women, and good times. Billboards equate cigarettes with excitement, relaxation, and being in style. Alcohol advertising in magazines has increased in recent years, and it seems that these ads are reaching girls more than boys. For example, between 2001 and 2002, exposure to alcohol ads for girls increased 216 percent, whereas exposure to such ads increased 46 percent for boys (Jernigan et al., 2004). A review of studies found that

F.T.C. Charges Joe Camel Ad Illegally Takes Aim at Minors

Internal Documents of R. J. Reynolds Are Cited by Agency

By JOHN M. BRODER

WASHINGTON, May 28 — In another blow to an industry under siege, the Federal Trade Commission charged today that the R. J. Reynolds Tobacco Company illegally aimed its Joe Camel advertising campaign at minors.

The agency asserted in an administrative complaint that the company violated Federal fair trade practice laws by promoting a lethal and addictive product to children and adolescents who could not legally purchase or use it.

This is the first time that the commission has accused the tobacco industry of peddling its products to minors. The complaint will be supported, agency officials said, by extensive citations from internal company documents.

The Government says it believes that R. J. Reynolds papers will prove that the company deliberately designed its cartoon-based advertising campaign in the mid-1980's to increase its shrinking market share among young smokers.

The complaint amounts to a civil ind[illegible] tment of [illegible] compan[illegible] [illegible] is s[illegible] ficial[illegible]

Linda Rosier for The New York Times

Advertising is an important factor in stimulating drug use. The Joe Camel campaign greatly increased Camel's share of the market among elementary and high school students. (New York Times.)

tobacco billboards were over two times more common in primarily African American neighborhoods than they were in primarily European American neighborhoods (Primack et al., 2007). It is clear that advertising for drinking targets girls and advertising for smoking targets African Americans, but does advertising change smoking or drinking patterns?

The evidence indicates that it does. An analysis of consumption in 17 countries between 1970 and 1983 supports the role of advertising in promoting alcohol use. Those countries that banned ads for alcohol had 16 percent less consumption than those that did not (Saffer, 1991). In a longitudinal study of nonsmoking adolescents, those who had a favorite cigarette ad were twice as likely subsequently to begin smoking or to be willing to do so (Pierce et al., 1998). A particularly striking example of this was the Joe Camel campaign for Camel cigarettes. Camel launched its campaign in 1988 with the Joe Camel character, which was modeled after either James Bond or the character played by Don Johnson in the television program *Miami Vice*, a popular show of the time. Before the campaign, in the period from 1976 to 1988, Camel was the preferred brand of less than 0.5 percent of seventh through twelfth graders. By 1991, Camel's share of this illegal market had increased to 33 percent (DiFranza et al., 1991)!

It seemed like the days of Joe Camel and other advertisements that appeal to young people were over. Indeed, the Liggett Group, manufacturers of cigarettes, agreed to stop using such advertising tools and to take other steps to discourage smoking among minors in 1996. These actions were part of a settlement in a class action lawsuit, which included 46 states, that charged U.S. tobacco companies with manipulating nicotine levels to keep smokers addicted. Another cigarette maker, Philip Morris, stopped advertising in magazines in 2004. Furthermore, the American Legacy Foundation was formed as part of the settlement that followed this class action lawsuit (www.americanlegacy.org). The goals of this group are to prevent smoking among young people and to make sure information about smoking and how to stop smoking is accessible to everyone. We will discuss the important efforts of this group later in the chapter when we discuss prevention.

Despite these efforts, a recent analysis of internal documents of several tobacco companies (made public thanks to the lawsuit mentioned above) by researchers at the Harvard School of Public Health revealed that tobacco companies were still targeting their advertising toward young people as recently as 2007 (Kreslake et al, 2008). Some tobacco companies, such as R.J. Reynolds, still advertise, and all magazine ads in 2005 were for menthol brands. The researchers found that tobacco companies' own research had found that cigarettes with lower levels of menthol appealed more to young people and that efforts were then made to market these milder menthol brands to young people. In 2005, nearly half of adolescent smokers chose menthol cigarettes.

Quick Summary

A number of etiological factors have been proposed to account for alcohol and drug dependence, and some have more support than others. Genetic factors play a role in alcohol dependence and perhaps also nicotine dependence. The ability to tolerate alcohol and metabolize nicotine may be what is passed on in the genes. Genes that are important for the operation of the dopamine system may be an important factor in explaining how genes influence substance dependence, although more research is needed. The most-studied neurobiological factors are brain systems associated with dopamine pathways—the major reward pathways in the brain. The incentive-sensitization theory describes brain pathways involved in liking (i.e., consuming) drugs and wanting (i.e., craving) drugs.

Psychological factors have also been evaluated, and there is support for the idea that tension reduction plays a role, but only under certain circumstances, such as when distractions are present. Expectancies about the effects of drugs, such as reducing tension, increasing aggression, and increasing sexual prowess, have been shown to predict drug and alcohol use. Expectancies about the effects of drugs are also powerful; the greater the perceived risk of a drug, the less likely it will be used. Studies of personality factors also help us understand why some people may be more prone to abuse drugs and alcohol.

Sociocultural factors play a role, including the culture, availability of a substance, family factors, social settings and networks, and advertising. There is support for both a social influence model and a social selection model.

Check Your Knowledge 10.4

Answer the questions.

1. Which of the following is not one of the sociocultural factors implicated in the etiology of substance abuse or dependence?
   - **a.** the media
   - **b.** gender
   - **c.** availability of a substance
   - **d.** social networks
2. Which of the following statements best captures the link between depression and smoking?
   - **a.** Depression causes smoking.
   - **b.** Smoking causes depression.
   - **c.** It does not predict initiation.
   - **d.** We just don't know yet.
3. Genetic research on substance dependence indicates that:
   - **a.** Genetic factors may be the same for many drugs.
   - **b.** Additional studies need to be done to determine heritability.
   - **c.** The dopamine receptor DRD1 may be faulty.
   - **d.** Twin studies show that the environment is just as important as genes.

Treatment of Substance-Related Disorders

> *The chronicity of addiction is really a kind of fatalism writ large. If an addict knows in his heart he is going to use again, why not today? But if a thin reed of hope appears, the possibility that it will not always be so, things change. You live another day and then get up and do it again. Hope is oxygen to someone who is suffocating on despair. (Excerpt from David Carr's book "The Night of the Gun" as adapted in an article for the New York Times Magazine, July 20, 2008.)*

The challenges in treating people who are dependent on substances are great, as illustrated by the quote above. Substance dependence is chronic, and relapse occurs often. In view of these challenges, the field is constantly working to develop new and effective treatments, many of which we review in this section. The author of the quote, David Carr, was formerly addicted to cocaine, crack, and alcohol. Currently, he is a media columnist for the *New York Times*. For him, residential treatment was successful.

Many who work with those dependent on alcohol or drugs suggest that the first step to successful treatment is admitting there is a problem. To a certain extent, this makes sense. Why would someone get treatment for something that is not deemed a problem? Unfortunately, a number of treatment programs require people not only to admit a problem but also to demonstrate their commitment to treatment by stopping their use of alcohol or drugs before beginning treatment. This requirement can exclude many who desire and need treatment. For example, James (in the clinical case presented earlier) might not have been admitted to a residential program had he not been free of heroin for a week before trying to gain admission. Imagine if people with lung cancer were told they had to demonstrate their commitment to treatment by stopping smoking before the cancer could be treated. In the next sections, we review treatments for alcohol-related problems, nicotine dependence, and other drug dependence.

Treatment of Alcohol Abuse and Dependence

In 2006, 4 million people over the age of 12 received treatment for alcohol abuse or dependence (SAMHSA, 2007). Unfortunately, over 21 million people over the age of 12 were in need of treatment for alcohol or drug problems in 2006 who did not receive it. A large epidemiological study found that only 24 percent of people with alcohol dependence ever receive treatment (Hasin et al., 2007). We have far to go in developing and providing effective treatments.

Inpatient Hospital Treatment Often, the first step in treatment for substance dependence is called **detoxification**. Withdrawal from substances including alcohol, can be difficult, both

physically and psychologically. Although detoxification does not have to occur in a hospital setting, it can be less unpleasant in a supervised setting. Many people have to go through the detoxification process multiple times. Unfortunately, multiple previous detoxifications are associated with a poorer response to treatment (Malcolm et al., 2000). In recent years, the population served in detoxification centers has changed demographically: There have been large increases in admissions of women, African Americans, and Hispanics, as well as a decline in the mean age at admission and an increase in people who are unemployed (McCarty et al., 2000). Alice, the woman described in the earlier clinical case, would likely need hospital treatment, at least for detoxification.

The number of for-profit hospitals treating alcohol abuse increased dramatically until the mid-1990s, in part because such treatment was covered in large measure by both private insurance companies and the federal government (Holder et al., 1991). Because inpatient treatment is much more expensive than outpatient treatment, its cost-effectiveness has been questioned. Is it worth the expense? Apparently not, at least in many cases. The therapeutic results of hospital treatment are not superior to those of outpatient treatment (Mundle et al., 2001; Soyka et al., 2001). In addition, short stays (less than 8 days) in detoxification hospitals may be as effective as longer stays (Foster, Marshall, & Peters, 2000). Some data even suggest that home detoxification may be a viable alternative to day hospital or inpatient treatment for selected groups of people (Allan, Smith, & Melting, 2000). However, an analysis of treatment for alcohol dependence concludes that an inpatient approach is probably necessary for people with few sources of social support who are living in environments that encourage the abuse of alcohol, especially people with serious psychological problems in addition to their substance abuse (Finney & Moos, 1998). Unfortunately, changes in health insurance in the United States over the past 10 years, including affordability, availability, and coverage, have made it more difficult for those dependent on alcohol to get hospital treatment when they need it. Between 2002 and 2003, the number of people receiving inpatient treatment at a hospital went from over 800,000 to just under 600,000 (SAMHSA, 2004).

Alcoholics Anonymous is the largest self-help group in the world. At their regular meetings, newcomers rise to announce their addiction and receive advice and support from others. (Hank Morgan/Photo Researchers.)

Alcoholics Anonymous The largest and most widely known self-help group in the world is Alcoholics Anonymous (AA), founded in 1935 by two recovering alcoholics. It has well over 70,000 chapters and a membership numbering more than 2 million people in the United States and in more than 100 other countries. In 2003, nearly two-thirds of people who received treatment for alcohol or drug dependence did so through a self-help program (SAMHSA, 2004).

Each AA chapter runs regular and frequent meetings at which newcomers rise to announce that they are alcoholics and older, sober members give testimonials, relating the stories of their problems with alcohol and indicating how their lives are better now. The group provides emotional support, understanding, and close counseling as well as a social network. Members are urged to call on one another around the clock when they need companionship and encouragement not to relapse. Programs modeled after AA are available for other substances, for example, Cocaine Anonymous and Marijuana Anonymous.

The AA program tries to instill in each member the belief that alcohol dependence is a disease that can never be cured and that continuing vigilance is necessary to resist taking even a single drink, lest uncontrollable drinking begin all over again. Even if the person has not consumed any alcohol for 15 years or more, the designation "alcoholic" is still necessary according to the tenets of AA, since the person is always an alcoholic, always carrying the disease, even if it is currently under control.

The spiritual aspect of AA is apparent in the 12 steps of AA shown in Table 10.2, and there is evidence that belief in this philosophy is linked with achieving abstinence (Fiorentine & Hillhouse, 2000; Tonigan, Miller, & Connors, 2000). Other self-help groups do not have the religious overtones of AA, relying instead on social support, reassurance, encouragement, and suggestions for leading a life without alcohol. One such approach, termed *Rational Recovery*, focuses on promoting renewed self-reliance rather than reliance on a higher power (Trimpey, Velton, & Dain, 1993).

Table 10.2 The 12 Steps of Alcoholics Anonymous

1. We admitted we were powerless over alcohol—that our lives had become unmanageable.
2. Came to believe that a power greater than ourselves could restore us to sanity.
3. Made a decision to turn our will and our lives over to the care of God as we understood Him.
4. Made a searching and fearless moral inventory of ourselves.
5. Admitted to God, to ourselves, and to another human being the exact nature of our wrongs.
6. Were entirely ready to have God remove all these defects of character.
7. Humbly asked Him to remove our shortcomings.
8. Made a list of all persons we had harmed, and became willing to make amends to them all.
9. Made direct amends to such people wherever possible, except when to do so would injure them or others.
10. Continued to take personal inventory and, when we were wrong, promptly admitted it.
11. Sought through prayer and meditation to improve our conscious contact with God as we understood Him, praying only for knowledge of His will for us and the power to carry that out.
12. Having had a spiritual awakening as the result of these steps, we tried to carry this message to alcoholics and to practice these principles in all our affairs.

Source: The Twelve Steps and Twelve Traditions. Copyright © 1952 by Alcoholics Anonymous World Services, Inc. Reprinted with permission of Alcoholics Anonymous World Services, Inc.

Noncontrolled trials show that AA provides significant benefit to participants (Ouimette, Finney, & Moos, 1997; Timko et al., 2001). A large prospective study of over 2,000 men with alcohol dependence found that participation in AA predicted a better outcome 2 years later (McKeller, Stewart, & Humphreys, 2003). In addition, becoming an AA member early in treatment and staying involved for a longer period of time is associated with a better outcome 8 years after treatment began (Moos & Humphreys, 2004).

All of this sounds like good news for people participating in AA. However, a review of the eight randomized controlled clinical trials found little benefit of AA over other types of treatment, including motivational enhancement, inpatient treatment, couples therapy, or cognitive behavior therapy (Ferri, Amato, & Davoli, 2008). In addition, AA has high dropout rates, and the dropouts are not always factored into the results of studies. There have been no controlled studies testing the efficacy of Rational Recovery, though two findings from preliminary studies suggest that it may be effective (Schmidt, Carns, & Chandler, 2001).

Couples Therapy Behaviorally oriented marital or couples therapy (O'Farrell & Fals-Stewart, 2000) has been found to achieve some reductions in problem drinking, even a year after treatment has stopped, as well as some improvement in couples' distress generally (McCrady & Epstein, 1995).

Cognitive and Behavioral Treatments Contingency management therapy is a cognitive behavior treatment for alcohol abuse and dependence that involves teaching people and those close to them to reinforce behaviors inconsistent with drinking—for example, taking Antabuse (on page 309) and avoiding situations that were associated with drinking in the past. It is based on the belief that environmental contingencies can play an important role in encouraging or discouraging drinking. Vouchers are provided for not using alcohol a substance (cocaine, heroin, marijuana; verified by urine samples), and the tokens are exchangeable for things that the person would like to have more of (Dallery et al., 2001; Katz et al., 2001; Silverman et al., 1996). This therapy also includes teaching job-hunting and social skills, as well as assertiveness training for refusing drinks. For socially isolated people, assistance and encouragement are provided to establish contacts with other people who are not associated with drinking. Other effective contingency-based treatments include providing reinforcers for sobriety, such as opportunities to win prizes (Petry et al., 2000) and abstinence-contingent partial support for housing, food, recreational activities, and access to supportive therapy (Gruber, Chutuape, & Stitzer, 2000). Often referred to as the *community-reinforcement approach*, contingency management therapy has generated very promising results (Bauemetol, 1998; Sisson & Azrin, 1989; Spitzer & Petry, 2006). A review of the literature shows that it is consistently found to be one of the most effective and cost-effective treatments available (Smith, Meyers, & Miller, 2001).

Relapse prevention is another cognitive behavioral treatment that has been effective with alcohol and drug dependence and abuse. It can be a stand-alone treatment or a part of other interventions. Broadly, the goal is to help people avoid relapsing back into drinking once they have stopped. Focus on Discovery 10.4 discusses this important treatment in more detail.

Brief Motivational Interventions As we described earlier, heavy drinking is particularly common among college students. One team of investigators designed a brief intervention to try to curb such heavy drinking in college (Carey et al., 2006). The intervention contained two parts: (1) a comprehensive assessment that included the Timeline Follow Back (TLFB) interview (Sobell & Sobell, 1996), an interview that carefully assess drinking in the past 3 months, and (2) a brief motivational treatment that included individualized feedback about a person's drinking in relation to community and national averages, education about the effects of alcohol,

FOCUS ON DISCOVERY 10.4

Relapse Prevention

Relapse prevention is an important part of any treatment for drug or alcohol dependence. Mark Twain quipped that stopping smoking was easy—he'd done it hundreds of times! Marlatt and Gordon (1985) developed an approach to treatment called relapse prevention specifically to prevent relapse in substance abuse. In this approach, people dependent on alcohol are encouraged to believe that a lapse will not inevitably precipitate a total relapse and should be regarded as a learning experience rather than as a sign that the battle is lost, a marked contrast from the AA perspective (Marlatt & Gordon, 1985). This noncatastrophizing approach to relapse after therapy—falling off the wagon—is important because the overwhelming majority of people who are dependent on alcohol who become abstinent experience one or more relapses over a 4-year period (Polich, Armor, & Braiker, 1980). People dependent on alcohol examine sources of stress in their work, family, and relationships so that they can become active and responsible in anticipating and resisting situations that might lead them into excessive drinking (Marlatt, 1983; Sobell, Toneatto, & Sobell, 1990). The sources of stress that precipitate a relapse in alcohol dependence may be different for men and women. For women, marital stress is a predictor of relapse. For men, however, marriage seems to protect them from relapse (Walitzer & Dearing, 2006).

Relapse prevention treatment appears to be more effective with some substances than with others. A meta-analysis of 26 randomized controlled clinical trials found that relapse prevention was most effective for alcohol and drug dependence and least effective for nicotine dependence (Irvin et al. 1999). Most smokers relapse within a year of stopping, regardless of the means used to stop. In a pattern we have already seen, people who smoked the most—and are presumably more addicted to nicotine—relapse more often and more quickly than moderate or light smokers. Frequent slips, intense cravings and withdrawal symptoms, low tolerance for distress, younger age, nicotine dependence, low self-efficacy, stressful life events, observations of other smokers, weight concerns, and previous quitting attempts are all predictors of relapse (Brown et al., 2005; McCarthy et al., 2006; Ockene et al., 2000; Piasecki, 2006). One very detailed analysis, using ecological momentary assessment, of smokers' thoughts, feelings, and symptoms both before and after they quit smoking revealed that many smokers experience high levels of negative affect before their target quit day and that this anticipatory negative affect predicted a greater likelihood of relapse (McCarthy et al., 2006). Despite these difficulties, there is some encouraging evidence that self-help relapse prevention programs can be effective in reducing smoking relapse (Brandon, Vidrine, & Litvin, 2007). In these programs, smokers receive booklets in the mail describing the relapse prevention approach. These brochures appear to be effective up to 1 year after smoking was stopped.

What factors contribute to success? Research results (and common sense) tell us that ex-smokers who do not live with a smoker do better at follow-up than those who do live with a smoker (McIntyre-Kingsolver, Lichtenstein, & Mermelstein, 1986). So-called booster or maintenance sessions help, but in a very real sense they represent a continuation of treatment; when they stop, relapse is the rule (Brandon, Zelman, & Baker, 1987). Intensive interventions, such as a telephone counseling (Brandon et al., 2000), also help; however, they reach relatively few smokers. Brief relapse prevention interventions during medical visits are cost-effective and could potentially reach most smokers but are not consistently delivered (Ockene et al., 2000). On a positive note, there is considerably more social support for not smoking than there was just 10 years ago, at least in the United States. Perhaps as time goes on, societal sanctions against smoking will help those who have succeeded in quitting remain abstinent. (It is certainly more difficult to find a place to light up nowadays.)

One specific approach to the relapse problem is to focus on the cognitions of ex-smokers (Baer & Lichtenstein, 1988). Using the articulated thoughts paradigm (see p. 87), a study found that recent ex-smokers who tended to think of smoking without prompting relapsed more readily 3 months later (Haaga, 1989). However, if ex-smokers learned some effective ways of countering these smoking-related thoughts, such as distracting themselves, their abstinence was better months later. Using a questionnaire measure, a study found that ex-smokers' self-efficacy in facing their most difficult challenge—for example, not smoking while having coffee and dessert after a pleasant dinner—was a good predictor of abstinence a year later (Haaga, 1990). These and related studies indicate that the prediction of continued abstinence or relapse is enhanced by measuring the cognitions of ex-smokers. Such information may help therapists design programs that will improve the ability of a specific person to remain a nonsmoker (Compas et al., 1998).

and tips for reducing harm and moderating drinking. Results from the study showed that the TLFB alone decreased drinking behavior, but that the combination of the TLFB and motivational intervention was associated with a longer lasting-reduction in drinking behavior, up to 1 year after the interview and intervention.

Moderation in Drinking At least since the advent of Alcoholics Anonymous, many have believed that people dependent on alcohol had to abstain completely if they were to be successfully treated, for they were assumed to have no control over drinking once they had taken that first drink. This continues to be the belief of Alcoholics Anonymous, but research mentioned earlier, indicating that drinkers' beliefs about themselves and alcohol may be as important as the addiction to the drug itself, has called this assumption into question. Considering the difficulty in society of avoiding alcohol altogether, it may be preferable to teach a person who does not abuse alcohol in an extreme fashion to drink with moderation. Drinkers' self-esteem will certainly benefit from being able to control a problem and from feeling in charge of their life.

The term **controlled drinking** was introduced into the domain of alcohol treatment by Mark and Linda Sobell (Sobell & Sobell, 1993). It refers to a pattern of alcohol consumption that is moderate, avoiding the extremes of total abstinence and inebriation. Findings of one well-known treatment program suggested that at least some people who abuse alcohol can learn to control their drinking and improve other aspects of their lives as well (Sobell & Sobell, 1976).

Controlled-drinking treatment programs were further developed to teach people to respond adaptively to situations in which they might otherwise drink excessively. They learn various social skills to help them resist pressures to drink; they receive assertiveness, relaxation, and stress-management training, sometimes including biofeedback and meditation; and they are encouraged to exercise and maintain a healthy diet.

The Sobells' current approach to teaching moderation to people with alcohol dependence has evolved even further. Termed *guided self-change*, this outpatient approach emphasizes personal responsibility and control. The basic assumption is that people have more potential control over their immoderate drinking than they typically believe and that heightened awareness of the costs of drinking to excess as well as of the benefits of abstaining or cutting down can be of material help. People are encouraged to view themselves as basically healthy people who have been making unwise, often self-destructive, choices about how to deal with life's inevitable stresses rather than as victims of an addiction.

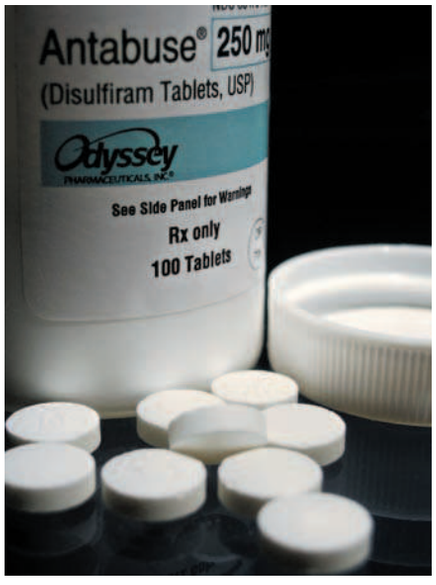
In guided self-change, the therapist is empathic and supportive while making salient to the person the negative aspects of excessive drinking that the person may have been overlooking. For example, getting the person to delay 20 minutes before taking a second or third drink can help him or her reflect on the costs versus the benefits of drinking to excess. Evidence supports the effectiveness of this approach in helping people moderate their intake and otherwise improve their lives (Sobell & Sobell, 1993).

Whether abstinence or controlled drinking should be the goal of treatment remains controversial. This issue pits influential forces, such as AA, that uphold abstinence as the only proper goal for people dependent on alcohol, against more recent researchers, such as the Sobells and those adopting their general approach, who have shown that moderation can work for many people, including those with severe drinking problems. If the therapeutic means of achieving the goal of moderate drinking are available—and research strongly suggests that they are—then controlled drinking may be a more realistic goal even for a person dependent on alcohol. Controlled drinking is currently much more widely accepted in Canada and Europe than it is in the United States.

Medications Some people who are in treatment for alcohol dependence, inpatient or outpatient, take disulfiram, or **Antabuse**, a drug that discourages drinking by causing violent vomiting if alcohol is ingested. As one can imagine, adherence to an Antabuse regimen can be a problem.

For it to be effective, a person must already be strongly committed to change. However, in a large, multicenter study, Antabuse was not shown to have any benefit, and dropout rates were as high as 80 percent (Fuller, 1988).

Mark and Linda Sobell introduced controlled drinking approaches to the treatment of alcohol abuse. (Courtesy of Mark Sobell; Courtesy of Linda Sobell.)



Antabuse is used to treat alcohol dependence, but it is not a very effective treatment because many people stop taking it. (Mark Alberhasky/imagema.com.)

The Food and Drug Administration has approved the opiate antagonists naltrexone and naloxone (discussed in the section on treatment for heroin dependence), which block the activity of endorphins that are stimulated by alcohol, thus reducing the craving for it. Evidence is mixed regarding whether these drugs are more effective than a placebo in reducing drinking when they are the only treatment (Krystal et al., 2001). But they do appear to add to overall treatment effectiveness when combined with cognitive behavioral therapy (Streeton & Whelan, 2001; Volpicelli et al., 1995, 1997).

Acamprosate, which has been in regular use in Europe for nearly 20 years under the brand name Campral, was approved by the FDA in 2004. Although its action is not completely understood, researchers believe that it impacts the glutamate and GABA neurotransmitter systems and thereby reduces the cravings associated with withdrawal. A review of data from all published double-blind, placebo-controlled clinical trials of acamprosate for people dependent on alcohol suggests that it is highly effective (Mason, 2001). A meta-analysis comparing the effectiveness of acamprosate and naltrexone found them equally effective (Kranzler & Van Kirk, 2001). There is, of course, the more general question of whether treating a substance abuse problem by giving another drug is necessarily a prudent strategy if one believes that some people come to rely on drugs in part because they are looking for a chemical solution to problems in their lives. Nevertheless, to the extent that medications are an effective treatment for alcohol dependence, disallowing them due to a concern over substituting one drug for another seems misguided.

Quick Summary

Inpatient hospital treatment for alcohol dependence is not as common today as it was in earlier years, primarily due to the cost. Detoxification from alcohol does often take place in hospitals, but treatment after this is more commonly done in outpatient settings.

Alcoholics Anonymous (AA) is the most common form of treatment for alcohol dependence. It is a group-based self-help treatment that instills the notion of alcohol dependence as disease. Though not widely studied, available research suggests that AA is an effective treatment.

There is some evidence that behavioral couples therapy is an effective treatment.

Contingency management therapy, which involves teaching people and those close to them to reinforce behaviors inconsistent with drinking, has shown some promise. Controlled drinking refers to a pattern of alcohol consumption that is moderate, avoiding the extremes of total abstinence and inebriation. The guided self-change treatment approach emphasizes control over moderate drinking, the costs of drinking to excess, and the benefits of abstaining.

Medications for alcohol dependence treatment include Antabuse, naltrexone and naloxone, and acamprosate. Antabuse is not an effective treatment in the long run. Noncompliance is a big problem. It is not clear that other medications are effective on their own, but they do seem to be beneficial in combination with cognitive behavior therapy. Early evidence suggests that acamprosate may be an effective medication.

Treatment of Nicotine Dependence

The numerous laws that currently prohibit smoking in restaurants, trains, airplanes, and public buildings are part of a social context that provides incentives and support to stop smoking. In addition, people are more likely to quit smoking if other people around them quit. A longitudinal study of over 12,000 people documented that if people in one's social network quit smoking (spouses, siblings, friends, co-workers), the odds that a person will quit smoking are much greater (Christakis & Fowler, 2008). For example, if a person's spouse stopped smoking, his or her chances of continued smoking decreased by nearly 70 percent. In short, peer pressure to quit smoking appears to be as effective as peer pressure to start smoking once was.

Some smokers who want to quit attend smoking clinics or consult with professionals for other specialized smoking-reduction programs. Even so, it is estimated that only about half of

those who go through smoking-cessation programs succeed in abstaining by the time the program is over; only about 20 percent of those who have succeeded in the short term actually remain nonsmoking after a year. The greatest success overall is found among smokers who are better educated, older, or have acute health problems (USDHHS, 1998b).

Laws that have banned smoking in many places have probably increased the frequency of quitting. (Digital Vision/SuperStock, Inc.)

Psychological Treatments Probably the most widespread psychological treatment consists of a physician telling the person to stop smoking. Each year millions of smokers are given this counsel—because of hypertension, heart disease, lung disease, or diabetes, on general grounds of preserving or improving health. Indeed, by age 65, most smokers have managed to quit (USDHHS, 1998b). There is some evidence that a physician's advice can get some people to stop smoking, at least for a while, especially when the person also chews nicotine gum (Law & Tang, 1995). But much more needs to be learned about the nature of the advice, the manner in which it is given, its timing, and other factors that must surely play a role in determining whether smokers are prepared and able to alter their behavior primarily on a physician's say-so (USDHHS, 1998b).

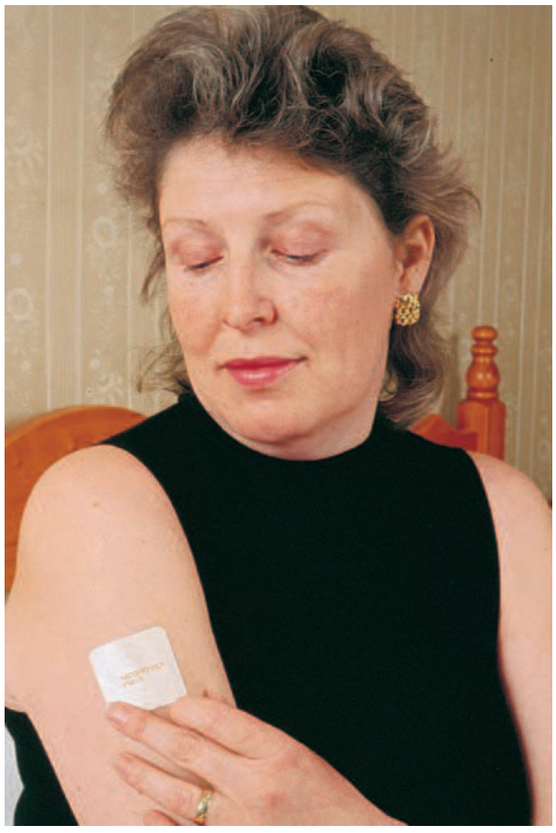
Cognitively oriented investigators have tried to encourage more control in people who smoke; treatments aim at having people develop and use coping skills, such as relaxation and positive self-talk, when confronted with tempting situations—for example, after a meal or when sitting down to read a book. Results are not very promising, however (Smith et al., 2001).

In contrast, a review indicated that scheduled smoking shows real promise (Compas et al., 1998). The strategy is to reduce nicotine intake gradually over a period of a few weeks by getting smokers to agree to increase the time between cigarettes. For example, during the first week of treatment, a one-pack-a-day smoker would be put on a schedule allowing only 10 cigarettes per day; during the second week, only 5 cigarettes a day would be allowed; and during the third week, the person would taper off to zero. The cigarettes would have to be smoked on a schedule provided by the treatment team, not when the smoker feels an intense craving. In this way, the person's smoking behavior is controlled by the passage of time rather than by urges, mood states, or situations. Smokers who are able to stay with the agreed-upon schedule showed a 44 percent abstinence rate after 1 year, a very impressive outcome (Cinciripini et al., 1994).

By age 18, about two-thirds of cigarette smokers regret having started smoking, one-half have already made an attempt to quit, and nearly 40 percent show interest in obtaining treatment for their dependence (Henningfield, Michaelides, & Sussman, 2000). A school-based program called Project EX includes training in coping skills and a psychoeducational component about the harmful effects of smoking. Two studies have found this program to be effective, both in the United States (Sussman, Dent, & Lichtman, 2001) and in China (Zheng et al., 2004), where the program was adapted to fit Chinese culture and language.

Nicotine Replacement Treatments and Medications Reducing a smoker's craving for nicotine by providing it in a different way is the goal of nicotine replacement treatments. Attention to nicotine dependence is clearly important because the more cigarettes people smoke daily, the less successful they are at quitting. Nicotine may be supplied in gum, patches, or inhalers. The idea is to help smokers endure the nicotine withdrawal that accompanies any effort to stop smoking. Although nicotine replacement alleviates withdrawal symptoms—which justifies its use in gum and in the nicotine patches to be described next—the severity of withdrawal is only minimally related to success in stopping smoking (Ferguson, Shiffman, & Gwaltney, 2006; Hughes, et al., 1990).

Gum containing nicotine has been available in the United States since 1984 by doctor's prescription, and it is now available over the counter. The nicotine in gum is absorbed much more slowly and steadily than that in tobacco. The long-term goal is for the former smoker to be able to cut back on the use of the gum as well, eventually eliminating reliance on nicotine altogether.



Nicotine patches are available over the counter to help relieve withdrawal symptoms. (Jim Selby/ Photo Researchers.)

This treatment involves some controversy, however. Ex-smokers can become dependent on the gum. Moreover, in doses that deliver an amount of nicotine equivalent to smoking one cigarette an hour, the gum causes cardiovascular changes, such as increased blood pressure, that can be dangerous to people with cardiovascular diseases. Nevertheless, some experts believe that even prolonged, continued use of the gum is healthier than obtaining nicotine by smoking, because at least the poisons in the smoke are avoided (de Wit & Zacny, 2000).

Nicotine patches became available in 1991 with a doctor's prescription and in 1996 over the counter. A polyethylene patch taped to the arm serves as a transdermal (through the skin) nicotine delivery system that slowly and steadily releases the drug into the bloodstream and thence to the brain. An advantage of the patch over nicotine gum is that the person need only apply one patch each day and not remove it until applying the next patch, making compliance easier. Treatment can be effective after 8 weeks of use for most smokers (Stead et al., 2008), with smaller and smaller patches used as treatment progresses. A drawback is that people who continue smoking while wearing the patch risk increasing the amount of nicotine in their body to dangerous levels.

Evidence suggests that the nicotine patch is superior to the use of a placebo patch in terms of both abstinence and subjective craving (Hughes et al., 1990). A meta-analysis of 111 trials of all types of nicotine replacement treatments (NRT: patch, gum, nasal spray, inhaler, tablets) found that NRT was more effective than placebo in smoking cessation (Stead et al., 2008). However, NRT is not a panacea. Abstinence rates are only about 50 percent at 12-month follow-ups. The manufacturers state that the patch is to be used only as part of a psychological smoking-cessation program and then for not more than 3 months at a time.

Combining the antidepressant medication buprioprion and nicotine patches yielded a 12-month abstinence rate of 35 percent in one study (Jorenby et al., 1999) but less promising results in others (Hughes, Stead, & Lancaster, 2004; Killen et al., 2006). Other promising non-nicotine pharmacotherapy for smoking cessation has included the drug clonidine and silver acetate (Benowitz & Peng, 2000). The FDA approved the prescription drug Varenicline in 2006 for treatment of nicotine dependence, and early results suggest that this medication is effective in combination with behavioral treatment and that is more effective than buprioprion (Cahill, Stead, & Lancaster, 2007; Tonstad et al., 2006).

Treatment of Illicit Drug Abuse and Dependence

Central to the treatment of people who use illegal drugs such as heroin and cocaine is detoxification—withdrawal from the drug itself. Heroin withdrawal reactions range from relatively mild bouts of anxiety, nausea, and restlessness for several days to more severe and frightening bouts of delirium and panic. The type of reaction depends primarily on the purity of the heroin that the person has been using. Withdrawal reactions from barbiturates are especially severe, even life threatening; they begin about 24 hours after the last dose and peak 2 or 3 days later. They usually abate by the end of the first week but may last for a month if large doses were taken. Withdrawal from barbiturates is best undertaken gradually, not cold turkey (a term that derives from the goosebumps that occur during withdrawal, making the person's skin resemble that of a plucked turkey), and should take place under close medical supervision.

Detoxification is the first way in which therapists try to help a person dependent on a drug, and it may be the easiest part of the rehabilitation process. Enabling the drug user to function without drugs after detoxification is extremely difficult—typically, both therapist and client experience more disappointment and sadness than success in this process. A variety of approaches to this task are available, including psychological treatments, drug substitution treatments, and medications.

Psychological Treatments In the first direct comparison in a controlled study, the antidepressant medication desipramine and cognitive behavioral therapy (CBT) were both found to be somewhat effective in reducing cocaine use as well as in improving a person's family, social, and general psychological functioning (Carroll, Rounsaville, Gordon, et al., 1994; Carroll et al.,

1995). In this 12-week study, desipramine was better than a placebo for people with a low degree of dependence on cocaine, whereas CBT was better for people with a high degree of dependence. This finding illustrates the significance of the psychological aspects of substance abuse.

In this study, people receiving CBT learned how to avoid high-risk situations (e.g., being around people using cocaine), recognize the lure of the drug for them, and develop alternatives to using cocaine (e.g., recreational activities with nonusers). People who abused cocaine in this study also learned strategies for coping with the craving and for resisting the tendency to regard a slip as a catastrophe ("relapse prevention training," see Focus on Discovery 10.4). A more recent study testing the effectiveness of CBT for drug abuse in a community setting found that there was no difference in outcomes between CBT and standard substance-abuse counseling (Morgenstern et al., 2001). We have a ways to go in order to make our treatments more effective in community settings.

Group therapy in residential settings is frequently used to treat heroin addiction. (David M. Grossman/Photo Researchers.)

Contingency management with vouchers has shown promise for cocaine, heroin, and marijuana dependence (Dallery et al., 2001; Katz et al., 2001; Petry et al., 2005; Silverman et al., 1996). For example, a randomized treatment trial for people with marijuana dependence compared a voucher treatment, CBT, and CBT plus vouchers (Budney et al., 2006). During the treatment, people who received the voucher treatment were more likely to remain abstinent than those in the CBT treatment or in the CBT plus vouchers treatment. After treatment was over, however, people who received CBT plus vouchers were most likely to remain abstinent. Thus, vouchers appear to work in the short term, but CBT appears to be an effective component of treatment for marijuana dependence in the long term with respect to maintaining abstinence after treatment is over.

Studies of contingency management for cocaine abuse find that it is associated not only with a greater likelihood of abstinence but also with a better quality of life (Petry, Alessi, & Hanson, 2007). In an analysis that looked at four different studies of contingency management treatment for cocaine abuse, the researchers found that people who received contingency management treatment were more likely to remain abstinent than people who received treatment as usual and that the duration of their abstinence during treatment was related to a higher quality of life after treatment. A meta-analysis of four randomized controlled clinical trials comparing contingency management, day treatment, or both treatments (combined condition) for cocaine abuse among homeless people found that the combined treatment and contingency management were both more effective than day treatment alone (Schumacher et al., 2007).

A treatment called *motivational interviewing* or *enhancement* therapy has also shown promise. This treatment involves a combination of CBT techniques and techniques associated with the humanistic therapy of Carl Rogers (see p. 491). A meta-analysis of this treatment found that it was effective for both alcohol and illegal drug dependence and abuse (Burke, Arkowitz, & Menchola, 2003). Another study found that motivational enhancement combined with CBT and contingency management was an effective treatment package for young people (ages 18–5) who were dependent on marijuana (Carroll et al. 2006).

Self-help residential homes are another psychological approach to treating heroin and other types of drug abuse and dependence. Daytop Village, Phoenix House, Odyssey House, and other drug-rehabilitation homes share the following features:

- Separation of people from previous social contacts, on the assumption that these relationships have been instrumental in maintaining the drug dependence
- A comprehensive environment in which drugs are not available and continuing support is offered to ease the transition from regular drug use to a drug-free existence

- The presence of charismatic role models, people formerly dependent on drugs who appear to be meeting life's challenges without drugs
- Direct, often intense confrontation in group therapy, in which people are goaded into accepting responsibility for their problems and for their drug habits and are urged to take charge of their lives
- A setting in which people are respected as human beings rather than stigmatized as failures or criminals

There are several obstacles to evaluating the efficacy of residential drug-treatment programs. Since entrance is voluntary, only a small minority of dependent users enter such settings. Furthermore, because the dropout rate is high, those who remain cannot be regarded as representative of the population of people addicted to illegal drugs; their motivation to stop using drugs is probably much stronger than that of people who don't volunteer for treatment or people who dropout. Any improvement participants in these programs make may reflect their uncommonly strong desire to rid themselves of the habit more than the specific qualities of the treatment program. Such self-regulating residential communities do, however, appear to help a large number of those who remain in them for a year or so (Institute of Medicine, 1990; Jaffe, 1985).

In 2000, voters in California approved Proposition 36, enacted into law in 2001 as the Substance Abuse and Crime Prevention Act (SACPA). The act allows nonviolent drug offenders to be sent to drug treatment rather than prison. Participation in this program is voluntary—someone meeting the criteria of SACPA has the choice of treatment or prison. In the first 4 years of the program, over 200,000 offenders were eligible and about 74 percent chose treatment over standard criminal justice proceedings. Researchers at UCLA studied the program for its first 4 years and released yearly reports. Findings from the first 4 years suggest that the program is working, at least with respect to treatment completion. Just over one-third completed the treatment. This may seem low, but it is actually quite favorable in comparison to completion rates of other programs, particularly those to which offenders are referred by the criminal justice system (Longshore et al., 2003, 2005). Cost savings from this program during its first 2 years were substantial. Every dollar invested in a SACPA participant would have cost as much as four times more had the participant been sent to prison (Longshore et al., 2006). The news is not all good, however. Participants who went into treatment under SACPA were more likely to be rearrested for drug offenses than people who had similar offenses before the beginning of SACPA (Longshore et al., 2005). Time will tell if the program is successful in keeping people out of the criminal justice system.

Drug Replacement Treatments and Medications Two widely used programs for heroin dependence involve the administration of *heroin substitutes*, drugs chemically similar to heroin that can replace the body's craving for it, or *opiate antagonists*, drugs that prevent the user from experiencing the heroin high. Recall from Chapter 2 (p. 36) that an antagonist is a drug that dampens the activity of neurotransmitters, and an agonist is a drug that stimulates neurotransmitters. The first category includes **methadone**, levomethadyl acetate, and bupreophine, synthetic narcotics designed to take the place of heroin. Since these drugs are themselves addicting, successful treatment essentially converts the person's dependence on heroin into dependence on a different substance. This conversion occurs because these synthetic narcotics are **cross-dependent** with heroin; that is, by acting on the same central nervous system receptors, they become a substitute for the original dependency. Abrupt discontinuation of methadone results in its own pattern of withdrawal reactions, but because these reactions are less severe than those of heroin, methadone has potential for weaning heroin users altogether from drug dependence (Strain et al., 1999).

Methadone is a synthetic heroin substitute. People formerly addicted to heroin come to clinics each day and swallow their dose. (John Giordano/Corbis SABA.)

Treatment with a heroin substitute usually involves going to a drug-treatment clinic and swallowing the drug in the presence of a staff member, once a day for methadone and three times a week for levomethadyl acetate and bupreophine. There is some evidence that methadone maintenance can be carried out more simply and just as effectively by weekly visits to a physician (Fiellin et al., 2001). The effectiveness of methadone treatment is improved if a high (80–100 milligram) dose is used as opposed to the more typical 40–50 milligram dose (Strain et al., 1999) and

if it is combined with regular psychological counseling (Ball & Ross, 1991). Drug treatment experts generally believe that treatment with heroin substitutes is best conducted in the context of a supportive social interaction, not merely as a medical encounter (Lilly et al., 2000).

Since methadone does not provide a euphoric high, many people will return to heroin if it becomes available to them. In an effort to improve outcomes, researchers have tried adding contingency management to the usual treatment at a methadone clinic. In one randomized controlled trial (Pierce et al., 2006), people receiving methadone from a clinic could draw for prizes each time they submitted a (carefully supervised and obtained) urine sample that had no trace of illegal drugs or alcohol. Prizes ranged from praise to televisions. People who were in the contingency group were more likely to remain drug-free than those people who received only usual care from the methadone clinic. Of course, it remains to be seen whether such abstinence gains can be maintained after treatment ends and therapists are no longer providing such incentives.

Unfortunately, many people drop out of methadone programs, in part because of side effects such as insomnia, constipation, excessive sweating, and diminished sexual functioning. The stigma associated with going to methadone clinics is also linked to dropout rates, as illustrated in the clinical case of James described earlier. Age of entry into treatment may be important—the older the person, the greater the likelihood that he or she will stick with the treatment regimen (Friedmann, Lemon, & Stein, 2001).

In treatment with the opiate or heroin antagonists such as naloxone or naltrexone, people are first gradually weaned from heroin. Then they receive increasing dosages of one of these drugs, which prevents them from experiencing any high should they later take heroin. These drugs work because they have great affinity for the receptors to which opiates usually bind; their molecules occupy the receptors without stimulating them. This leaves heroin molecules with no place to go, and therefore heroin does not have its usual effect on the user. As with methadone, however, treatment with heroin antagonists involves frequent and regular visits to a clinic, which requires motivation. In addition, people do not lose the craving for heroin for some time. Both clinical effectiveness and treatment compliance can be increased by adding a contingency management component to the therapy (Carroll et al., 2001). Giving people vouchers that they can exchange for food and clothing in return for taking naltrexone and having drug-free urine samples markedly improves effectiveness.

Given the limitations of heroin substitutes such as methadone and other opiate antagonists, researchers have been searching for alternative medications. In 2003, a new prescription drug was introduced for the treatment of heroin dependence. Buprenorphine (Suboxone) is a medication that actually contains two agents: buprenorphine and naloxone. Buprenorphine is a partial opiate agonist, which means it does not have the same powerfully addicting properties as heroin, which is a full agonist. Naloxone is one of the opiate antagonists described above. This unique combination in Suboxone does not produce an intense high, is only mildly addictive, and lasts for as long as 3 days. Heroin users do not need to go to a clinic to receive this medication since it can be prescribed to individual people. Thus, this treatment avoids the stigma associated with visiting methadone clinics. Suboxone is effective at relieving withdrawal symptoms, and because it lasts longer than methadone, researchers are hopeful that relapse will be less likely. Still, some users may miss the more euphoric high associated with heroin, thus hastening a relapse.

Drug replacement does not appear to be an effective treatment for cocaine abuse and dependence. A meta-analysis of nine randomized controlled clinical trials of stimulant medication as a treatment for cocaine abuse revealed little evidence that this type of medication is effective (Castells et al., 2007). Two double-blind experiments found poor results for the antidepressant desipramine (Norpramine) (Arndt et al., 1992; Kosten et al., 1992). Researchers are also working on a possible vaccine to help stave off the cravings for cocaine. The vaccine contains tiny amounts of cocaine attached to otherwise harmless pathogens. The body's immune system responds to this invasion by developing antibodies that then squelch the cocaine. It is hoped that with repeated exposure, the antibodies will be able to keep a good deal of the cocaine from reaching the brain.

Developing effective treatments for methamphetamine dependence remains a challenge for the field. People like Anton, described in the clinical case earlier, do not have many places to

turn for treatment. The largest effort to date is a randomized controlled clinical trial conducted across eight different sites referred to as the Methamphetamine Treatment Project (Rawson et al., 2004). This study compared a multifaceted treatment called Matrix with treatment as usual. The Matrix treatment consisted of 16 cognitive behavior therapy group sessions, 12 family education sessions, 4 individual therapy sessions, and 4 social support group sessions. Treatment as usual (TAU) consisted of the best available treatment currently offered at the eight outpatient clinics. This varied quite a bit across the sites, with some offering individual counseling and others offering group counseling; some offering 4 weeks of treatment, others offering 16 weeks. Results of the study are somewhat supportive of the Matrix treatment. Compared to those in TAU, those people receiving Matrix stayed in treatment longer and were less likely to use methamphetamine during treatment (confirmed with urine analysis). Unfortunately, at the end of treatment and at the 6-month follow-up, people who received Matrix were no less likely to have used methamphetamine than those in TAU. The good news is that all participants were less likely to use methamphetamine after 6 months, regardless of whether they received Matrix or TAU. Although these results are promising, additional work is clearly needed to develop effective treatments for methamphetamine abuse and dependence.

Quick Summary

Psychological treatments have not been all that effective for nicotine dependence. Scheduled smoking involves reducing nicotine intake gradually over a period of a few weeks, and it has shown some promise. Nicotine gum appears to be somewhat effective, though users can become dependent on the gum. Nicotine patches are more effective than placebo patches, but 9 months after the treatment, abstinence differences between these receiving the drug and those receiving a placebo disappear. Adding buprioprion or therapy along with nicotine patches may be effective.

Detoxification is usually the first step in treatment for drug dependence. There is some evidence that CBT is an effective treatment for cocaine dependence. Motivational interviewing has shown promise for the treatment of alcohol and other drug dependence. Residential treatment homes have not been adequately evaluated for their efficacy, though they are a common form of treatment.

The use of heroin substitutes, such as methadone, is an effective treatment for heroin dependence. Methadone can only be administered in a special clinic, and there is stigma associated with this type of treatment. A newly approved prescription drug called buprenorphine can be taken at home. Treating methamphetamine dependence remains a challenge.

Check Your Knowledge 10.5

Match the treatment approach to the type of substance(s).

Treatment	Substance
1. Suboxone	**a.** alcohol
2. AA	**b.** heroin
3. couples therapy	**c.** cocaine
4. opiate antagonist	**d.** nicotine
5. antidepressant	**e.** methamphetamine
6. patch	
7. Matrix	

Prevention of Substance-Related Disorders

Many prevention efforts have been aimed at adolescents because substance abuse in adulthood often follows experimentation in the teens and earlier. Programs, usually conducted in schools, have been directed at enhancing the young adolescent's self-esteem, teaching social skills, and encouraging the young person to say no to peer pressure. The results are mixed (Hansen, 1993; Jansen et al., 1996). Self-esteem enhancement has not demonstrated its effectiveness. In contrast, social skills training and resistance training (learning to say no) have shown some pos-

itive results, particularly with girls. A highly publicized program, Project DARE (Drug Abuse Resistance Education), which combines effective education and resistance training and is delivered by police officers in fifth- and sixth-grade classrooms, has shown disappointing results (Clayton, Catterello, & Walden, 1991; Ringwalt, Ennett, & Holt, 1991).

Half of adult smokers began their habit before the age of 15, and nearly all before the age of 19 (USDHHS, 1998b). Thus, developing ways of discouraging young people from experimenting with tobacco has become a top priority among health researchers and politicians, with encouragement from the Surgeon General and funding from the National Cancer Institute, one of the National Institutes of Health. The American Legacy Foundation is an organization developed to prevent smoking among young people, and this organization was funded in part from the settlement that followed this class action lawsuit against tobacco companies in 1999.

The measures that hold promise for persuading young people to resist smoking may also be useful in dissuading them from trying illicit drugs and alcohol. Brief family interventions show such promise. In Iowa, the Iowa Strengthening Families Program and the five-session Preparing for the Drug Free Years Program have been found to forestall the onset of nicotine and alcohol use among teens (Spoth et al., 2004). For adolescents, family treatments may also have preventative effects. Research has shown that two different brief family interventions were associated with less initiation of alcohol use among teens (Spoth, Guyll, & Day, 2002). Other evidence suggests that the longer alcohol use is delayed, the less likely alcohol dependence will develop (Grant & Dawson, 1997), suggesting that preventive interventions can play a big role in keeping the prevalence of alcohol dependence down.

These programs target families with early adolescents and include skills-based training in risk and protective factors linked to substance abuse.

Statewide comprehensive tobacco control programs, which include increasing taxes on cigarettes, restricting tobacco advertising, conducting public education campaigns, and creating smoke-free environments, appear to be an effective strategy for reducing teenage smoking (Wakefield & Chaloupka, 2000). In addition, recent years have seen scores of school-based programs aimed at preventing young people from starting to use tobacco. By and large, such programs have succeeded in delaying the onset of smoking (Sussman et al., 1995). These programs share some common components, not all of them shown to be effective (Evans, 2001; Hansen, 1992; Sussman, 1996):

- *Peer-pressure resistance training*. Students learn about the nature of peer pressure and ways to say no. Overall, programs based on peer-pressure resistance training appear to be effective in reducing the onset and level of tobacco use, as well as illegal drug use, in young people (Tobler et al., 2000).
- *Correction of beliefs and expectations*. Many young people believe that cigarette smoking is more prevalent (and by implication, more okay) than it actually is. Changing beliefs about the prevalence of smoking has been shown to be an effective strategy, perhaps because young people are so sensitive to what others their age do and believe. Establishing that it is not standard behavior to smoke cigarettes (or drink alcohol or use marijuana) appears to be significantly more effective than resistance training (Hansen & Graham, 1991).
- *Inoculation against mass media messages*. Some prevention programs try to counter the positive images of smokers that have been put forth in the media (e.g., the Joe Camel ads mentioned earlier). Sophisticated mass media campaigns, similar to the ones that have made tobacco a profitable consumer product, can be successful in discouraging smoking. For example, the *truth* campaign, instituted by the American Legacy Foundation, developed websites (www.thetruth.com and www.fairenough.com) and radio and television ads to tell youth about the health and social consequences of smoking and the ways in which the tobacco industry targets them so that they can make informed choices about whether to smoke. This campaign has been well received among young people, and one study found that awareness and agreement with the *truth* messages were associated with less smoking among teens (Niederdeppe, Farrelly, & Haviland, 2004). These findings are particularly encouraging since we know that teenagers' receptivity to tobacco marketing is strongly related to whether or not they will actually smoke (Unger et al., 2001).
- *Peer leadership*. Most smoking and other drug prevention programs involve peers of recognized status, which adds to the impact of the messages being conveyed.

Summary

Clinical Descriptions

- DSM-IV-TR distinguishes between substance dependence and substance abuse. Dependence refers to a pattern of substance use and consequent serious psychological and physical impairments, often including tolerance and withdrawal. In substance abuse, drug use leads to failure to meet obligations and to interpersonal and legal problems.
- Alcohol has a variety of short-term and long-term effects on human beings, ranging from poor judgment and impaired motor coordination to chronic health problems.
- People can become dependent on nicotine, most often via smoking cigarettes. Despite somberly phrased warnings from public health officials, it continues to be used. Medical problems associated with long-term cigarette smoking include many cancers, emphysema, and cardiovascular disease. Moreover, the health hazards of smoking are not restricted to those who smoke, for secondhand (environmental) smoke can also cause lung damage and other problems.
- When used regularly, marijuana can damage the lungs and cardiovascular system and lead to cognitive impairments. Tolerance to marijuana can develop. Ironically, just as the possible dangers of marijuana began to be uncovered, it was found to have therapeutic effects, easing the nausea of people undergoing chemotherapy and easing discomfort associated with AIDS.
- Opiates slow the activities of the body and, in moderate doses, are used to relieve pain and induce sleep. Heroin has been a focus of concern because usage is up and stronger varieties have become available. Another group is the synthetic sedatives and tranquilizers. Barbiturates are particularly lethal when taken with alcohol.
- Stimulants, which include amphetamines and cocaine, act on the brain and the sympathetic nervous system to increase alertness and motor activity. Tolerance and withdrawal are associated with all these drugs. Abuse of methamphetamine, a derivative of amphetamine, has risen dramatically since the 1990s.
- The hallucinogens—LSD, mescaline, and psilocybin—alter or expand consciousness. Use of the hallucinogen-like drug Ecstasy has dramatically risen, and it is also considered a threat to health. PCP use often leads to violence.

Etiology

- Several factors are related to the etiology of substance abuse and dependence. Neurobiological factors, most notably a genetic predisposition or diathesis and the brain's reward pathways, appear to play a role in the use of some substances. Many substances are used to alter mood (e.g., to reduce tension or increase positive affect), and people with certain personality traits, such as those high in negative affect or constraint, are especially likely to use drugs. Cognitive variables, such as the expectation that the drug will yield positive effects, are also important. Finally, sociocultural variables, such as attitudes toward the substance, peer pressure, and how the substance is portrayed by the media, are all related to how frequently a substance is used.

Treatment

- Treatments of all kinds have been used to help people refrain from the use of both legal drugs (e.g., alcohol and nicotine) and illegal drugs (e.g., heroin and cocaine). Biological treatments have attempted to release users from their dependency, often by substituting another drug. Some benefits have been observed for treatments using such drugs as clonidine, naltrexone, and methadone. Nicotine replacement via gum, patches, or inhalers has met with some success in reducing cigarette smoking. None of these approaches appears to lead to enduring change, however, unless accompanied by psychological treatments with such goals as helping people resist pressures to indulge, cope with normal life stress, control emotions without relying on chemicals, and make use of social supports, such as Alcoholics Anonymous.
- Since it is far easier never to begin using drugs than to stop using them, considerable effort has been expended to prevent substance abuse by implementing educational and social programs to equip young people to develop their lives without a reliance on drugs.

Answers to Check Your Knowledge Questions

10.1 1. F; 2. T; 3. T
10.2 1. lung, larynx, esophagus, pancreas, bladder, cervix, stomach; 2. short-term, long-term; 3. pain relief, reduction of nausea, increased appetite, relief from the discomfort from AIDS
10.3 1. F; 2. F; 3. F; 4. T
10.4 1. b; 2. c; 3. a
10.5 1. b; 2. a; 3. a; 4. b; 5. a, c, d; 6. d; 7. e

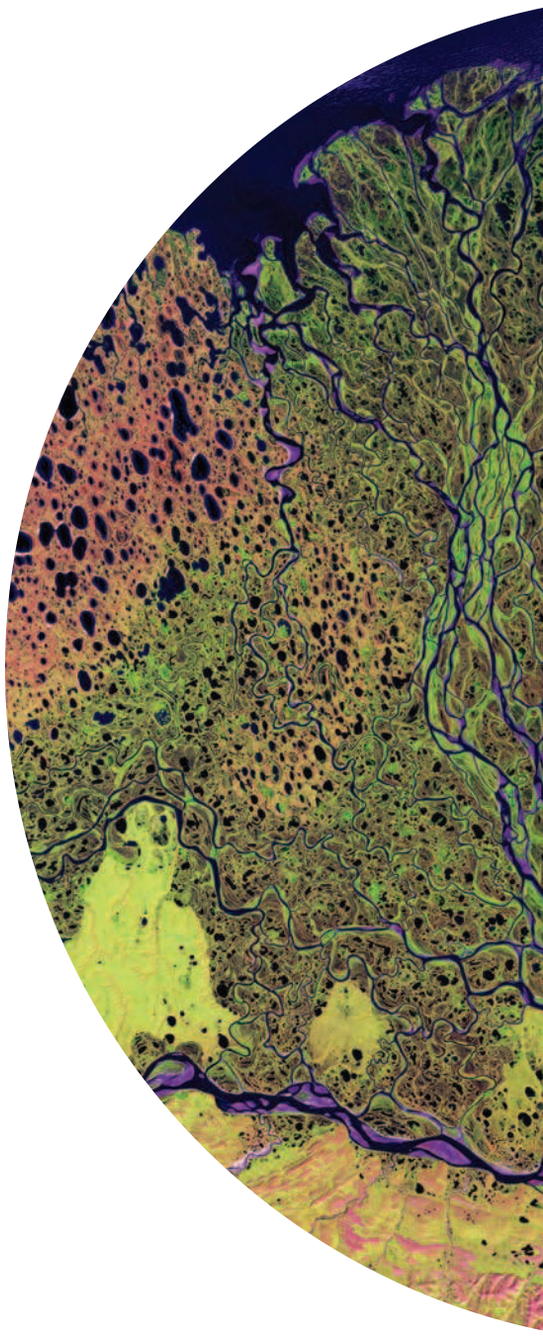
Key Terms

addiction
amphetamines
Antabuse
barbiturates
caffeine
cocaine
controlled drinking
crack
cross-dependent
delirium tremens (DTs)
detoxification
Ecstasy
fetal alcohol syndrome (FAS)
flashback
hallucinogen
hashish
heroin
hydrocodone
LSD
marijuana
MDA
MDMA
mescaline
methadone
methamphetamine
morphine
nicotine
nitrous oxide
opiates
opium
oxycodone
PCP
polydrug abuse
psilocybin
secondhand smoke
stimulants
substance abuse
substance dependence
substance-related disorders
tolerance
withdrawal

11 Schizophrenia

LEARNING GOALS

1. Be able to describe the clinical symptoms of schizophrenia, including positive, negative, and disorganized symptoms.
2. Be able to differentiate the genetic factors, both behavioral and molecular, in the etiology of schizophrenia.
3. Be able to discuss how the brain has been implicated in schizophrenia.
4. Be able to describe the role of stress and other psychosocial factors in the etiology and relapse of schizophrenia.
5. Be able to distinguish the medication treatments and psychological treatments for schizophrenia.



All of a sudden things weren't going so well. I began to lose control of my life and, most of all, myself. I couldn't concentrate on my schoolwork, I couldn't sleep, and when I did sleep, I had dreams about dying. I was afraid to go to class, imagined that people were talking about me, and on top of that I heard voices. I called my mother in Pittsburgh and asked for her advice. She told me to move off campus into an apartment with my sister.

After I moved in with my sister, things got worse. I was afraid to go outside and when I looked out of the window, it seemed that everyone outside was yelling, "Kill her, kill her." My sister forced me to go to school. I would go out of the house until I knew she had gone to work; then I would return home. Things continued to get worse. I imagined that I had a foul body odor and I sometimes took up to 6 showers a day. I recall going to the grocery store one day, and I imagined that the people in the store were saying, "Get saved, Jesus is the answer." Things worsened—I couldn't remember a thing. I had a notebook full of reminders telling me what to do on that particular day. I couldn't remember my schoolwork, and I would study from 6:00 P.M. until 4:00 A.M. but never had the courage to go to class on the following day. I tried to tell my sister about it, but she didn't understand. She suggested that I see a psychiatrist, but I was afraid to go out of the house to see him.

One day I decided that I couldn't take this trauma anymore, so I took an overdose of 35 Darvon pills. At the same moment, a voice inside me said, "What did you do that for? Now you won't go to heaven." At that instant, I realized that I didn't really want to die. I wanted to live, and I was afraid. I got on the phone and called the psychiatrist whom my sister had recommended.

I told him I had taken an overdose of Darvon and that I was afraid. He told me to take a taxi to the hospital. When I arrived at the hospital, I began vomiting, but I didn't pass out. Somehow, I just couldn't accept the fact that I was really going to see a psychiatrist. I thought that psychiatrists were only for crazy people, and I definitely didn't think I was crazy. As a result, I did not admit myself right away. As a matter of fact, I left the hospital and ended up meeting my sister on the way home. She told me to turn right back around because I was definitely going to be admitted. We then called my mother, and she said she would fly down the following day. (quoted in O'Neal, 1984, pp. 109–110)

THE YOUNG WOMAN DESCRIBED in this case study was diagnosed with schizophrenia. **Schizophrenia** is a disorder characterized by disturbances in thought, emotion, and behavior—disordered thinking, in which ideas are not logically related; faulty perception and attention; a lack of emotional expressiveness or, at times, inappropriate expressions; and disturbances in movement and behavior, such as a disheveled appearance. People with schizophrenia may withdraw from other people and from everyday reality, often into a life of odd beliefs (delusions) and hallucinations. Given that schizophrenia is associated with such widespread disruptions in the person's life, we should not be surprised that it has been difficult to uncover the causes of the disorder and develop methods to treat it. We still have a long way to go before we fully understand the multiple factors that trigger schizophrenia and have treatments that are both effective and free of unpleasant side effects.

The symptoms of schizophrenia can make stable employment difficult, often leading to impoverishment and homelessness. Strange behavior and social skills deficits lead to loss of friends, a solitary existence, and sometimes ridicule and persecution. Substance abuse rates are high (Fowler et al., 1998), perhaps reflecting an attempt to achieve some relief from negative emotions (Blanchard et al., 1999). Little wonder, then, that the suicide rate among people with schizophrenia is high. Indeed, people with schizophrenia are 12 times more likely to die of suicide than people in the general population (Saha, Chant, & McGrath, 2007). The symptoms of schizophrenia also have a profound effect on the lives of families and friends. Delusions and hallucinations may cause considerable distress, compounded by the fact that hopes and dreams have been shattered.

Schizophrenia is one of the most severe disorders we will describe in this book. Its lifetime prevalence is slightly less than 1 percent, and it affects men slightly more often than women (Kirkbride et al., 2006; Walker et al., 2004). Schizophrenia is diagnosed more frequently among some groups, such as African Americans, though it remains unclear whether this reflects an actual difference among groups or bias among clinicians (Kirkbride et al., 2006; [U.S. Department of Health and Human Services (USDHHS), 2001a]. Schizophrenia sometimes begins in childhood, but it usually appears in late adolescence or early adulthood, and usually somewhat earlier in men than in women. People with schizophrenia typically have a number of acute episodes of their symptoms and less severe but still debilitating symptoms between episodes. Comorbid substance abuse occurs in about 50 percent of people with schizophrenia, and so it is a major problem (Kesten & Ziedonis, 1997). Not only are people with schizophrenia more likely to die from suicide than people in the general population, they are also more likely to die from any cause (Saha et al., 2007).

In this chapter, we first describe the clinical features of schizophrenia. Then we discuss the etiology of schizophrenia and treatments for the disorder.

Clinical Descriptions of Schizophrenia

The range of symptoms in the diagnosis of schizophrenia is extensive, although people with schizophrenia typically have only some of these problems at any given time. No single essential symptom must be present for a diagnosis of schizophrenia (see DSM-IV-TR criteria box in the margin). Thus, people with schizophrenia can differ from one another quite a bit.

About 30 years ago, symptoms were divided into two categories called positive and negative (Crow, 1980; Strauss, Carpenter, & Bartko, 1974). Subsequently, the original category of positive symptoms was divided into two categories—positive (hallucinations and delusions) and disorganized (disorganized speech and behavior) (Lenzenweger, Dworkin, & Wethington, 1991). The distinction between positive, negative, and disorganized symptoms has been very useful in research on etiology and treatment of schizophrenia—even more useful than the DSM-IV-TR subtypes that we describe later. Table 11.1 shows the symptoms that comprise these categories.

In the following sections, we describe in some detail the individual symptoms that make up the positive, negative, and disorganized categories. We also describe some symptoms that do not fit neatly into these three categories.

DSM-IV-TR Criteria for Schizophrenia

- Two or more of the following symptoms for a significant portion of time for at least 1 month: delusions, hallucinations, disorganized speech, disorganized or catatonic behavior, negative symptoms
- Social and occupational functioning have declined since onset
- Signs of disturbance for at least 6 months; at least 1 month duration for delusions, hallucinations, disorganized speech, disorganized or catatonic behavior; during the remaining time either negative symptoms or other symptoms in attenuated form

Positive Symptoms

Positive symptoms comprise excesses and distortions, such as hallucinations and delusions. For the most part, acute episodes of schizophrenia are characterized by positive symptoms.

Delusions No doubt all of us at one time or another have been concerned because we believed that others thought ill of us. Some of the time this belief may be justified. After all, who is universally loved? Consider, though, the anguish that you would feel if you were firmly convinced that many people did not like you—indeed, that they disliked you so much that they were plotting against you. Imagine that your persecutors have sophisticated listening devices that let them tune in on your most private conversations and gather evidence in a plot to discredit you. Those around you, including your loved ones, are unable to reassure you that people are not spying on you. Even your closest friends are gradually joining forces with your tormentor. Anxious and angry, you begin taking counteractions against the persecutors. You carefully check any new room you enter for listening devices. When you meet people for the first time, you question them at great length to determine whether they are part of the plot against you.

Such **delusions**, which are beliefs held contrary to reality and firmly held in spite of disconfirming evidence, are common positive symptoms of schizophrenia. Persecutory delusions such as those just described were found in 65 percent of a large, cross-national sample of people diagnosed with schizophrenia (Sartorius, Shapiro, & Jablonsky, 1974). Delusions may take several other forms as well, including the following:

- A person may believe that thoughts that are not his or her own have been placed in his or her mind by an external source; this is called *thought insertion*. For example, a woman may believe that the government has inserted a computer chip in her brain so that thoughts can be inserted into her head.
- A person may believe that his or her thoughts are broadcast or transmitted, so that others know what he or she is thinking; this is called *thought broadcasting*. When walking down the street, a man may look suspiciously at passersby, thinking that they are able to hear what he is thinking even though he is not saying anything out loud.

Table 11.1 Summary of the Major Symptom Domains in Schizophrenia

Positive Symptoms	Negative Symptoms	Disorganized Symptoms
Delusions, hallucinations	Avolition, alogia, anhedonia, flat affect, asociality	Disorganized behavior, disorganized speech

- A person may believe that his or her feelings or behaviors are controlled by an external force. For example, a person may believe that his or her behavior is being controlled by the radiofrequency (RF) waves emitted from cell phone towers.
- A person may believe that he or she is being persecuted by others. For example, a man may believe that his friends and neighbors are plotting together to get him arrested by the CIA because he can read signals from cloud formations about the government's plans.
- A person may have **grandiose delusions**, in which a person has an exaggerated sense of his or her own importance, power, knowledge, or identity. For example, a woman may believe that she can cause the wind to change direction just by moving her hands.
- A person may have **ideas of reference** in which he or she incorporates unimportant events within a delusional framework and reads personal significance into the trivial activities of others. For instance, people with this symptom might think that overheard segments of conversations are about them, that the frequent appearance of the same person on a street where they customarily walk means that they are being watched, and that what they see on television or read in magazines somehow refers to them.

Although delusions are found among more than half of people with schizophrenia, they are also found among people with other diagnoses, particularly bipolar disorder, depression with psychotic features, and delusional disorder.

Hallucinations and Other Disturbances of Perception People with schizophrenia frequently report that the world seems somehow different or even unreal to them. A patient may mention changes in how his or her body feels, or a person may become so depersonalized that his or her body feels as though it is a machine. As in the case at the beginning of this chapter, some people report difficulties in paying attention to what is happening around them:

> *I can't concentrate on television because I can't watch the screen and listen to what is being said at the same time. I can't seem to take in two things like this at the same time especially when one of them means watching and the other means listening. On the other hand I seem to be always taking in too much at the one time, and then I can't handle it and can't make sense of it. (quoted in McGhie & Chapman, 1961, p. 106)*

The most dramatic distortions of perception are **hallucinations**, sensory experiences in the absence of any relevant stimulation from the environment. They are more often auditory than visual; 74 percent of one sample of people with schizophrenia reported having auditory hallucinations (Sartorius et al., 1974). Like delusions, hallucinations can be very frightening experiences.

Some types of hallucinations are thought to be particularly important diagnostically because they occur more often in people with schizophrenia than in people with other psychotic disorders. For example, some people with schizophrenia report hearing their own thoughts spoken by another voice. Other people may claim that they hear voices arguing, and others hear voices commenting on their behavior. Many people with schizophrenia experience their hallucinations as frightening or annoying. In one study of nearly 200 people with schizophrenia, those who had hallucinations that were longer, louder, more frequent, and experienced in the third person found them unpleasant. Hallucinations that were believed to come from a known person were experienced more positively (Copolov, Mackinnon, & Trauer, 2004).

Some theorists propose that a person who has auditory hallucinations misattributes their own voice as being someone else's voice. Behavioral studies have shown that people with hallucinations are more likely to misattribute recordings of their own speech to a different source than are people without hallucinations or healthy controls (Allen et al., 2004). Neuroimaging studies have examined what happens in the brain during auditory hallucinations. For example, studies using fMRI have found greater activity in Broca's area, the productive language area of the brain, when people with schizophrenia report hearing voices (McGuire, Shah, & Murray, 1993). Why might people make this misattribution? There may be a problem in the connections between the frontal lobe areas that enable the production of speech and the temporal lobe areas that enable the understanding of speech. Studies using both psychophysiological (Ford et al., 2002) and brain imaging methods (McGuire, Silbersweig, & Frith 1996; Shergill et al., 2000) support this idea.

Negative Symptoms

The **negative symptoms** of schizophrenia consist of behavioral deficits; they include avolition, alogia, anhedonia, flat affect, and asociality (Kirkpatrick et al., 2006), all of which we describe below. These symptoms tend to endure beyond an acute episode and have profound effects on the lives of people with schizophrenia. They are also important prognostically; the presence of many negative symptoms is a strong predictor of a poor quality of life (e.g., occupational impairment, few friends) 2 years following hospitalization (Ho et al., 1998).

When assessing negative symptoms, it is important to distinguish among those that are truly symptoms of schizophrenia and those that are due to some other factor (Carpenter, Heinrichs, & Wagman, 1988). For example, flat affect (a lack of emotional expressiveness) can be a side effect of antipsychotic medication. Observing people over extended time periods is probably the only way to address this issue.

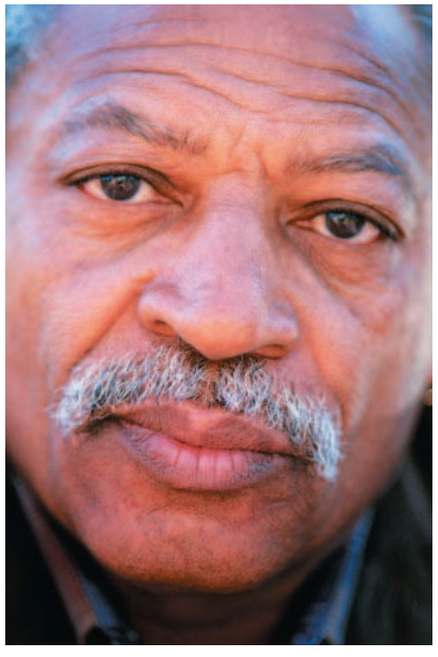
Avolition Apathy, or **avolition**, refers to a lack of motivation and a seeming absence of interest in or an inability to persist in what are usually routine activities, including work or school, self-care, hobbies, or social activities. For example, people with avolition may become inattentive to grooming and personal hygiene, with uncombed hair, dirty nails, unbrushed teeth, and disheveled clothes. They may have difficulty persisting at work, school, or household chores and may spend much of their time sitting around doing nothing.

Alogia **Alogia** refers to a significant reduction in the amount of speech. Simply put, people with this symptom do not talk much. A person may answer a question with one or two words and will not be likely to elaborate on an answer with additional detail. For example, if you ask a person with alogia to describe a happy life experience, the person might respond "getting married" and then fail to elaborate even when asked for additional information.

Anhedonia A loss of interest in or a reported lessening of the experience of pleasure is called **anhedonia**. There are two types of pleasure experiences in the anhedonia construct. The first, called **consummatory pleasure**, refers to the amount of pleasure experienced in-the-moment or in the presence of something pleasurable. For example, the amount of pleasure you experience as you are eating a good meal is consummatory pleasure. The second type of pleasure, called **anticipatory pleasure**, refers to the amount of expected or anticipated pleasure from future events or activities. For example, the amount of pleasure you expect to receive after graduating from college is anticipatory pleasure. People with schizophrenia appear to have a deficit in anticipatory pleasure but not consummatory pleasure (Gard et al., 2007; Kring, 1999). That is, when people with schizophrenia are asked about expected future situations or activities that are pleasurable for most people (e.g., good food, recreational activities, social interactions) on an anhedonia questionnaire, people with schizophrenia report that they derive less pleasure from these sorts of activities than people without schizophrenia (Gard et al., 2007; Horan, Kring, & Blanchard, 2006). However, when presented with actual pleasant activities, such as amusing films or tasty beverages, people with schizophrenia report experiencing as much pleasure as do people without schizophrenia (Gard et al., 2007). Thus, the anhedonia deficit in schizophrenia appears to be in anticipating pleasure, not experiencing pleasure in-the-moment or in the presence of pleasurable things.

Flat Affect **Flat affect** refers to a lack of outward expression of emotion. A person with this symptom may stare vacantly, the muscles of the face motionless, the eyes lifeless. When spoken to, the person may answer in a flat and toneless voice and not look at his or her conversational partner. Flat affect was found in 66 percent of a large sample of people with schizophrenia (Sartorius et al., 1974).

The concept of flat affect refers only to the outward expression of emotion, not to the patient's inner experience, which is not impoverished at all. In one study, people with schizophrenia and a control group of people without schizophrenia watched excerpts from films while their facial reactions and skin conductance were recorded (Kring & Neale, 1996). After each film clip, participants self-reported on the emotions the films had elicited. As expected, the people with schizophrenia were much less facially expressive than were the people without



People with schizophrenia who have flat affect may not outwardly show happiness, but they will feel it as strongly as people who smile. (Top: Blend Images/SuperStock,Inc.; bottom: ThinkStock/SUPERSTOCK)

schizophrenia, but they reported experiencing the same amount of emotion and were even more physiologically aroused (as measured by skin conductance). This same pattern—diminished expression and comparable experience in people with schizophrenia compared to people without schizophrenia—has been found in over 20 different studies (Kring & Moran, 2008).

Asociality Some people with schizophrenia have severe impairments in social relationships, referred to as **asociality**. They may have few friends, poor social skills, and very little interest in being with other people. They may not desire close relationships with family, friends, or romantic partners. Instead, they may wish to spend much of their time alone. When around others, people with this symptom may interact only superficially and briefly and appear aloof or indifferent to the social interaction.

Disorganized Symptoms

Disorganized symptoms include disorganized speech and disorganized behavior.

Disorganized Speech Also known as *formal thought disorder*, **disorganized speech** refers to problems in organizing ideas and in speaking so that a listener can understand. The following excerpt illustrates the incoherence sometimes found in the conversation of people with schizophrenia as an interviewer tries to ask John, a person with schizophrenia, several questions.

> ***Interviewer:*** *Have you been nervous or tense lately?*
> ***John:*** *No, I got a head of lettuce.*
> ***Interviewer:*** *You got a head of lettuce? I don't understand.*
> ***John:*** *Well, it's just a head of lettuce.*
> ***Interviewer:*** *Tell me about lettuce. What do you mean?*
> ***John:*** *Well . . . lettuce is a transformation of a dead cougar that suffered a relapse on the lion's toe. And he swallowed the lion and something happened. The . . . see, the . . . Gloria and Tommy, they're two heads and they're not whales. But they escaped with herds of vomit, and things like that.*
> ***Interviewer:*** *Who are Tommy and Gloria?*
> ***John:*** *Uh, . . . there's Joe DiMaggio, Tommy Henrich, Bill Dickey, Phil Rizzuto, John Esclavera, Del Crandell, Ted Williams, Mickey Mantle, Roy Mantle, Ray Mantle, Bob Chance . . .*
> ***Interviewer:*** *Who are they? Who are those people?*
> ***John:*** *Dead people . . . they want to be fucked . . . by this outlaw.*
> ***Interviewer:*** *What does all that mean?*
> ***John:*** *Well, you see, I have to leave the hospital. I'm supposed to have an operation on my legs, you know. And it comes to be pretty sickly that I don't want to keep my legs. That's why I wish I could have an operation.*
> ***Interviewer:*** *You want to have your legs taken off?*
> ***John:*** *It's possible, you know.*
> ***Interviewer:*** *Why would you want to do that?*
> ***John:*** *I didn't have any legs to begin with. So I would imagine that if I was a fast runner, I'd be scared to be a wife, because I had a splinter inside of my head of lettuce. (Neale & Oltmanns, 1980, pp. 103–104)*

Although John may make repeated references to central ideas or themes, the images and fragments of thought are not connected; it is difficult to understand what he is trying to tell the interviewer.

Speech may also be disorganized by what are called **loose associations**, or **derailment**, in which case the person may be more successful in communicating with a listener but has difficulty sticking to one topic. Steve Lopez, a reporter for the *Los Angeles Times*, befriended a man with schizophrenia named Nathanial in the LA area who was a gifted musician (and also homeless). Lopez wrote about their friendship in the book *The Soloist* (Lopez, 2008). Nathanial often exhibited loose associations. For example, in response to a question about Beethoven, Nathanial replied:

> *Cleveland doesn't have the Beethoven statue. That's a military-oriented city, occupied, preoccupied, with all the military figures of American history, the great soldiers and generals, but you don't see the musicians on parade, although you do have Severance Hall, Cleveland Music School Settlement, Ohio*

University Bobcats, Buckeyes of Ohio State. All the great soldiers are there from the United States Military, World War Two, Korean War, whereas in Los Angeles you have the LAPD, Los Angeles County Jail, Los Angeles Times, Mr. Steve Lopez. That's an army, right? (quoted in Lopez, 2008, pp. 23–24)

As this quote illustrates, a person with this symptom seems to drift off on a train of associations evoked by an idea from the past. People with schizophrenia have also described what it is like to experience disorganized speech.

My thoughts get all jumbled up. I start thinking or talking about something but I never get there. Instead, I wander off in the wrong direction and get caught up with all sorts of different things that may be connected with things I want to say but in a way I can't explain. People listening to me get more lost than I do. My trouble is that I've got too many thoughts. You might think about something, let's say that ashtray and just think, oh yes, that's for putting my cigarette in, but I would think of it and then I would think of a dozen different things connected with it at the same time. (quoted in McGhie & Chapman, 1961, p. 108)

It would seem logical to expect disorganized speech to be associated with problems in language production, but this does not appear to be the case. Instead, disorganized speech is associated with problems in what is called *executive functioning*—problem solving, planning, and making associations between thinking and feeling. Disorganized speech is also related to the ability to perceive semantic information (i.e., the meaning of words) (Kerns & Berenbaum, 2002, 2003)

Disorganized Behavior **Disorganized behavior** takes many forms. People with this symptom may go into inexplicable bouts of agitation, dress in unusual clothes, act in a childlike or silly manner, hoard food, or collect garbage. They seem to lose the ability to organize their behavior and make it conform to community standards. They also have difficulty performing the tasks of everyday living.

Other Symptoms

Two other symptoms of schizophrenia do not fit neatly into the categories we have just presented: catatonia and inappropriate affect.

Catatonia Several motor abnormalities define **catatonia**. People with this symptom may gesture repeatedly, using peculiar and sometimes complex sequences of finger, hand, and arm movements, which often seem to be purposeful. Some people manifest an unusual increase in their overall level of activity, including much excitement, wild flailing of the limbs, and great expenditure of energy similar to that seen in mania. At the other end of the spectrum is **catatonic immobility**: people adopt unusual postures and maintain them for very long periods of time. Catatonia can also involve *waxy flexibility*—another person can move the patient's limbs into positions that the patient will then maintain for long periods of time.

Catatonia is seldom seen today, perhaps because medications work effectively on these disturbed motor processes. Alternatively, Boyle (1991) has argued that the apparent high prevalence of catatonia during the early part of the twentieth century reflected misdiagnosis. Specifically, the similarities between encephalitis lethargica (sleeping sickness) and catatonic schizophrenia suggest that many cases of the former were misdiagnosed as the latter. This idea was portrayed in the film *Awakenings*, which was based on the career and writings of Oliver Sacks. See Focus on Discovery 11.1 for more on the history of schizophrenia and its symptoms.

An 1894 photo showing a woman with catatonic schizophrenia. She held this unusual posture for long periods of time. (The Burns Archive.)

Inappropriate Affect Some people with schizophrenia show **inappropriate affect**—their emotional responses are out of context. Such a person may laugh on hearing that his or her mother just died or become enraged when asked a simple question about how a new jacket fits. People with this symptom are likely to shift rapidly from one emotional state to another for no discernible reason. Like catatonia, this symptom is rare, and it is relatively specific to schizophrenia.

FOCUS ON DISCOVERY 11.1

History of the Concept of Schizophrenia

Two European psychiatrists, Emil Kraepelin and Eugen Bleuler, initially formulated the concept of schizophrenia. Kraepelin first described **dementia praecox,** his term for what we now call schizophrenia, in 1898. Dementia praecox included several diagnostic subtypes—dementia paranoides, catatonia, and hebephrenia—that had been regarded as distinct entities by clinicians in the previous few decades. Although these disorders were symptomatically diverse, Kraepelin believed that they shared a common core, and the term **dementia praecox** reflected what he believed was that core—an early onset (praecox) and a progressive, inevitable intellectual deterioration (dementia). The dementia in dementia praecox is not the same as the dementias we discuss in the chapter on late life (Chapter 15), which are defined principally by severe memory impairments. Kraepelin's term referred to a general "mental enfeeblement."

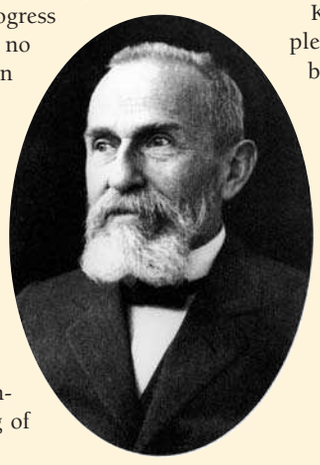
Emil Kraepelin (1856–1926), German psychiatrist, articulated descriptions of schizophrenia (then called dementia praecox) that have proved remarkably durable in the light of contemporary research. (Hueton Archive Getty Images.)

Bleuler broke with Kraepelin's description on two major points: he believed that the disorder did not necessarily have an early onset, and he believed that it did not inevitably progress toward dementia. Thus the label "dementia praecox" was no longer appropriate, and in 1908 Bleuler proposed his own term, *schizophrenia*, from the Greek words *schizein* ("to split"), and *phren* ("mind"), capturing what he viewed as the essential nature of the condition.

With age of onset and deteriorating course no longer considered defining features of the disorder, Bleuler faced a conceptual problem. The symptoms of schizophrenia could vary widely among people, so he had to provide some justification for putting them into a single diagnostic category. That is, he needed to specify some common denominator, or essential property, that would link the various disturbances. The metaphorical concept that he adopted for this purpose was the "breaking of associative threads."

For Bleuler, associative threads joined not only words but also thoughts. Thus, goal-directed, efficient thinking and communication were possible only when these hypothetical structures were intact. The notion that associative threads were disrupted in people with schizophrenia could then be used to account for the range of other disturbances. Bleuler viewed attentional difficulties, for example, as resulting from a loss of purposeful direction in thought, in turn causing passive responses to objects and people in the immediate surroundings.

Kraepelin had recognized that a small percentage of people with symptoms of dementia praecox did not deteriorate, but he preferred to limit this diagnostic category to people who had a poor prognosis. Bleuler's work, in contrast, led to a broader concept of the disorder. He diagnosed some people with a good prognosis as having schizophrenia, and he also diagnosed schizophrenia in many people who would have received different diagnoses from other clinicians.



Eugen Bleuler (1857–1939), Swiss psychiatrist, contributed to our conceptions of schizophrenia and coined the term. (Corbis Bettmann.)

Schizophrenia in DSM-IV-TR

DSM-IV-TR requires that the symptoms last for at least 6 months for the diagnosis. The 6-month period must include at least 1 month of an acute episode, or active phase, defined by the presence of at least two of the following: delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, and negative symptoms. (Only one of these symptoms is required if the delusions are bizarre or if the hallucinations consist of voices commenting or arguing.) The remaining time required for the diagnosis can occur either before the active phase or after the active phase. This time criterion eliminates people who have a brief psychotic episode and then recover quickly.

Are the DSM-IV-TR diagnostic criteria applicable across cultures? Evidence bearing on this question was collected in a World Health Organization study of both industrialized and developing countries (Jablonsky et al., 1994). The symptomatic criteria held up well cross-culturally. However, for reasons not yet fully understood, people with schizophrenia in developing countries have a more acute onset and a more favorable course than those in industrialized societies (Susser & Wanderling, 1994).

Table 11.2 Key Features of DSM-IV-TR Subtypes of Schizophrenia

Disorganized schizophrenia The subtype called **disorganized schizophrenia** in DSM-IV-TR is manifested by speech that is disorganized and difficult for a listener to follow. The person may have flat affect or experience constant shifts of emotion, breaking into inexplicable fits of laughter and crying. The person's behavior is also generally disorganized and not goal directed.

Catatonic schizophrenia The most obvious symptoms of **catatonic schizophrenia** are the catatonic symptoms. A person may alternate between catatonic immobility and wild excitement, but one of these symptoms may predominate. Negative symptoms are also likely present.

Paranoid schizophrenia The key to the diagnosis of **paranoid schizophrenia** is the presence of prominent delusions, such as delusions of persecution, grandiose delusions, or ideas of reference. Vivid auditory hallucinations may accompany the delusions. Speech is not disorganized, and flat affect is not typically present even though a person may be somewhat stilted, formal, and intense with others.

Undifferentiated schizophrenia The subtype of **undifferentiated schizophrenia** is applied to people who meet the diagnostic criteria for schizophrenia but not for any of the three main subtypes.

Residual schizophrenia The subtype of **residual schizophrenia** is used when a person no longer meets the full criteria for schizophrenia but still shows some signs of the illness.

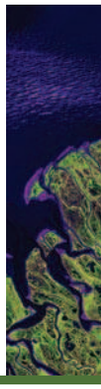
Table 11.2 presents the subtypes of schizophrenia in the DSM-IV-TR. Although the subtypes of schizophrenia in DSM-IV-TR form the basis of current diagnostic practices, their usefulness is often questioned. Actually, diagnosing the subtypes is extremely difficult, so diagnostic reliability is very low. Furthermore, the subtypes have little predictive validity; that is, the diagnosis of one or another type of schizophrenia provides little information helpful in either treating the disorder or predicting its course. There is also considerable overlap of symptoms among the subtypes. For example, people with all subtypes of schizophrenia may have delusions.

Other Psychotic Disorders in the DSM-IV-TR

Two brief psychotic disorders are **schizophreniform disorder** and **brief psychotic disorder.** The symptoms of schizophreniform disorder are the same as those of schizophrenia but last only from 1 to 6 months. Brief psychotic disorder lasts from 1 day to 1 month and is often brought on by extreme stress, such as bereavement. **Schizoaffective disorder** comprises a mixture of symptoms of schizophrenia and mood disorders.

A person with **delusional disorder** is troubled by persistent delusions of persecution or by delusional jealousy, the unfounded conviction that a spouse or lover is unfaithful. Other delusions seen in this disorder include delusions of being followed, delusions of erotomania (believing that one is loved by some other person, usually a complete stranger with a higher social status), and somatic delusions (believing that some internal organ is malfunctioning). Unlike the person with paranoid schizophrenia, the person with delusional disorder does not have hallucinations, and his or her delusions are less bizarre.

Quick Summary



Schizophrenia is a very heterogeneous disorder. It affects men slightly more than women and typically begins in late adolescence or early adulthood. Symptoms can be distinguished as positive, negative, and disorganized. Positive symptoms include hallucinations and delusions. Negative symptoms include avolition, alogia, flat affect, anhedonia, and asociality. Disorganized symptoms include disorganized speech and disorganized behavior. No one of these symptoms is critical for the diagnosis of schizophrenia. The DSM-IV-TR subtypes include catatonic, paranoid, disorganized, undifferentiated, and residual. Despite their presence in the DSM-IV-TR, they do not have a good deal of validity and are not that useful. Other psychotic disorders include schizophreniform disorder and brief psychotic disorder, which differ from schizophrenia in duration. Schizoaffective disorder involves symptoms of both schizophrenia and mood disorders. Delusional disorder involves delusions but no other symptoms of schizophrenia, and the delusions are less bizarre than those in schizophrenia.

Check Your Knowledge 11.1 (Answers are at the end of the chapter.)

List the symptom that each clinical vignette describes.

1. Charlie enjoyed going to movies. He particularly liked to see horror movies because they made him feel really scared. His sister was surprised to learn this, because when she went to movies with Charlie, he didn't gasp out loud or show fear on his face.
2. Marlene was convinced that Christian Bale was sending her messages. In his movie *The Dark Knight*, his battles with the Joker were a signal that he was prepared to fight for them to be together. That he signed autographs at his movie opening also told her that he was trying to get in touch with her.
3. Sophia didn't want to go out to dinner with her family. She reasoned that these dinners were always the same food and conversation, so why bother? Later in the week, her mother mentioned that Sophia was not doing much around the house. Sophia said that nothing she could think of to do would be fun.
4. Jevon was talking with his doctor about the side effects of his medication. He talked about having dry mouth and then immediately began talking about cottonmouth snakes and jungle safaris and how hiking was good for your health but that Barack Obama was in better shape than George Bush.

Etiology of Schizophrenia

What can explain the scattering and disconnection of thoughts, the lack of emotion expression, the odd delusions, and bewildering hallucinations of people with schizophrenia? Broad theoretical perspectives, such as psychoanalysis, have not had much of an impact in research on schizophrenia. Other perspectives, however, have yielded many interesting research results, as we discuss in the following sections.

Genetic Factors

A good deal of research supports the idea that schizophrenia has a genetic component, as we discuss in the sections below on behavior genetics and molecular genetics research. The evidence is somewhat more convincing from behavior genetics studies, largely because they have been well replicated. Many molecular genetics studies are still in need of replication to bolster confidence in their findings.

Behavior Genetics Research The family, twin, and adoption methods employed in this research, as in other behavior genetics research projects, have led researchers to conclude that a predisposition to schizophrenia is inherited. It should be noted that many genetic studies of schizophrenia were conducted when the definition of schizophrenia was considerably broader than it is now. However, genetic investigators collected extensive descriptive data on their samples, allowing the results to be reanalyzed later using newer diagnostic criteria.

Family Studies Table 11.3 presents a summary of the risk for schizophrenia in various relatives of index cases with schizophrenia. (In evaluating the figures, bear in mind that the risk for schizophrenia in the general population is a little less than 1 percent.) Quite clearly, relatives of people with schizophrenia are at increased risk, and the risk increases as the genetic relationship between proband and relative becomes closer (Kendler, Karkowski-Shuman, & Walsh, 1996).

Furthermore, people who have schizophrenia in their family histories have more negative symptoms than those whose families are free of schizophrenia (Malaspina et al., 2000), suggesting that negative symptoms may have a stronger genetic component. The relatives of people with schizophrenia are also at increased risk for other disorders (e.g., schizotypal personality disorder) that are thought to be less severe forms of schizophrenia (Kendler, Neale, & Walsh, 1995).

The results of family studies thus support the notion that a predisposition for schizophrenia can be transmitted genetically. Yet the relatives of a person with schizophrenia share not only genes but also common experiences. Recall from Chapter 2 that genes do much of their work via the environment. Therefore, the influence of the environment cannot be discounted in explaining the higher risks among relatives.

Table 11.3 Summary of Major Family and Twin Studies of the Genetics of Schizophrenia

Relation to Proband	Percentage with Schizophrenia
Spouse	1.00
Grandchildren	2.84
Nieces/nephews	2.65
Children	9.35
Siblings	7.30
DZ twins	12.08
MZ twins	44.30

Source: After Gottesman, McGuffin, & Farmer (1987).

Twin Studies Table 11.3 also shows the risk for identical (MZ) and fraternal (DZ) twins of people with schizophrenia. The risk for MZ twins (44.3 percent), although greater than that for DZ twins (12.08 percent), is still much less than 100 percent. Similar results have been obtained in more recent studies (Cannon et al., 1998; Cardno et al., 1999). The less-than-100-percent concordance in MZ twins is important: if genetic transmission alone accounted for schizophrenia and one twin had schizophrenia, the other twin would also have schizophrenia because MZ twins are genetically identical. The importance of genetic factors is supported, however, by the fact that the risk among MZ twins increases when the twin with schizophrenia is more severely ill (Gottesman & Shields, 1972). As with the family studies, twin study research suggests that negative symptoms may have a stronger genetic component than do positive symptoms (Dworkin & Lenzenweger, 1984; Dworkin, Lenzenweger, & Moldin, 1987).

Childhood photograph of the Genain quadruplets. Each of the girls developed schizophrenia later in life. (Courtesy of Monte S. Buchsbaum, M.D., Mt. Sinai School of Medicine, New York, NY.)

As with family studies, of course, there is a critical problem in interpreting the results of twin studies. A common environment rather than common genetic factors could account for some portion of the increased risk. By common environment, we mean not only similar shared and nonshared environmental factors, such as child-rearing practices or peer relationships, but also a more similar intrauterine environment, for MZ twins are more likely than DZ twins to share a single blood supply.

A clever analysis supporting a genetic interpretation of the high risk found for identical twins was performed by Fischer (1971). She reasoned that if these rates indeed reflected a genetic effect, the twins without schizophrenia should be at high risk for the disorder. These MZ twins without schizophrenia would presumably have the genotype for schizophrenia, even though it was not expressed behaviorally, and thus might pass along an increased risk for the disorder to their children. In agreement with this line of reasoning, the rate of schizophrenia and schizophrenia-like psychoses in the children of the MZ twins without schizophrenia was 9.4 percent, while the rate among the children of the twins with schizophrenia was only slightly and nonsignificantly higher, 12.3 percent. Both rates are substantially higher than the 1 percent prevalence found in the general population, and this lends further support to the importance of genetic factors in schizophrenia.

Adoption Studies The study of children whose mothers had schizophrenia but who were reared from early infancy by adoptive parents without schizophrenia has provided clearer confirmation of the role of genes in schizophrenia because such studies eliminate the possible effects of being reared in an environment where a parent has schizophrenia. In a now-classic study, Heston (1966) followed up 47 people born between 1915 and 1945 to women with schizophrenia. The infants were separated from their mothers at birth and raised by foster or adoptive parents. Fifty control participants were selected from the same adoption agency that had placed the children of the women with schizophrenia.

The follow-up assessment revealed that none of the controls was diagnosed with schizophrenia, versus 16.6 percent (five) of the offspring of women with schizophrenia. Children of women with schizophrenia were also more likely to be diagnosed with mental retardation, psychopathy, and neuroses (the older term for anxiety) (Table 11.4). This study provides strong support for the importance of genetic factors in the development of schizophrenia.

Another large study of adopted offspring of mothers with schizophrenia found similar results. In this study, the risk for developing schizophrenia among the 164 adoptees who had a biological parent with schizophrenia was 8.1 percent; the risk for the 197 control adoptees who did not have a biological parent with schizophrenia was significantly lower at 2.3 percent. The risk for other disorders, such as schizoaffective, schizophreniform, and schizotypal personality disorder, was also greater among the adoptees with a biological parent with schizophrenia than among the control adoptees (Tienari et al., 2000).

A similar study was carried out in Denmark (Kety et al., 1976, 1994), where researchers examined the records of children who had been adopted at a young age. All adoptees who had

Table 11.4 Characteristics of Participants Separated from Their Mothers in Early Infancy

Characteristic	Offspring of Mothers with Schizophrenia	Control Offspring
Number of participants	47	50
Mean age at follow-up	35.8	36.3
Overall ratings of disability (low score indicates more pathology)	65.2	80.1
Number diagnosed with schizophrenia	5	0
Number diagnosed with mental retardation	4	0
Number diagnosed with psychopathy	9	2
Number diagnosed with neurosis	13	7

Source: From Heston (1966).

later been admitted to a psychiatric facility and diagnosed with schizophrenia were selected as the index cases. From the remaining cases, the investigators chose a control group of people who had no psychiatric history and who were matched to the index group on such variables as sex and age. Both the adoptive and the biological parents and the siblings and half-siblings of the two groups were then identified, and a search was made to determine who among them had a psychiatric history. As might be expected if genetic factors figure in schizophrenia, the biological relatives of the group with schizophrenia were diagnosed with schizophrenia more often than were members of the general population; the adoptive relatives were not.

Molecular Genetics Research Knowing that schizophrenia has a genetic component is in many ways just the starting point for research. Understanding exactly what constitutes the genetic predisposition is the challenge faced by molecular genetics researchers. As with nearly all of the disorders we cover in this book, it does not appear that the predisposition for schizophrenia is transmitted by a single gene.

The results of linkage analysis studies (see p.108), in which family pedigrees are studied to try to determine on which chromosome or chromosomes the schizophrenia genes are located, have been inconsistent. Studies have reported positive findings for linkage at locations on a number of different chromosomes, including 1, 2, 5, 6, 8, 10, 11, 13, 15, 18, and 22 (Faraone, Taylor, & Tsuang, 2002: Lewis et al., 2003). Although finding so many chromosomal locations to be possibly connected with schizophrenia is consistent with the idea that multiple genes are involved, the results of these studies are simply too varied to justify any firm conclusions. A meta-analysis of 20 genome-wide studies of schizophrenia found some support for linkage on chromosome 2 (Lewis et al., 2003). However, such results have a history of not being replicated (DeLisi et al., 2002), possibly because these types of studies work better for conditions with a predisposition that is transmitted by a single gene or a small set of genes. It is also highly likely that schizophrenia is genetically heterogeneous—that is, the genetic diathesis may vary from case to case—mirroring the fact, noted earlier, that schizophrenia is certainly symptomatically heterogeneous. As with the case of any gene or genes, they do their work via the environment, so gene–environment interaction studies are likely to help more clearly pinpoint the nature of the genetic contribution to schizophrenia (Walker & Tessner, 2008).

Association studies (see p. 109) have begun to focus on specific genes associated with schizophrenia. In an association study, the goal is to establish how often a specific gene and a particular phenotype co-occur. As with the linkage studies, positive findings are often followed by failures to replicate. For example, research was initially focused on genes associated with the dopamine D2 receptor because, as we discuss below, this receptor is associated with the positive effectiveness of some medications used to treat schizophrenia. Although there are some positive findings (Glatt, Faraone, & Tsuang, 2003), a number of other studies are negative (Owen, Williams, & O'Donovan, 2004). Other studies have found associations with the serotonin receptor 5HT2 gene, though its role appears to be very small (Lohmueller et al., 2003; J. Williams et al., 1997).

Two promising candidate genes have received some recent support from association studies (Owen et al., 2004). One, a gene called DTNBP1, encodes a protein called dysbindin that is expressed throughout the brain, but it is not yet clear what the function is of either the gene or the protein. However, it appears to impact the glutamate neurotransmitter system throughout the brain (MacDonald & Chafee, 2006), and five studies have replicated an association between DTNBP1 and schizophrenia. In addition, a postmortem study has shown that compared to people without schizophrenia, those with schizophrenia appear to have less dysbindin in a number of brain areas, including the frontal cortex, temporal cortex, hippocampus, and limbic system structures (Weickert et al., 2004). Another gene, NGR1, which has been linked to the neurotransmitter glutamate's NMDA (*N*-methyl-*D*-aspartate) receptor and is helpful with the process of myelination (see p. 36), has also been found to be associated with schizophrenia. Time will tell if these results can be replicated.

Another approach to research on specific genes that may improve our understanding of schizophrenia is association studies that examine the relationship between genes and cognitive functions among people without psychopathology. For example, some research has found that a gene called COMT is associated with executive functions that rely on the **prefrontal cortex** (reviewed by Goldberg & Weinberger, 2004). A number of studies have demonstrated that people with schizophrenia have deficits in executive functions, which include planning, working memory, and problem solving, and other studies have shown problems in the prefrontal cortex. A few association studies have implicated COMT in schizophrenia (Harrison & Weinberger, 2004; Owen et al., 2004). Another gene called BDNF has been studied and linked with cognitive function in people with and without schizophrenia. This gene has a polymorphism called Val66Met, where a person can have two Val alleles (Val/Val), two Met alleles (Met/Met), or one Val and one Met allele (Val/Met). In a large study of people with and without schizophrenia, verbal memory was better for people who had two Val alleles (Val/Val) compared to people who had either one or two Met alleles (Val/Met or Met/Met) (Ho et al., 2006).

Finally, newer techniques in molecular genetics that allow for the rapid scanning of a person's entire genome, a so-called genome-wide scan, have been applied to the study of schizophrenia. This technique allows researchers to identify rare mutations in genes rather than just known gene loci from previous linkage and association studies. Mutations are changes in a gene that occur randomly and for unknown reasons. In one study, researchers identified over 50 such mutations that were three times more common among people with schizophrenia than in people without schizophrenia across two different samples of people (Walsh et al., 2008). Some of the identified gene mutations are known to be associated with other presumed risk factors in the etiology of schizophrenia, including the neurotransmitter glutamate (discussed below) and proteins that promote the proper placement of neurons in the brain during brain development. Although encouraging, these findings will need to be replicated. Furthermore, even though the identified mutations were more common in people with schizophrenia than people without schizophrenia, they were identified only in about 20 percent of the people with schizophrenia. Thus, other genetic factors await discovery in future studies.

This apparatus is used to assess a person's ability to track a moving target. This ability is impaired both in people with schizophrenia and in their relatives, suggesting that eye tracking is a genetic marker for the disorder. (Courtesy of Dr. William Iacono, University of Minnesota.)

Evaluation of the Genetic Research Research results indicate that genetic factors play an important role in the development of schizophrenia. Of particular importance, adoption studies that do a better job of separating genetic and environmental effects provide support for the heritability of schizophrenia.

Despite this evidence, we cannot conclude that schizophrenia is a disorder completely determined by genetic transmission, for we must always keep in mind the distinction between phenotype and genotype (see p. 30). Like other mental disorders, schizophrenia is defined by behavior; it is a phenotype, and thus it reflects the influence of both genes and environment. The diathesis–stress model introduced in Chapter 2 seems appropriate for guiding theory and research into the etiology of schizophrenia. Genetic factors can only predispose people to schizophrenia. Some kind of stress is required to cause this predisposition to be expressed as an observable disorder.

The genetic research in schizophrenia has some further limitations as well. First, as reviewed in the molecular genetics section above, it has not yet been possible to specify exactly how a predisposition for schizophrenia is transmitted. Second, the nature of the inherited diathesis remains unknown. What exactly is inherited that puts some people at risk for schizophrenia? One way of addressing this question is to study relatives of people with schizophrenia. Although not necessarily disordered, these people, who are at increased risk for schizophrenia, may reveal signs of the genetic predisposition. One area of research has been the study of how well the eyes track a moving target, such as a pendulum. People with schizophrenia do poorly on this task, as do about 50 percent of their first-degree relatives (Holzman, 1985). The importance of eye tracking is supported by data showing that it is influenced by genetic factors (Greenwood et al., 2007; Iacono et al., 1992). Deficient eye tracking may reflect a problem in several areas of the brain, including the frontal and temporal lobes as well as the cerebellum (Chen et al., 1999). We will soon see that these brain areas are thought to be very important in schizophrenia.

Despite the problems and loose ends, the results of genetics research represent an impressive body of evidence. The strong positive correlation between genetic relatedness and the prevalence of schizophrenia remains one of the strongest links in the chain of information about the causes of schizophrenia.

Neurotransmitters

Present research is examining several different neurotransmitters, such as norepinephrine, serotonin, and glutamate, to see what role they might play in the etiology of schizophrenia. The first neurotransmitter to receive substantial research attention was dopamine. We trace the history of this research here, highlighting how it has both helped and hindered efforts toward identifying causes and treatments for schizophrenia.

Dopamine Theory The theory that schizophrenia is related to excess activity of the neurotransmitter dopamine is based principally on the knowledge that drugs effective in treating schizophrenia reduce dopamine activity. Researchers noted that antipsychotic drugs, in addition to being useful in treating some symptoms of schizophrenia, produce side effects resembling the symptoms of Parkinson's disease. Parkinson's disease is known to be caused in part by low levels of dopamine in a particular nerve tract of the brain. It was subsequently confirmed that antipsychotic drugs fit into and thereby block a particular type of postsynaptic dopamine receptors, called D2 receptors. From this knowledge about the action of the drugs that help people with schizophrenia, it was natural to conjecture that schizophrenia resulted from excess activity in dopamine nerve tracts.

Further indirect support for this **dopamine theory** of schizophrenia came from the literature on *amphetamine psychosis*. Amphetamines can produce a state that closely resembles paranoid schizophrenia, and they can exacerbate the symptoms of people with schizophrenia (Angrist, Lee, & Gershon, 1974). The amphetamines cause the release of norepinephrine and dopamine into the synaptic cleft and prevent their inactivation. We can be relatively confident that the psychosis-inducing effects of amphetamines are a result of increasing activity of dopamine rather than of norepinephrine, because antipsychotics are effective in treating amphetamine psychosis.

Based on the evidence just reviewed, researchers at first assumed that schizophrenia was caused by an excess of dopamine. But as other studies progressed, this assumption did not gain support. For example, the major metabolite of dopamine, homovanillic acid (HVA), was not found in greater amounts in people with schizophrenia (Bowers, 1974).

Such evidence, plus improved technologies for studying neurotransmitters in humans, led researchers to propose excess numbers of dopamine receptors or oversensitive dopamine receptors, rather than a high level of dopamine, as factors in schizophrenia. Research on the antipsychotics' mode of action suggests that the dopamine receptors are a more likely locus of disorder than the level of dopamine itself. Some postmortem studies of brains of people with schizophrenia, as well as PET scans of people with schizophrenia, have revealed that dopamine receptors are greater in number or are hypersensitive in some people with schizophrenia (Hietala et al., 1994; Tune et al., 1993; Wong et al., 1986). Having too many dopamine receptors would be functionally akin to having an overactive dopamine system. The reason is that when dopamine

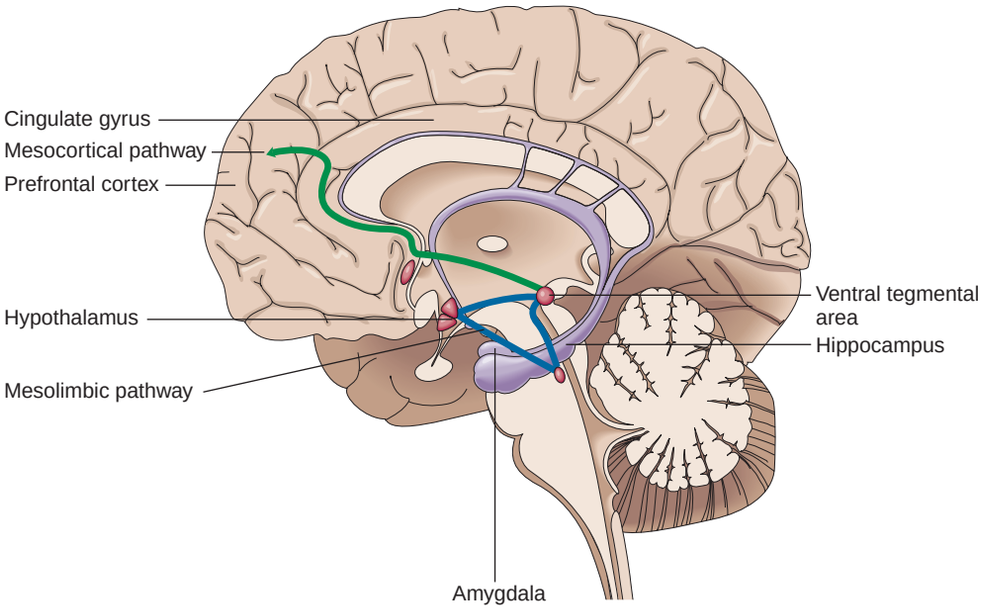


Figure 11.1 The brain and schizophrenia. The mesocortical pathway begins in the ventral tegmental area and projects to the prefrontal cortex. The mesolimbic pathway also begins in the ventral tegmental area but projects to the hypothalamus, amygdala, hippocampus, and nucleus accumbens.

(or any neurotransmitter) is released into the synapse, only some of it actually interacts with postsynaptic receptors. Having more receptors gives a greater opportunity for the dopamine that is released to stimulate a receptor, hence a greater opportunity for dopamine activity.

An excess of dopamine receptors may not be responsible for all the symptoms of schizophrenia; such an excess appears to be related mainly to positive symptoms. Amphetamines worsen positive symptoms. Antipsychotics lessen positive symptoms but have little or no effect on negative symptoms.

Subsequent developments in the dopamine theory (e.g., Davis et al., 1991) expanded its scope. The key change involved the recognition of differences among the neural pathways that use dopamine as a transmitter. The excess dopamine activity that is thought to be most relevant to schizophrenia is localized in the mesolimbic pathway (see Figure 11.1), and the therapeutic effects of antipsychotics on positive symptoms occur by blocking dopamine receptors in this neural system, thereby lowering dopamine activity.

The mesocortical pathway is another scene of dopamine activity. It begins in the same brain region as the mesolimbic pathway but projects to the prefrontal cortex. The prefrontal cortex also projects to other areas that are innervated by dopamine. The dopamine neurons in the prefrontal cortex may be underactive and thus fail to exert inhibitory control over the dopamine neurons in the limbic area, with the result that there is dopamine overactivity in the pathways. Because the prefrontal cortex is thought to be especially relevant to the negative symptoms of schizophrenia, the underactivity of the dopamine neurons in this part of the brain may also be the cause of the negative symptoms of schizophrenia (see Figure 11.2). This proposal has the advantage of accounting for the simultaneous presence of positive and negative symptoms in the same person with schizophrenia. Furthermore, because antipsychotics do not have major effects on the dopamine neurons in the prefrontal cortex, we would expect them to be relatively ineffective as treatments for negative symptoms, and they are. When we examine research on structural abnormalities in the brains of people with schizophrenia, we will see some close connections between these two domains.

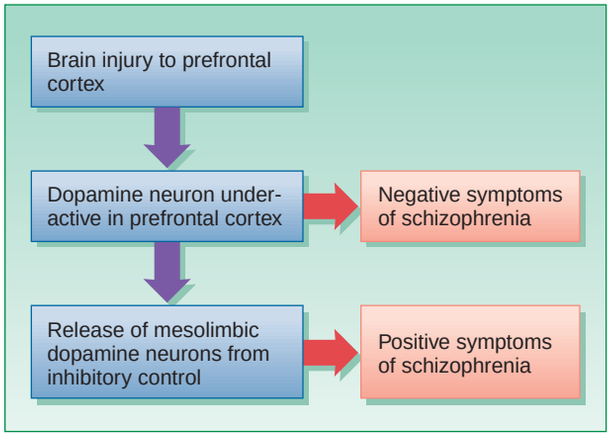


Figure 11.2 Dopamine theory of schizophrenia.

Evaluation of the Dopamine Theory Despite the positive evidence we have reviewed, the dopamine theory does not appear to be a complete theory of schizophrenia. For example, it takes several weeks for antipsychotics to begin lessening the positive symptoms of schizophrenia, although they begin blocking dopamine receptors rapidly (Davis, 1978). This disjunction between the behavioral and pharmacological effects of antipsychotics is difficult to understand within the context of the theory. One possibility is that although antipsychotics do indeed block D2 receptors, their ultimate therapeutic effect may result from the effect this blockade has on other brain areas and other neurotransmitter systems (R. M. Cohen et al., 1997).

It is also puzzling that to be therapeutically effective, antipsychotics must reduce dopamine levels or receptor activity to below normal, in some cases producing side effects like the symptoms of Parkinson's disease. According to the theory, reducing dopamine levels or receptor activity to normal should be sufficient for a therapeutic effect.

In sum, although dopamine remains the most actively researched neurotransmitter in schizophrenia, it is not likely to provide a complete explanation of the etiology of schizophrenia. Schizophrenia is a disorder with widespread symptoms covering perception, cognition, motor activity, and social behavior. It is unlikely that a single neurotransmitter could account for all of them. Thus, schizophrenia researchers have cast a broader neurotransmitter net, moving away from an almost exclusive emphasis on dopamine.

Other Neurotransmitters As we discuss later, newer drugs used in treating schizophrenia implicate other neurotransmitters, such as serotonin, in the disorder. These newer drugs partially block D2 receptors, but they also work by blocking the serotonin receptor 5HT2 (e.g., Burris et al., 2002). Dopamine neurons generally modulate the activity of other neural systems; for example, in the prefrontal cortex they regulate GABA neurons. Thus, it is not surprising that GABA transmission is disrupted in the prefrontal cortex of people with schizophrenia (Volk et al., 2000). Similarly, serotonin neurons regulate dopamine neurons in the mesolimbic pathway.

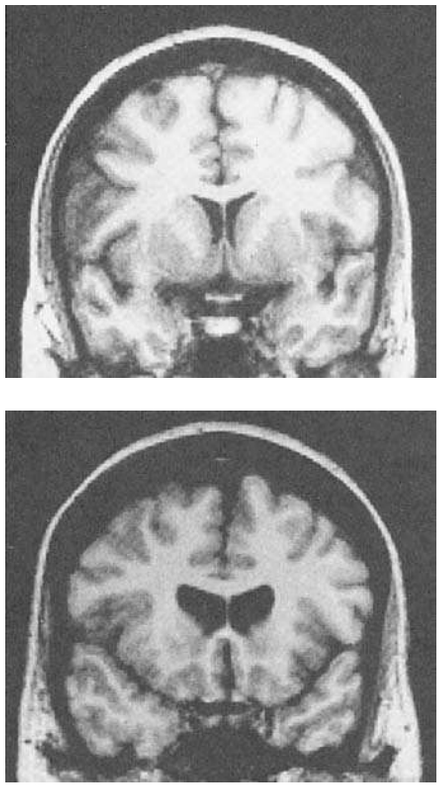
Glutamate, a neurotransmitter that is widespread in the human brain, may also play a role (Carlsson et al., 1999). Low levels of glutamate have been found in the cerebrospinal fluid of people with schizophrenia (Faustman et al., 1999), and postmortem studies have revealed low levels of the enzyme needed to produce glutamate (Tsai et al., 1995). Studies have found elevated levels of the amino acid homocysteine, a substance that is known to interact with the NMDA receptor among people with schizophrenia and in the blood of pregnant women during their third trimester whose offspring developed schizophrenia as adults (Brown et al., 2007; Regland et al., 1995). The street drug PCP (p. 296) can induce both positive and negative symptoms in people without schizophrenia, and it produces this effect by interfering with one of glutamate's receptors (O'Donnell & Grace, 1998). Furthermore, a decrease in glutamate inputs from either the prefrontal cortex or the hippocampus (both of these brain structures are implicated in schizophrenia) to the corpus striatum (a temporal lobe structure) could result in increased dopamine activity (O'Donnell & Grace, 1998). Additional evidence suggests that cognitive deficits in schizophrenia supported by the prefrontal cortex as well as symptoms of disorganization may be connected to deficits involving NMDA (MacDonald & Chafee, 2006). A new medication that targets glutamate receptors is currently being tested, and the early results are promising (Patel et al., 2007).

Brain Structure and Function

The search for a brain abnormality that causes schizophrenia began as early as the syndrome was identified, but studies did not begin to yield consistent findings until fairly recently. The challenge of such a task is indeed daunting. Schizophrenia affects everything about us that makes us human—our thinking, feeling, and behaving. It is thus unlikely that a single type of brain abnormality can account for schizophrenia's wide array of symptoms. In the last two decades, however, spurred by a number of technological advances, research has yielded some promising results. Among the most well-replicated findings of brain abnormalities in schizophrenia are enlargement of the ventricles and dysfunction in the prefrontal cortex.

Enlarged Ventricles Postmortem studies of the brains of people with schizophrenia consistently reveal enlarged ventricles, which implies a loss of brain cells, although there are also contradictory findings. Findings from neuroimaging studies are even more impressive. Thus far, these studies have most consistently revealed that some people with schizophrenia, especially men (Nopoulos, Flaum, & Andreasen, 1997), have enlarged ventricles[1]. Further evidence concerning enlarged ventricles comes from two MRI studies of pairs of MZ twins only one of whom had schizophrenia (McNeil, Cantor-Graae, & Weinberger, 2000; Suddath et al., 1990). In both studies the ill twin had larger ventricles than the well twin, and in one of the studies most of the twins with schizophrenia could be identified by simple visual inspection of the scan. Because the twins were genetically identical in these studies, these results suggest that the origin of these brain abnormalities may not be genetic.

Large ventricles in people with schizophrenia are correlated with impaired performance on neuropsychological tests, poor adjustment prior to the onset of the disorder, and poor response to drug treatment (Andreasen et al., 1982; Weinberger et al., 1980). The extent to which the ventricles are enlarged, however, is modest, and many people with schizophrenia do not differ from people without schizophrenia in this respect. Furthermore, enlarged ventricles are not specific to schizophrenia, as they are also evident in the CT scans of people with other disorders, such as bipolar disorder with psychotic features (Rieder et al., 1983). People with these disorders can show ventricular enlargement almost as great as that seen in schizophrenia (Elkis et al., 1995)[2].



MRI of the brain of a woman with schizophrenia (bottom) and the brain of a woman without schizophrenia (top). Enlarged ventricles (the dark spaces at center of photos) are one of the best-validated biological features of schizophrenia. (Courtesy of J. Lieberman, American Journal of Psychiatry.)

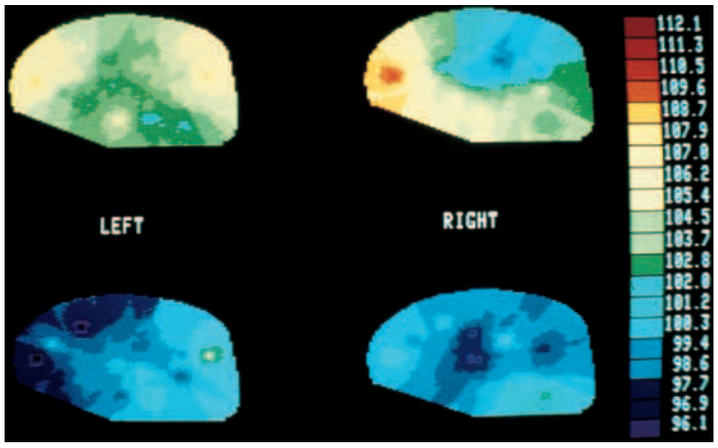
Factors Involving the Prefrontal Cortex A variety of evidence suggests that the prefrontal cortex is of particular importance in schizophrenia.

- The prefrontal cortex is known to play a role in behaviors such as speech, decision making, and goal-directed behavior, which are disrupted in schizophrenia.
- MRI studies have shown reductions in gray matter in the prefrontal cortex (Buchanan, Vladar, et al., 1998).
- People with schizophrenia perform more poorly on neuropsychological tests designed to tap functions promoted by the prefrontal region, including working memory or the ability to hold bits of information in memory (Barch et al., 2002, 2003; Heinrichs & Zakzanis, 1998).
- In a type of functional imaging in which glucose metabolism is studied in various brain regions while people perform psychological tests, people with schizophrenia have shown low metabolic rates in the prefrontal cortex (Buchsbaum et al., 1984). Glucose metabolism in the prefrontal cortex has also been studied while people with schizophrenia are performing neuropsychological tests of prefrontal function. Because the tests place demands on the prefrontal cortex, glucose metabolism normally goes up as energy is used. People with schizophrenia, especially those with prominent negative symptoms, do poorly on the tests and also fail to show activation in the prefrontal region (Potkin et al., 2002; Weinberger, Berman, & Illowsky, 1988). Failure to show frontal activation has also been found using fMRI (Barch et al., 2001; MacDonald & Carter, 2003).
- Finally, failure to show frontal activation is related to the severity of negative symptoms (O'Donnell & Grace, 1998) and thus parallels the work on dopamine underactivity in the frontal cortex already discussed.

Despite the reduced volume of the gray matter in the prefrontal cortex (and also the temporal cortex), the number of neurons in this area does not appear to be reduced. More detailed studies indicate that what is lost may be what are called "dendritic spines" (Goldman-Rakic & Selemon, 1997; McGlashan & Hoffman, 2000). Dendritic spines are small projections on

[1]This difference between men and women with schizophrenia prompts us to mention that there are other gender differences as well. For example, men with schizophrenia have an earlier age of onset and are more likely to express negative symptoms and to have a more deteriorating course than are women with schizophrenia (Salem & Kring, 1998).

[2]Other findings also suggest that the schizophrenia and psychotic mood disorders should not perhaps be totally separate diagnostic categories. The disorders share some symptoms (notably, delusions) and some possible etiological factors (e.g., genetic factors, increased dopamine activity), and they respond similarly to medications. An important implication is that researchers would be well served to focus some of their efforts on psychotic symptoms in other disorders as well as in schizophrenia.



Differences in regional cerebral blood flow between people with schizophrenia (bottom) and people without schizophrenia (top) for each hemisphere. The values shown were scored as the percentage change in cerebral blood flow while performing a control task to the Wisconsin Card Sort that was expected to activate the prefrontal cortex. The participants without schizophrenia showed greater prefrontal cortical activation as indicated by the "hotter" color of this brain region. *Source:* Weinberger et al., 1988. (Courtesy of Daniel Weinberger, National Institute of Health.)

the shafts of dendrites where nerve impulses are received from other neurons (see Figure 11.3). The loss of these dendritic spines would mean that communication among neurons would be disrupted, resulting in what some have termed a "disconnection syndrome." One possible result of the failure of neural systems to communicate could be the speech and behavioral disorganization seen in schizophrenia.

Congenital and Developmental Factors A possible cause of some of these brain abnormalities is damage during gestation or birth. Many studies have shown high rates of delivery complications in people with schizophrenia (Walker et al., 2004); such complications could have resulted in a reduced supply of oxygen to the brain, resulting in loss of cortical gray matter (Cannon et al., 2002). These obstetrical complications do not raise the rate of schizophrenia in everyone who experiences them; rather, the risk for schizophrenia is increased in those who experience complications and have a genetic diathesis (Cannon & Mednick, 1993).

Although the data are not entirely consistent (Westergaard et al., 1999), another possibility is that a virus invades the brain and damages it during fetal development (Mednick, Huttonen, & Machon, 1994; Mednick et al., 1988). During a 5-week period in 1957, Helsinki, Finland, experienced an epidemic of influenza virus. Researchers examined rates of schizophrenia among adults who had likely been exposed during their mothers' pregnancies. People who had been exposed to the virus during the second trimester of pregnancy had much higher rates than those who had been exposed in either of the other trimesters and much higher rates than in nonexposed control adults. This finding was intriguing because we know that the second trimester is a critical period for cortical development; however, only half of nearly 30 later studies were able to replicate this finding. And a more recent study found evidence that mothers' exposure to the flu during the *first* trimester of pregnancy, as directly measured by the presence of flu antibodies in the blood, was associated with a sevenfold increase in the risk for schizophrenia among their children (Brown et al., 2004). Though the increase in risk sounds large, the difference from the control group was not quite statistically different, suggesting that it will be important to replicate this finding.

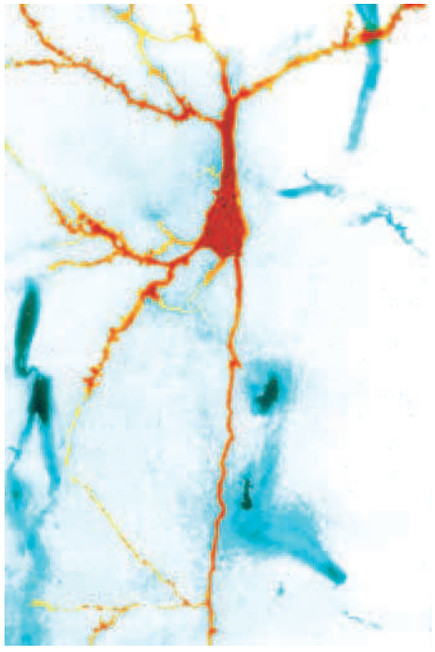


Figure 11.3 Micrograph of a neuron. The bumps on the dendrites are dendritic spines, which receive inputs from other neurons. Fewer dendritic spines may impair connections among neurons and may be a factor in schizophrenia. (BSIP/Sercomi/Photo Researchers, Inc.)

Additional research suggests that other types of maternal infections during pregnancy are associated with greater risk of their children developing schizophrenia when they become adults (Brown, 2006). Specifically, one study found that maternal exposure to the parasite toxoplasma gondii was associated with a nearly 2.5 times greater risk of schizophrenia among the mothers' children when they became adults (A.S. Brown et al., 2005). This is a common parasite, and many people carry it with no ill effects.

If, as the findings we have just reviewed suggest, the development of the brains of people with schizophrenia goes awry very early, why does the disorder begin many years later, in adolescence or early adulthood? The prefrontal cortex is a brain structure that matures late, typically in adolescence or early adulthood. Thus a problem in this area, even one that begins early in the course of development, may not show itself in the person's behavior until the period of development when the prefrontal cortex begins to play a larger role in behavior (Weinberger, 1987). Notably, dopamine activity also peaks in adolescence, which may further set the stage for the onset of schizophrenia symptoms (Walker et al., 2008). Adolescence is also typically a developmental period that is fraught with stress. Recall from our discussions in Chapter 2 that stress activates the hypothalamic–pituitary–adrenal (HPA) axis (see p. 38), causing cortisol to be secreted. Research in the past 10 years has demonstrated that cortisol increases dopamine activity, particularly in the mesolimbic pathway, perhaps increasing the likelihood of the development of schizophrenia symptoms (Walker et al., 2008).

Another proposed explanation is that the development of symptoms in adolescence could reflect a loss of synapses due to excessive pruning, the elimination of synaptic connections. Pruning is a normal part of brain development that occurs at different rates in different areas

of the brain. It is mostly complete in sensory areas by about 2 years of age but continues in the prefrontal cortex until mid-adolescence. If too extensive, pruning would result in the loss of necessary communication among neurons (McGlashan & Hoffman, 2000).

Current Research Further work on the relationship of schizophrenia to brain structure and function is proceeding at a rapid rate. Recognizing that the symptoms of schizophrenia implicate many areas of the brain, researchers have moved away from trying to find a highly specific "lesion" and are beginning to examine neural systems and the ways in which different areas of the brain interact. This work is beginning to call attention to the possible roles of a wider range of brain structures, such as the thalamus and the cerebellum, in schizophrenia (Byne et al., 2002; Gilbert et al., 2001). Research also shows a reduction in cortical gray matter in both the temporal and frontal regions (Gur et al., 2000) and reduced volume in basal ganglia (e.g., the caudate nucleus), hippocampus, and limbic structures (Chua & McKenna, 1995; Gur & Pearlson, 1993; Keshavan et al., 1998; Lim et al., 1998; Nelson et al., 1998; Velakoulis et al., 1999; Walker et al., 2008). A twin study found reduced hippocampus volume among twins with schizophrenia, but not among the twins without schizophrenia (van Erp et al., 2004). A meta-analysis of MRI studies conducted with people during their first episode of schizophrenia concluded that the volume of the hippocampus was significantly reduced compared to people without schizophrenia (Steen et al., 2006).

What makes these findings about the hippocampus all the more intriguing is the fact that the HPA axis is closely connected to this area of the brain. Chronic stress is associated with reductions in hippocampal volume in other disorders, such as PTSD. Although people with schizophrenia do not necessarily experience more stress compared to people without schizophrenia, they are more reactive to stress. Other evidence indicates that the HPA axis is disrupted in schizophrenia. Taken together, stress reactivity and a disrupted HPA axis likely contribute to the reductions in hippocampal volume observed in people with schizophrenia (Walker et al., 2008). An additional interesting piece of evidence regarding the hippocampus comes from a meta-analysis of 9 studies assessing brain volume of over 400 first-degree relatives of people with schizophrenia and over 600 first-degree relatives of people without schizophrenia (Boos et al., 2007). Relatives of people with schizophrenia had smaller hippocampal volumes than relatives of people without schizophrenia. These findings suggest that reduced hippocampal volume in people with schizophrenia may reflect a combination of genetic and environmental factors.

Psychological Stress

We have discussed several possible neurobiological diatheses for schizophrenia, but more than a diathesis is required to produce schizophrenia. Psychological stress plays a role by interacting with a genetic or neurobiological vulnerability to produce this illness. Research shows that, as with many of the disorders we have discussed, increases in life stress increase the likelihood of a relapse (Ventura et al., 1989; Walker et al., 2008). People with schizophrenia do not appear to experience more stress in daily life than people without schizophrenia (Phillips et al., 2007; Walker, Mittal, & Tessner, 2008). However, people with schizophrenia appear to be very reactive to the stressors we all encounter in daily living. In one study, people with psychotic disorders (92 percent with schizophrenia), their first-degree relatives, and people without any psychiatric disorder participated in a 6-day ecological momentary assessment study in which they recorded stress and mood several times each day. Stress led to greater decreases in positive moods in both people with schizophrenia and their relatives compared with controls. Stress also led to greater increases in negative moods in the people with schizophrenia compared with both relatives and controls (Myin-Gremeys et al., 2001). Thus, people with schizophrenia were particularly vulnerable to daily stress.

Additional research on the role of life stress in the development and relapse of schizophrenia has focused on socioeconomic status and the family.

Socioeconomic Status For many years we have known that the highest rates of schizophrenia are found in urban areas inhabited by people of the lowest socioeconomic status (SES) in several countries, including the United States, Denmark, Norway, and the United Kingdom (Hollingshead & Redlich, 1958; Kohn, 1968). The relationship between SES and schizophrenia

is not such that the prevalence of schizophrenia goes up as SES goes down. Rather, there is a sharp upturn in the prevalence of schizophrenia in people of the lowest socioeconomic status.

The correlation between SES and schizophrenia is consistent but difficult to interpret in causal terms. Some people believe that stressors associated with SES may cause or contribute to the development of schizophrenia—the **sociogenic hypothesis**. Degrading treatment by others of higher status, low levels of education, and lack of rewards and opportunities may, taken together, make very low SES so stressful that people who are predisposed to develop schizophrenia readily develop the disorder. Alternatively, these stressors could have neurobiological effects; for example, children of mothers whose nutrition during pregnancy was poor are at increased risk for schizophrenia (Susser et al., 1996).

Another explanation of the correlation between schizophrenia and low SES is the **social selection theory**, which reverses the direction of causality. The theory proposes that during the course of their developing illness, people with schizophrenia may drift into poor neighborhoods because their illness impairs their earning power and they cannot afford to live elsewhere.

A study in Israel evaluated the two theories by investigating both SES and ethnic background (Dohrenwend et al., 1992). The rates of schizophrenia were examined in Israeli Jews of European ethnic background and in more recent immigrants to Israel from North Africa and the Middle East. The latter group experienced considerable racial prejudice and discrimination in Israel. The sociogenic hypothesis would predict that because they experienced high levels of stress regardless of socioeconomic status, the members of the disadvantaged ethnic group should have consistently higher rates of schizophrenia regardless of status. However, this pattern did not emerge, supporting the social selection theory.

In sum, research results are more supportive of the social selection theory than of the sociogenic hypothesis. But we should not conclude that the social environment plays no role in schizophrenia. For example, the prevalence of schizophrenia among Africans from the Caribbean who remain in their native country is much lower than among those who have emigrated to London (Hutchinson et al., 1996). This difference could well be caused by the stress associated with trying to assimilate into a new culture.

Family-Related Factors Early theorists regarded family relationships, especially those between a mother and her son, as crucial in the development of schizophrenia. At one time the view was so prevalent that the term "*schizophrenogenic mother*" was coined for the supposedly cold and dominant, conflict-inducing parent who was said to produce schizophrenia in her offspring (Fromm-Reichmann, 1948). These mothers were characterized as rejecting, overprotective, self-sacrificing, impervious to the feelings of others, rigid and moralistic about sex, and fearful of intimacy. Controlled studies evaluating the schizophrenogenic-mother theory have not supported it. The damage done to families by this theory, however, was significant. For generations, parents blamed themselves for their child's illness, and until the 1970s, psychiatrists often joined in this blame game.

How Do Families Influence Schizophrenia? Other studies continued to explore the possibility that the family plays some role in the etiology of schizophrenia. For the most part, the findings are only suggestive, not conclusive. For example, a few studies of families of people with schizophrenia have found that they communicate more vaguely with one another and have higher levels of conflict than families of people without schizophrenia. It is plausible, though, that the conflict and unclear communication are a response to having a young family member with schizophrenia.

Some other findings suggest that faulty communications by parents may play a role in the etiology of schizophrenia. One type of communication pattern studied is called *communication deviance (CD)*, which is characterized by hostility and poor communication. In a longitudinal study of adolescents with behavior problems, CD in the families was found to predict the later onset of schizophrenia (Norton, 1982). However, not all people who develop schizophrenia exhibit behavior problems as adolescents. Furthermore, it does not appear that CD is specifically associated with schizophrenia, since parents of people with bipolar disorder are equally likely to show CD (Miklowitz, 1985).

Further evidence favoring some role for the family comes from the Finnish adoption study described above (Tienari et al., 2000). Various aspects of family life in the adoptive families were

extensively studied and then related to the adjustment of the children (Tienari et al., 1994). The families were categorized into levels of maladjustment based on material from clinical interviews and psychological tests. More serious psychopathology was found among the adoptees reared in a disturbed family environment. Furthermore, among children reared in a disturbed family environment, those having a biological parent with schizophrenia showed more psychopathology than did the control participants. Although it is tempting to conclude that both a genetic predisposition and a noxious family environment are necessary to increase risk for psychopathology, a problem in interpretation remains: the disturbed family environment could be a response to a disturbed child. Thus we cannot firmly conclude that an etiological role for the family has been established.

Families and Relapse A series of studies initiated in London indicate that the family can have an important impact on the adjustment of patients after they leave the hospital. In one study, investigators conducted a 9-month follow-up study of a sample of people with schizophrenia who returned to live with their families after being discharged from the hospital (Brown et al., 1966). Interviews were conducted with parents or spouses before discharge and rated for the number of critical comments made about the patient and for expressions of hostility toward or emotional overinvolvement with the patient. The following is an example of a critical comment made by a father remarking on his daughter's behavior, in which he is expressing the idea that his daughter is deliberately symptomatic to avoid housework: "My view is that Maria acts this way so my wife doesn't give her any responsibilities around the house" (quoted in Weisman et al., 1998). On the basis of this variable, called **expressed emotion (EE)**, families were divided into two groups: those revealing a great deal of expressed emotion (high-EE families) and those revealing little (low-EE families). At the end of the follow-up period, only 10 percent of the patients returning to low-EE homes had relapsed, but 58 percent of the patients returning to high-EE homes had gone back to the hospital.

This research, which has since been replicated (see Butzlaff & Hooley, 1998, for a meta-analysis), indicates that the environment to which people with schizophrenia are discharged has great bearing on how soon they are rehospitalized. Researchers have also found that negative symptoms of schizophrenia are most likely to elicit critical comments, as in the example presented in the previous paragraph, and that the relatives who make the most critical comments are the most likely to view people with schizophrenia as being able to control their symptoms (Lopez et al., 1999; Weisman et al., 1998).

What is not yet clear is exactly how to interpret the effects of EE. Is EE causal, or does it reflect a reaction to the ill relative's behavior? For example, if the condition of a patient with schizophrenia begins to deteriorate, family concern and involvement may increase. Indeed, disorganized or dangerous behavior by the patient might seem to warrant limit setting and other familial efforts that could increase the level of EE. Research indicates that both interpretations of the operation of EE may be correct. Recently discharged people with schizophrenia and their high- or low-EE families were observed as they engaged in a discussion of a family problem. Two key findings emerged (Rosenfarb et al., 1994).

1. The expression of unusual thoughts by the people with schizophrenia ("If that kid bites you, you'll get rabies") elicited a greater number of critical comments by family members who had previously been characterized as high in EE than by those characterized as low in EE.
2. In high-EE families, critical comments by family members led to increased expression of unusual thoughts by the people with schizophrenia.

Thus, this study found a bidirectional relationship in high-EE families: critical comments by family members elicited more unusual thoughts by relatives with schizophrenia, and unusual thoughts expressed by the relatives with schizophrenia led to increased critical comments.

Expressed emotion, which includes hostility, critical comments, and emotional overinvolvement, has been linked with relapse in schizophrenia. (Lisette Le Bon/SUPERSTOCK.)

How does stress, such as a high level of EE, increase the symptoms of schizophrenia and precipitate relapses? One answer to this question relates the effects of stress on the HPA axis and its link to dopamine (Walker et al., 2008). Stress activates the HPA axis, causing cortisol to be secreted, which can then increase dopamine activity (Walker et al., 2008). Furthermore, heightened dopamine activity itself can increase HPA activation, which may make a person overly sensitive to stress. Thus, there is a bidirectional relationship between HPA activation and dopamine activity.

Developmental Studies

What are people who develop schizophrenia like before their symptoms begin? An early method of answering this question was to construct developmental histories by examining the childhood records of those who had later developed schizophrenia. In the 1960s, researchers found that children who later developed schizophrenia had lower IQs and were more often delinquent and withdrawn than members of various control groups, usually comprising siblings and neighborhood peers (Albee, Lane, & Reuter, 1964; Lane & Albee, 1965; Berry, 1967). Other studies found that boys who later developed schizophrenia were rated by teachers as disagreeable, whereas girls who later developed schizophrenia were rated as passive (Watt, 1974; Watt et al., 1970).

More recently, researchers have examined home movies before the onset of schizophrenia, made as part of normal family life (Walker, Davis, & Savoie, 1994; Walker et al., 1993). Compared with their siblings who did not later develop schizophrenia, the children who later developed schizophrenia as young adults showed poorer motor skills and more expressions of negative emotions.

As intriguing as these findings are, the major limitation of such developmental research is that the data were not originally collected with the intention of predicting the development of schizophrenia from childhood behavior. More specific information is required if developmental histories are to provide clear evidence regarding etiology.

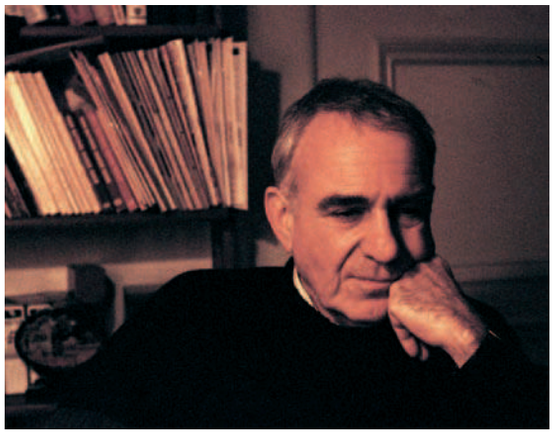
The high-risk method can yield this information. The first such study of schizophrenia was begun in the 1960s (Mednick & Schulsinger, 1968). The researchers chose Denmark because Danish registries make it possible to keep track of people for long periods of time. The high-risk participants were 207 young people whose mothers had schizophrenia (The researchers decided that the mother should be the parent with the disorder because paternity is not always easy to determine.) Then, 104 low-risk participants, people whose mothers did not have schizophrenia, were matched to the high-risk subjects on variables such as sex, age, father's occupation, rural or urban residence, years of education, and institutional upbringing versus rearing by the family. In 1972 the now-grown men and women were followed up with a number of measures, including a battery of diagnostic tests. Fifteen of the high-risk participants were diagnosed with schizophrenia; none of the control participants was so diagnosed.

Additional analyses of the group of participants who were diagnosed with schizophrenia suggested that positive and negative symptoms of schizophrenia may have different etiologies (Cannon, Mednick, & Parnas, 1990). People with predominantly negative symptoms had a history of pregnancy and birth complications and a failure to show electrodermal responses to simple stimuli. By contrast, people with predominantly positive symptoms had a history of family instability, such as separation from parents and placement in foster homes or institutions for periods of time.

In the wake of this pioneering study, other high-risk investigations were undertaken, some of which have also yielded information concerning the possible causes of adult psychopathology, but not necessarily schizophrenia specifically. The New York High-Risk Study found that a composite measure of attentional dysfunction predicted behavioral disturbance at follow-up (Cornblatt & Erlenmeyer-Kimling, 1985). Furthermore, low IQ was a characteristic of the first high-risk children to be hospitalized (Erlenmeyer-Kimling & Cornblatt, 1987). In an Israeli study, poor neurobehavioral functioning (poor concentration, poor verbal ability, lack of motor control and coordination) predicted schizophrenia-like outcomes, as did earlier interpersonal problems (Marcus et al., 1987).

One of the difficulties with these types of high-risk studies has to do with the large sample sizes that are required. As shown in Table 11.3, the percentage of children with a biological parent who has schizophrenia who go on to themselves develop schizophrenia is around 10 percent. If a study begins with 200 high-risk children, only about 20 of them may go on to develop schizophrenia. In addition, is not particularly easy to locate a large sample of women or men with schizophrenia who have had their own children.

Because of these difficulties, other high-risk research designs have been used in more recent research. One such study has been ongoing in Australia for the past several years, following people between the ages of 14 and 30 who were referred to a mental health clinic in the mid-1990s (Yung et al., 1995). None of the participants had schizophrenia when they entered the study, but many later exhibited varying degrees of schizophrenia symptoms and some, but not all, had a biological relative with a psychotic disorder. These participants were deemed to be at "ultra-high risk" of developing schizophrenia or psychotic disorders. Since the study began, 41 of the original 104 participants have developed some type of psychotic disorder (Yung et al., 2004). An MRI study of 75 of the 104 participants found that those people who later developed a psychotic disorder had lower gray matter volumes than those who had not developed a psychotic disorder (Pantelis et al., 2003). Recall that reduced gray matter volume has been found in people with schizophrenia; this study suggests that this characteristic may predate the onset of schizophrenia and other psychotic disorders.



Sarnoff Mednick, a psychologist at the University of Southern California, pioneered the use of the high-risk method for studying schizophrenia. He has also contributed to the hypothesis that a maternal viral infection is implicated in this disorder. (Sarnoff Mednick.)

A similar study is ongoing in the United States and Canada, called the North American Prodrome Longitudinal Study (NAPLS). Prodrome refers to the period before a person meets diagnostic criteria for schizophrenia but nonetheless shows some symptoms. In this study, 82 of the 291 ultra-high risk participants had developed schizophrenia or some type of psychotic disorder (Cannon et al., 2008). The researchers identified a number of factors that predicted a greater likelihood of developing a psychotic disorder, including having a biological relative with schizophrenia, a recent decline in functioning, high levels of positive symptoms, and high levels of social impairment. It will be important in future studies to see if these factors can prospectively predict the onset of schizophrenia.

Quick Summary

Given its complexity, a number of causal factors are likely to contribute to schizophrenia. The genetic evidence is strong, with much of the evidence coming from family, twin, and adoption studies. Learning what is inherited remains a challenge for molecular genetics studies. Linkage studies have found linkage on several chromosomes, but these studies need to be replicated. Promising genes from association studies include DTNBP1, NGR1, and COMT, but replication is also needed here.

Neurotransmitters play a role in schizophrenia. For years, dopamine was the focus of study, but later findings led investigators to conclude that this one neurotransmitter could not fully account for schizophrenia. Other neurotransmitters are also the focus of study, such as serotonin, GABA, and glutamate. A number of different brain areas have been implicated in schizophrenia. One of the most widely replicated findings is of enlarged ventricles. Other research supports the role of the prefrontal cortex, particularly reduced activation of this area, in schizophrenia.

Research has examined the role of socioeconomic status in schizophrenia, and generally this work supports the social selection theory more than the sociogenic hypothesis. Early theories blamed families, particularly mothers, for causing schizophrenia, but research does not support this view. Communication in families is important and could perhaps constitute the stress in the diathesis–stress theory for schizophrenia. Expressed emotion has also been found to predict relapse in schizophrenia.

Early developmental studies looked back at the childhood records of adults with schizophrenia and found that some adults with schizophrenia had lower IQs and were withdrawn and delinquent as children. Other studies found that adults who later developed schizophrenia expressed a lot of negative emotion and had poor motor skills. The problem with these studies is that the studies were not designed to predict the onset of schizophrenia. High-risk designs deal with this problem, and these studies have found that children at risk for adult psychopathology have difficulties with attention and motor control, among other things.

Check Your Knowledge 11.2

Fill in the blanks.

1. _____ studies do not do such a good job of teasing out genetic and environmental effects: _____ studies do a better job.
2. _____ and _____ are two genes that have recently been associated with schizophrenia.
3. Some studies showing the _____ area of the brain to be disrupted in schizophrenia also show that people with schizophrenia do poorly on tasks that rely on this area, such as planning and problem solving.
4. _____, _____, and _____ are the three components of expressed emotion.

Treatment of Schizophrenia

Treatments for schizophrenia most often include a combination of short-term hospital stays (during the acute phases of the illness), medication, and psychosocial treatment. A problem with any kind of treatment for schizophrenia is that some people with schizophrenia lack insight into their impaired condition and refuse any treatment at all (Amador et al., 1994). Results from one study suggest that gender (female) and age (older) are predictors of better insight among people in their first episode of the illness (McEvoy et al., 2006), and this may help account for why women with schizophrenia tend to respond better to treatment (Salem & Kring, 1998). For those who lack insight and thus don't believe they have an illness, they don't see the need for professional help, particularly when it includes hospitalization or drugs. This may be especially true for those with paranoid schizophrenia, who may regard treatment as a threat from hostile outside forces. Family members therefore face a major challenge in getting their relatives into treatment, which is one reason they sometimes turn to involuntary hospitalization via civil commitment.

Before we examine the range of treatments for schizophrenia, it is important to point out that the appropriateness of a given treatment depends on the stage of illness that the patient is in. That is, when a patient is in an acutely psychotic phase of the illness, psychological interventions are not likely to be successful because the patient is too distracted, unable to concentrate on what the therapist is saying. In such a phase some sort of medication is likely necessary, and perhaps a short hospital stay. Once the person becomes less psychotic, a psychological intervention can begin to have a beneficial impact, and the dosage of the medication can be reduced as the person learns ways to reduce the stress that may have precipitated the episode (Kopelowicz, Liberman, & Zarate, 2002).

Medications

One of the most important developments in the treatment of schizophrenia was the advent in the 1950s of several medications collectively referred to as **antipsychotic drugs**, also referred to as *neuroleptics* because they produce side effects similar to the symptoms of a neurological disease. Focus on Discovery 11.2 presents a brief history of the development of these drugs.

First-Generation Antipsychotic Drugs and Their Side Effects The discovery of the phenothiazines, including the drug Thorazine, in the 1950s led to a complete change in the treatment of schizophrenia. Just 20 years after their discovery, these drugs were the primary form of treatment for schizophrenia. Other antipsychotics that have been used for years to treat schizophrenia include the butyrophenones (e.g., haloperidol, trade name Haldol) and the thioxanthenes (e.g., thiothixene, trade name Navane). Both types seem generally as effective as the phenothiazines and work in similar ways. These classes of drugs can reduce the positive and disorganized symptoms of schizophrenia but have little or no effect on the negative symptoms, perhaps because their primary mechanism of action involves blocking dopamine D2 receptors. Recall from our discussion earlier that the dopamine theory helps account for positive symptoms, but not negative symptoms. Despite their effectiveness at reducing some of the symptoms of schizophrenia

FOCUS ON DISCOVERY 11.2

Stumbling Toward a Cure: The Development of Antipsychotic Medications

One of the more frequently prescribed antipsychotic drugs, phenothiazine, was first produced by a German chemist in the late nineteenth century. But it was not until the discovery of the antihistamines, which have a phenothiazine nucleus, in the 1940s, that phenothiazines received much attention.

Reaching beyond their use to treat the common cold and asthma, the French surgeon Henri Laborit pioneered the use of antihistamines to reduce surgical shock. He noticed that they made his patients somewhat sleepy and less fearful about the impending operation. Laborit's work encouraged pharmaceutical companies to reexamine antihistamines in light of their tranquilizing effects. Shortly thereafter the French chemist Paul Charpentier prepared a new phenothiazine derivative, which he called chlorpromazine. This drug proved very effective in calming people with schizophrenia. Phenothiazines derive their therapeutic properties by blocking dopamine receptors in the brain, thus reducing the influence of dopamine on thought, emotion, and behavior.

Chlorpromazine (trade name Thorazine) was first used therapeutically in the United States in 1954 and rapidly became the preferred treatment for schizophrenia. By 1970, more than 85 percent of all patients in state mental hospitals were receiving chlorpromazine or another phenothiazine.

and allowing many patients to be released from the hospital, these so-called first-generation antipsychotics are not a cure. They are referred to as first-generation antipsychotics because they came out of the first "wave" of significant research discoveries of effective medication treatments for schizophrenia. The second wave produced a group of drugs referred to as second-generation antipsychotics, a class of drugs we will discuss in more detail later. About 30 percent of people with schizophrenia do not respond favorably to the first-generation antipsychotics, and about half the people who take any antipsychotic drug quit after 1 year and up to three-quarters quit before 2 years because the side effects are so unpleasant (Harvard Mental Health Letter, 1995; Lieberman et al. 2005).

People who respond positively to the antipsychotics are kept on so-called maintenance doses of the drug, just enough to continue the therapeutic effect. Some people who are maintained on medication may make only marginal adjustment to the community, however. For example, they may be unable to live unsupervised or to hold down the kind of job for which they would otherwise be qualified, and their social relationships may be sparse. And again, although the first-generation antipsychotics keep positive and disorganized symptoms from returning, they tend to have little effect on negative symptoms, such as flat affect. The first-generation antipsychotics significantly reduced long-term hospitalization, but they have also initiated the revolving-door pattern of admission, discharge, and readmission seen in some people with schizophrenia.

Commonly reported side effects of the antipsychotics include sedation, dizziness, blurred vision, restlessness, and sexual dysfunction. In addition, some particularly disturbing side effects, termed *extrapyramidal side effects*, resemble the symptoms of Parkinson's disease. People taking antipsychotics may develop tremors of the fingers, a shuffling gait, and drooling. Other side effects include dystonia, a state of muscular rigidity, and dyskinesia, an abnormal motion of voluntary and involuntary muscles, producing chewing movements as well as other movements of the lips, fingers, and legs; together they cause arching of the back and a twisted posture of the neck and body. Another side effect is akasthesia, an inability to remain still; people pace constantly and fidget. These perturbing symptoms can be treated by drugs used with people who have Parkinson's disease.

In a rare muscular disturbance called *tardive dyskinesia*, the mouth muscles involuntarily make sucking, lip-smacking, and chin-wagging motions. In more severe cases, the whole body can be subject to involuntary motor movements. This syndrome is observed mainly in older people with schizophrenia who had been treated with first-generation medications before drugs were developed to prevent tardive dyskinesia from developing. It affects about 10 to 20 percent of these older people treated with first-generation antipsychotics for a long period of time and is not responsive to any known treatment (Sweet et al., 1995). Finally, a side effect called *neuroleptic malignant syndrome* occurs in about 1 percent of cases. In this condition, which can sometimes be fatal, severe muscular rigidity develops, accompanied by fever. The heart races, blood pressure increases, and the patient may lapse into a coma.

Because of these serious side effects, some clinicians believe it is unwise to prescribe high doses of first-generation antipsychotics for extended periods of time. Current clinical practice guidelines from the American Psychiatric Association call for treating people with the smallest possible doses of drugs (APA, 2004). The clinician is put in a bind by this situation: if medication is reduced, the chance of relapse increases; but if medication is continued, serious and untreatable side effects may develop.

Second-Generation Antipsychotic Drugs and Their Side Effects In the decades following the introduction of the first-generation antipsychotic drugs, there appeared to be little interest in developing new drugs to treat schizophrenia. This situation changed about 20 years ago, with the introduction of clozapine (trade name Clozaril) in the United States. Early studies of this drug suggested it could produce therapeutic gains in people with schizophrenia who did not respond well to first-generation antipsychotics (Kane et al., 1988). Additional studies suggested that clozapine has greater therapeutic gains in reducing positive and disorganization symptoms (Rosenheck et al., 1999; Wahlbeck et al., 1999), is associated with less treatment dropout (Kane et al., 2001), reduces relapse (Conley et al., 1999), and produces fewer motor side effects than the first-generation antipsychotics. Although the precise mechanism of the therapeutic effects of clozapine is not yet completely understood, we do know that it has a major impact on serotonin receptors.

However, researchers and clinicians soon learned that clozapine has its own set of serious side effects. It can impair the functioning of the immune system in a small percentage of people (about 1 percent) by lowering the number of white blood cells, a condition called agranulocytosis, which makes people vulnerable to infection and even death. For this reason, people taking clozapine have to be carefully monitored with routine blood tests. It also can produce seizures and other side effects, such as dizziness, fatigue, drooling, and weight gain (Meltzer, Cola, & Way, 1993).

Nevertheless, the apparent success of clozapine stimulated drug companies to begin a more earnest search for other drugs that might be more effective than first-generation antipsychotics. These drugs, including clozapine, are referred to as the **second-generation antipsychotic drugs** because their mechanism of action is not like that of the typical or first-generation antipsychotic medications. Two second-generation antipsychotics developed after clozapine are olanzapine (trade name Zyprexa) and risperidone (trade name Risperdal). Early studies showed that olanzapine and risperidone produced fewer of the side effects that first-generation antipsychotics produce, suggesting people were somewhat less likely to discontinue treatment (Dolder et al., 2002), but later studies have not always replicated this (Lieberman, 2006). The second-generation antipsychotics appear to be equally as effective as first-generation antipsychotics in reducing positive and disorganized symptoms (Conley & Mahmoud, 2001), particularly for people who have not responded to at least two other medications (Lewis et al., 2006), and some studies suggest that they are superior to the first-generation antipsychotics in reducing rehospitalization rates and relapse and in reducing negative symptoms (Csernansky, Mahmoud, & Brenner, 2002; Leucht et al., 2003). A meta-analysis of 124 studies comparing first- and second-generation antipsychotic drugs found that some, but not all, second-generation drugs were modestly more effective than the first-generation drugs in reducing negative symptoms and improving cognitive deficits (Davis, Chen, & Glick, 2003).

However, the news is not all good. A comprehensive randomized controlled clinical trial compared four second-generation drugs (olanzapine, risperidone, ziprasidone, and quetiapine) and one first-generation drug (perphenazine) against one another (Lieberman et al., 2005). Close to 1,500 people from all over the United States were in the study. What set this study apart from others included in the meta-analysis mentioned above was that it was not sponsored by one of the drug companies that makes the drugs (see p. 224 in Chapter 8 for a discussion of publication bias). Among the many findings from this study, three stand out. First, the second-generation drugs were not more effective than the older, first-generation drug. Second, the second-generation drugs did not produce fewer unpleasant side effects. And third, nearly three-quarters of the people stopped taking the medications before the 18 months of the study design had ended. Similar results have been found in another large study (Jones et al., 2006). Despite the early promise of second-generation drugs, more work is needed to develop better treatments for schizophrenia.

In addition, other studies suggest that second-generation antipsychotics may have serious side effects of their own (Freedman, 2003). For example, clozapine and olanzapine have been related to the development of type 2 diabetes (Leslie & Rosenheck, 2004); however, it is not clear whether the medicine itself increases this risk, perhaps via the side effect of weight gain, or whether people taking the medications were predisposed to developing diabetes independent of their medication usage. Other evidence suggests that these drugs may increase the risk for pancreatitis (Koller et al., 2003). In 2005, the drug company that produces olanzapine, Eli Lilly, agreed to settle a series of lawsuits, paying out over $700 million to patients taking the drug. The company was sued for failing to adequately warn patients of these serious side effects. The drug's label now contains warnings about possible side effects, including weight gain, elevated blood sugar, and elevated cholesterol levels.

Another disturbing aspect of the second-generation antipsychotic medications is that they tend not to be used among people of color. Two different studies recently found that African Americans were more likely to be prescribed the first-generation antipsychotics and less likely to be prescribed the second-generation antipsychotics (Kreyenbuhl et al., 2003; Valenti, Narendran, & Pristach, 2003). This is unfortunate for a number of reasons, but particularly since there is some evidence that African Americans may experience more side effects than whites in response to the first-generation medications (Frackeiwicz et al., 1997). More broadly, these results echo the findings of the Surgeon General's supplement to his landmark report on mental health in 2001 that elucidated a number of disparities in mental health treatment among members of ethnic minority groups (USDHHS, 2001a). Compared with other disorders reviewed in this book, there has been relatively less research on schizophrenia across different ethnic groups. This must be a focus of future research.

Second-generation antipsychotic drugs such as olanzapine may have fewer side effects than first-generation antipsychotic drugs, but they still have side effects. (Copyright Eli Lilly and Company. All Rights Reserved. Used with permission.)

A psychological approach to the study of the second-generation antipsychotics examines fundamental aspects of cognition, such as attention and memory, that are known to be deficient in many people with schizophrenia (Heinrichs & Zakzanis, 1998) and are associated with poor social adaptation (Green, 1996). A number of studies suggest that these medications may be more effective than the first-generation drugs at improving cognitive functioning (P. D. Harvey, et al., 2003, 2004; Keefe et al., 2007). For example, evidence suggests that risperidone improves short-term memory—involved in, for example, remembering an email address long enough to be able to type it—more than other antipsychotic drugs, apparently by reducing the activity of serotonin-sensitive receptors in the frontal cortex (Green et al., 1997). Research has also shown that improvements in memory are correlated with improvements in learning social skills in psychosocial rehabilitation programs (Green, 1996; Marder et al., 1999). More generally, the second-generation antipsychotics may thus make possible more thoroughgoing changes in schizophrenia and its behavioral consequences than do drugs that do not have these cognitive effects. However, other evidence suggests that psychological treatments (reviewed below) are also effective, perhaps more so, at alleviating cognitive deficits.

Development of New Drugs Some people with schizophrenia do not respond to any of the available medications, suggesting the need for new medications to be developed. One exciting approach in this area was the MATRICS project. MATRICS (Measurement and Treatment Research to Improve Cognition in Schizophrenia) was a collaborative effort among psychologists, psychiatrists, pharmaceutical companies, the FDA, and the National Institute of Mental Health. One goal of this project was to develop a consensus battery of cognitive and neuropsychological tests that can be used to evaluate and compare the efficacy of medications to treat schizophrenia (Green et al., 2004). To achieve this goal, several systematic and transparent steps were followed, which included deciding on the most important cognitive domains to be studied, finding the best and most practical ways to measure these domains, and determining the extent to which improving performance in those domains is related to a better outcome in schizophrenia. Results from each step were made available to the public via a website (www.matrics.ucla.edu).

Table 11.5 Summary of Major Drugs Used in Treating Schizophrenia

Drug Category	Generic Name	Trade Name
First-Generation Drugs	Chlorpromazine	Thorazine
	Fluphenazine decanoate	Prolixin
	Haloperidol	Haldol
	Thiothixene	Navane
	Trifluoperazine	Stelazine
Second-Generation Drugs	Clozapine	Clozaril
	Aripiprazole	Ablify
	Olanzapine	Zyprexa
	Risperidone	Risperdal
	Ziprasidone	Geodon
	Quetiapine	Seroquel

Evaluation of Drug Treatments Antipsychotic drugs are an indispensable part of treatment for schizophrenia and will undoubtedly continue to be an important component. Furthermore, the limited success of clozapine, olanzapine, and risperidone has stimulated a continued effort to find new and more effective drug therapies for schizophrenia. Many other drugs are currently being evaluated, so we may be on the verge of a new era in the treatment of schizophrenia. See Table 11.5 for a summary of major drugs used to treat schizophrenia.

Psychological Treatments

Our growing knowledge about neurobiological factors in schizophrenia and the continuing improvement in antipsychotic medications should not lead us to neglect the importance of psychosocial factors in both the etiology and treatment of schizophrenia. This is made clear in the following excerpt from a review of empirically supported psychological treatments for schizophrenia:

> *For veteran practitioners who have long considered only biological treatments as effective in protecting schizophrenic individuals from stress-induced relapse and disability . . . evidence [on reducing expressed emotion in families, reviewed later] that supports the protective value of psychosocial treatments . . . may serve as an antidote to the insidious biological reductionism that often characterizes the field of schizophrenia research and treatment. . . . It is essential to view treatments of schizophrenia in their biopsychosocial matrix—leaving out any of the three components . . . will diminish the impact and efficacy of treatment. (Kopelowicz & Liberman, 1998, p. 192)*

Neglecting the psychological and social aspect of schizophrenia compromises efforts to help people and their families who are struggling with this illness. Indeed, the current treatment recommendations for schizophrenia as compiled by the schizophrenia Patient Outcomes Research Team (PORT) are medications plus psychosocial interventions (Lehman et al., 2004). The PORT recommendations are based on extensive reviews of treatment research. In addition, review of 37 prospective studies of people after their first episode of schizophrenia found that the combination of medication and psychosocial treatment predicted the best outcome (Menezes, Arenovich, & Zipursky, 2006).

For example, a promising procedure for reducing rehospitalization rates involves both medication and psychosocial treatment. In one study, people with schizophrenia were randomly assigned to maintenance treatment as usual (medication and supportive group therapy) or a new treatment involving the following components (Herz et al., 2000):

1. Educating people with schizophrenia about relapse and recognizing early signs of relapse
2. Monitoring early signs of relapse by staff
3. Weekly supportive group or individual therapy
4. Family educational sessions
5. Quick intervention, involving both increased doses of medication and crisis-oriented problem-solving therapy, when early signs of relapse were detected

Importantly, staff were able to accurately recognize early signs of relapse and implement procedures to deal with them. Over 18 months, the new treatment cut relapse rates in half and reduced rehospitalization rates by about 44 percent. Other psychosocial treatments have been developed for schizophrenia, some with more success than others. We turn to these next.

Psychoanalytic Therapy Freud did little, either in his clinical practice or through his writings, to adapt psychoanalysis to the treatment of people with schizophrenia. He believed that they were incapable of establishing the close interpersonal relationship essential for analysis. Later analysts, such as Harry Stack Sullivan and Frieda Fromm-Reichmann, promoted the use

FOCUS ON DISCOVERY 11.3

Living with Schizophrenia

A heartening example of one woman's struggles with and triumphs over schizophrenia is found in the 2007 book entitled *The Center Cannot Hold: My Journey Through Madness.* This book was written by Elyn Saks, an endowed professor of law at the University of Southern California who also happens to have schizophrenia. In the book, she describes her lifelong experience with this illness. Prior to the publication of the book, only a few of Professor Saks' close friends even knew that she had schizophrenia. Why did she keep it a secret? Certainly stigma is part of the reason. As we have discussed throughout this book, stigma toward people with mental illness is very much alive in the 21st century, and stigma can have seriously negative consequences for people with illnesses like schizophrenia.

Elyn Saks, a law professor at USC, has schizophrenia. (Photo courtesy Will Vinet.)

What makes Professor Saks' life story particularly encouraging is that she has achieved exceptional professional and personal success in her life despite having such a serious mental illness. She grew up in a loving and supportive family, earned a bachelor's degree from Vanderbilt University, graduating as her class valedictorian, earned a prestigious Marshall fellowship to study philosophy at Oxford in the United Kingdom, graduated from Yale Law School as editor of the prestigious *Yale Law Review*, and is a tenured professor of law at a major university. How did she do it?

She believes that a combination of treatments, including psychoanalysis and medications, social support from family and friends, hard work, and acknowledging that she has a serious illness have all helped her cope with schizophrenia and its sometimes unpredictable and frightening symptoms. Although psychoanalysis does not have a good deal of empirical support for its efficacy with schizophrenia, it was and remains a central part of Professor Saks' treatment regimen. This illustrates nicely the fact that even though some treatments may not be effective for a group of people, they can nonetheless be effective for individuals (see Chapter 16 for more on this). One of the things that appears to have been helpful for Professor Saks, from her early days in psychoanalysis as a Marshall scholar at Oxford University until the present, has been her ability to "be psychotic" when she is with her psychoanalyst. So much of her energy was spent trying to hide her symptoms and keep them from interfering with her life, psychoanalysis became a safe place for her to let these symptoms more fully out into the open. The different analysts she has had over the year were also among the chief proponents of adding antipsychotic medication to her treatment, something that Professor Saks resisted for many years. Having the unwavering support of close friends and her husband has also been a tremendous help, particularly during her more symptomatic periods. Her loved ones would not turn and run the other way when she was psychotic. Instead, they would support her and help her get additional treatment if it was needed.

She still experiences symptoms, sometimes every day. Her symptoms include paranoid delusions, which she describes as very frightening (e.g., believing that her thoughts have killed people). She also experiences disorganization symptoms, which she eloquently describes in the book:

> *Consciousness gradually loses its coherence. One's center gives way. The center cannot hold. The "me" becomes a haze, and the solid center from which one experiences reality breaks up like a bad radio signal. There is no longer a sturdy vantage point from which to look out, take things in, assess what's happening. No core holds things together, providing the lens through which to see the world, to make judgments and comprehend risk. (Saks, 2007, p. 13).*

Even though she still experiences symptoms, she has been able to come to terms with the fact that schizophrenia is a part of her life. Would she prefer not to have the illness? Sure. But she also recognizes that she has a wonderful life filled with friends, loved ones, and meaningful work. She is not defined by her illness, and she importantly notes that "the humanity we all share is more important than the mental illness we may not" (Saks, 2007, p. 336). Her life is an inspiration to all, not just those with mental illness. Her story reminds us that life is difficult, more so for some than others, but that it can be lived, and lived to the fullest.

of psychoanalysis for people with schizophrenia. However, research results do not support the efficacy of this treatment for schizophrenia. For some people, it may do more harm than good (Katz & Gunderson, 1990; Mueser & Berenbaum, 1990; Stanton et al., 1984). Nevertheless, anecdotal reports and case studies point to some successes with this type of treatment. See Focus on Discovery 11.3 for an example of this.

More recent types of psychosocial treatments are more active, present-focused, and reality-oriented than psychoanalytic approaches, as therapists try to help patients and their families deal more directly with the everyday problems they face in coping with this disruptive and debilitating illness. Inherent to this work is the assumption that a good deal of the stress experienced by people with schizophrenia is due to their difficulties in negotiating everyday social challenges, including the pressures that arise in their families when they return home after hospitalization. We turn now to these newer and more effective approaches.

Social Skills Training

Social skills training is designed to teach people with schizophrenia how to successfully manage a wide variety of interpersonal situations—discussing their medications with their psychiatrist, ordering meals in a restaurant, filling out job applications, interviewing for jobs, saying no to drug dealers on the street, and reading bus schedules. Most of us take these skills for granted and give little thought to them in our daily lives, but people with schizophrenia cannot take them for granted—they need to work hard to acquire or reacquire such skills (Heinssen, Liberman, & Kopelowicz, 2000; Liberman et al., 2000). Social skills training typically involves role-playing and other group exercises to practice skills, both in a therapy group and in actual social situations.

Research has shown that people with schizophrenia can be taught new social behaviors that help them achieve fewer relapses, better social functioning, and a higher quality of life (Kopelowicz et al., 2002). Some of the studies are noteworthy in demonstrating benefits over a period of 2 years following treatment (Liberman et al., 1998; Marder et al., 1999), though not all results are positive (Pilling et al., 2002). Social skills training is usually a component of treatments for schizophrenia that go beyond the use of medications alone, including family therapies for lowering expressed emotion, which we discuss next. For example, social skills training that included family therapy was found to be more effective than treatment as usual (medication plus a 20-minute monthly meeting with a psychiatrist) in a randomized controlled trial conducted in Mexico (Valencia et al., 2007).

Family Therapies

Many people with schizophrenia who are discharged from hospitals go home to their families. Earlier we discussed research showing that high levels of expressed emotion (EE) within the family, including being hostile, hypercritical, and overprotective, have been linked to relapse and rehospitalization. Based on this finding, a number of family therapies have been developed. These therapies may differ in length, setting, and specific techniques, but they have several features in common:

- *Education about schizophrenia—specifically about the genetic or neurobiological factors that predispose some people to the illness, the cognitive problems associated with schizophrenia, the symptoms of schizophrenia, and the signs of impending relapse.* High-EE families are typically not well informed about schizophrenia, and giving them some basic information helps them be less critical of the relative with schizophrenia. Knowing, for example, that neurobiology has a lot to do with having schizophrenia and that the illness involves problems in thinking clearly and rationally might help family members be more accepting and understanding of their relative's inappropriate or ineffectual actions. Therapists encourage family members to lower their expectations of their relative with schizophrenia, and they make clear to family and the person with schizophrenia alike that proper medication and therapy can reduce stress on the patient and prevent deterioration.
- *Information about antipsychotic medication.* Therapists impress on both the family and the ill relative the importance of taking antipsychotic medication, becoming better informed about the intended effects and the side effects of the medication, taking responsibility for monitoring response to medication, and seeking medical consultation rather than just discontinuing the medication if adverse side effects occur.
- *Blame avoidance and reduction.* Therapists encourage family members to blame neither themselves nor their relative for the illness and for the difficulties all are having in coping with it.
- *Communication and problem-solving skills within the family.* Therapists focus on teaching the family ways to express both positive and negative feelings in a constructive, empathic, nondemanding manner rather than in a finger-pointing, critical, or overprotective way. They focus as well on making personal conflicts less stressful by teaching family members ways to work together to solve everyday problems.
- *Social network* expansion. Therapists encourage people with schizophrenia and their families to expand their social contacts, especially their support networks.
- *Hope.* Therapists instill hope that things can improve, including the hope that the person with schizophrenia may not have to return to the hospital.

Therapists use various techniques to implement these strategies. Examples include identifying stressors that could cause relapse, training families in communication skills and problem solving, and having high-EE family members watch videotapes of interactions of low-EE families (Penn & Mueser, 1996). Compared with standard treatments (usually just medication), family therapy plus medication has typically lowered relapse over periods of 1 to 2 years. This positive finding is evident particularly in studies in which the treatment lasted for at least 9 months (Falloon et al., 1982, 1985; Hogarty et al., 1986, 1991; Kopelowicz & Liberman, 1998; McFarlane et al., 1995; Penn & Mueser, 1996).

Cognitive Behavior Therapy At one time, researchers assumed that it was futile to try to alter the cognitive distortions, including delusions, of people with schizophrenia. Now, however, a growing body of evidence demonstrates that the maladaptive beliefs of some people with schizophrenia can in fact benefit from cognitive behavior therapy (CBT) (Garety, Fowler, & Kuipers, 2000; Wykes et al., 2008).

Family therapy can help educate people with schizophrenia and their families about schizophrenia and reduce expressed emotion. (Bruce Ayres/Stone/Getty Images.)

People with schizophrenia can be encouraged to test out their delusional beliefs in much the same way as people without schizophrenia do. Through collaborative discussions (and in the context of other modes of treatment, including antipsychotic drugs), some people with schizophrenia have been helped to attach a nonpsychotic meaning to paranoid symptoms and thereby reduce their intensity and aversive nature, similar to what is done for depression and panic disorder (Beck & Rector, 2000; Drury et al., 1996; Haddock et al., 1998). Researchers have found that CBT can also reduce negative symptoms, for example, by challenging belief structures tied to low expectations for success (avolition) and low expectations for pleasure (anticipatory pleasure deficit in anhedonia) (Beck, Rector, & Stolar, 2004; Rector, Beck, & Stolar, 2005; Wykes et al., 2008).

Findings from the first few randomized controlled trials of CBT in schizophrenia suggest that this treatment, along with medication, can help reduce hallucinations and delusions (Bustillo et al., 2001). A more recent meta-analysis of 34 studies of close to 2,000 people with schizophrenia across 8 different countries found small to moderate effect sizes for positive symptoms, negative symptoms, mood, and general life functioning (Wykes et al., 2008). CBT has been used as an adjunctive treatment for schizophrenia in Great Britain for over 10 years, and the results have been positive, even in community settings (Sensky et al., 2000; Turkington, Kingdom, & Turner, 2002; Wykes et al., 2008). One study has found that stress management training (discussed in Chapter 7) was effective in reducing stress among people with schizophrenia—a noteworthy outcome indeed, given the link between stress and relapse (Norman et al., 2002).

Therapies That Focus on Basic Cognitive Functions In recent years researchers have been attending to fundamental aspects of cognition that are disordered in schizophrenia, in an attempt to improve these functions and thereby favorably affect behavior. The fact that positive clinical outcomes from risperidone are associated with improvements in certain kinds of memory (Green et al., 1997) lends support to the more general notion that therapies directed at basic cognitive processes—the kind that nonclinical cognitive scientists study—holds promise for improving the social and emotional lives of people with schizophrenia. This general approach concentrates on trying to normalize such functions as attention and memory, which are known to be deficient in many people with schizophrenia and are associated with poor social adaptation (Green et al., 2000).

Recently developed treatments that seek to enhance basic cognitive functions such as verbal learning ability are referred to as **cognitive enhancement therapy (CET)** or *cognitive training*. A 2-year randomized controlled clinical trial compared group-based CET with enriched supportive therapy (EST). CET consisted of nearly 80 hours of computer-based training in attention, memory, and problem solving. Groups also worked on such daily-life, social-cognitive skills as reading

and understanding newspaper editorials, solving social problems, and starting and maintaining conversations. EST included supportive and educational elements. All people were also taking medications. At the 1- and 2-year follow-up assessments, CET was more effective than EST in improving cognitive abilities in problem solving, attention, social cognition, and social adjustment, while symptom reduction was the same for both treatments (Hogarty et al., 2004). People who received CET were also rated as being more ready for employment and, in fact, tended to be employed at the end of 2 years, largely driven by the fact that these people were more likely to be in volunteer positions than those in the EST group. Thus, CET is effective at reducing symptoms and improving cognitive abilities, and it appears to be linked to good functional outcomes, such as employment.

A recent review of 17 other randomized trials of cognitive training therapies shows that these interventions, for the most part, improve cognitive abilities, whether the treatments focus on specific tasks (e.g., a memory test) or on broader strategies (e.g., problem solving) or whether done via computer-based training (Twamley, Jeste, & Bellack, 2003). Only a few of these studies included measures of symptoms and functional outcomes, such as employment or general functioning, but those that did generally found that cognitive training improved symptoms and functional outcomes. As promising as these findings are, nearly all of the studies have been with white men; thus, their generalizability remains to be established. And not all studies yield positive results (Pilling et al., 2002).

Case Management After large numbers of people were discharged from hospitals (referred to as deinstitutionalization) in the 1960s, many people with schizophrenia no longer resided in hospitals and thus had to fend for themselves in securing needed services. Lacking the centralized hospital as the site where most services were delivered, the mental health system became more complex. In 1977, fearing that many people with schizophrenia were not accessing services, the National Institute of Mental Health established a program giving grants to states to help people with schizophrenia cope with the mental health system. Out of this program, a new mental health specialty, the case manager, was created.

Initially, case managers were basically brokers of services; because they were familiar with the system, they were able to get people with schizophrenia into contact with providers of whatever services they required. As the years passed, different models of case management developed. The major innovation was the recognition that case managers often needed to provide direct clinical services and that services might best be delivered by a team rather than brokered out. The Assertive Community Treatment model (Stein & Test, 1980) and the Intensive Case Management model (Surles et al., 1992) both entail a multidisciplinary team that provides services in the community, such as medication, treatment for substance abuse, help in dealing with stressors people with schizophrenia face regularly (such as managing money), psychotherapy, vocational training, and assistance in obtaining housing and employment. Case managers hold together and coordinate the range of medical and psychological services that people with schizophrenia need to keep functioning outside of institutions and with some degree of independence and peace of mind (Kopelowicz et al., 2002).

Indications are that this more intensive treatment is superior to less intensive methods in reducing time spent in the hospital, improving housing stability, and ameliorating symptoms (Mueser et al., 1998). However, more intensive case management has not shown positive effects in other domains, such as improvement in social functioning. In order for this approach to be effective, there have to be enough case managers for people with schizophrenia. Too often, the caseloads of these mental health professionals are much too high.

Residential Treatment Residential treatment homes, or "halfway houses," are sometimes good alternatives for people who do not need to be in the hospital but are not quite well enough to live on their own or even with their family. These are protected living units, typically located in large, formerly private residences. Here people discharged from the hospital live, take their meals, and gradually return to ordinary community life by holding a part-time job or going to school. As part of what is called *vocational rehabilitation*, residents learn marketable skills that can help them secure employment and thereby increase their chances of remaining in the community. Living arrangements may be relatively unstructured; some houses set up money-making enterprises that help train and support the residents.

Depending on how well funded the residential treatment facility is, the staff may include psychiatrists or clinical psychologists or both. The frontline staff members are paraprofessionals, often undergraduate psychology majors or graduate students in clinical psychology or social work, who live at the facility and act both as administrators and as friends to the residents. Group meetings, at which residents talk out their frustrations and learn to relate to others in honest and constructive ways, are often part of the routine. There are many such programs across the United States that have helped thousands of people with schizophrenia make enough of a social adaptation to be able to remain out of the hospital.

The need in the United States for effective residential treatment cannot be underestimated, especially in light of the deinstitutionalization that has seen tens of thousands of people discharged from hospitals. People with schizophrenia almost always need follow-up community-based services, and these are scarce. Indeed, today a large percentage of homeless people in the United States are mentally ill, including many people with schizophrenia. Social Security benefits are available to those with schizophrenia, but if they do not have an address, they often do not receive all the benefits to which they are entitled. Though there are good residential treatment programs available, there are not enough of them.

Integrating therapy with gainful employment is important in keeping people with schizophrenia out of hospitals (Kopelowicz & Liberman, 1998; Kopelowicz et al., 2002). For example, the U.S. government has begun to recognize the importance of employment by allowing people with schizophrenia to continue receiving Social Security benefits for up to 2 years while they are earning money from (low-paying) jobs that can increase their chances of living independently or at least outside of the hospital. This welcome change in policy (from one that terminated such benefits once the person began earning money) represents a recognition of the harmful effects of not working and not being able to live in a reasonably independent manner.

Still, obtaining employment can pose a major challenge because of bias and stigma against people with schizophrenia. Although the Americans with Disabilities Act of 1990 prohibits employers from asking applicants if they have a history of serious mental illness, people with schizophrenia still have a difficult time obtaining regular employment because their symptoms make negatively biased employers fearful of hiring them. Also a factor is how much leeway employers are willing to give people whose thinking, emotions, and behavior can be unconventional to some degree.

Despite these difficulties, the trend seems to be to do whatever is necessary to assist people in working and living in as autonomous a manner as their physical and mental condition will allow (Kopelowicz & Liberman, 1998). Additional funding will be needed to create more residential treatment facilities with the hope of reducing the number of people with schizophrenia who are without treatment.

Remaining Challenges in the Treatment of Schizophrenia

It is increasingly recognized that early intervention is important and useful in affecting the course of schizophrenia over time. That is, getting people with schizophrenia onto the right medications and providing support and information to the family and appropriate psychotherapy can reduce the severity of relapses in the future (Drury et al., 1996). It is also important to teach people with schizophrenia social skills and more reality-based thinking so that they can function outside the hospital and probably reduce the EE encountered both inside and outside the home. Families affected by schizophrenia are encouraged to join support groups and formal organizations, such as the National Alliance on Mental Illness, to reduce the isolation and stigma associated with having a family member who has schizophrenia.

Despite the promise of these interventions, there is often a gap between what treatments are available and what treatments are actually received. This issue was highlighted in a study that involved interviewing over 700 people with schizophrenia and reviewing their medical records (Lehman et al., 1998). As expected, almost 90 percent had been prescribed antipsychotic drugs, but of these people only 62 percent received a dose in the recommended range. About 15 percent got too little, and the remainder got too much. Further, although over 90 percent of people with schizophrenia were prescribed maintenance doses of drugs, only 29 percent of these received a dose in the recommended range; of the 71 percent who did not receive

a recommended dose, about half were getting too much and half too little. African Americans were much more likely than whites to be prescribed maintenance doses that were too high.

Psychosocial treatments were also examined, but these were more difficult to evaluate because records of patient reports did not allow the researchers to know whether the treatment was one of those considered effective (such as family therapies or social skills training). Just in terms of whether any psychosocial treatments at all were prescribed for people with schizophrenia, the study shows that some sort of individual or group therapy was provided for over 90 percent of patients in the hospital. But for people with schizophrenia who had regular contact with their families, family treatment of some sort was prescribed for only about 40 percent. For unemployed people with schizophrenia, vocational rehabilitation (teaching job skills) was prescribed for only about 30 percent.

Conclusion? Many people with schizophrenia are not getting anything near optimal therapy. Indeed, though the kind of integrated treatment we have been describing is promising, the sad fact is that it is not widely available or accessible to most people with schizophrenia and their families. The reasons for this are unclear (Baucom et al., 1998; Dixon et al., 1997).

Preventing substance abuse among people with schizophrenia is largely an unmet challenge. The lifetime prevalence rate for substance abuse among people with schizophrenia is an astounding 50 percent (Kosten & Ziedonis, 1997); the rate is even higher among the homeless mentally ill population. Programs for treating substance abuse usually exclude people who are seriously mentally ill, and programs for treating people who are seriously mentally ill usually exclude substance abusers. In both instances the reason is that the comorbid condition is considered disruptive to the treatment (Mueser, Bellack, & Blanchard, 1992). This is a situation that simply must be turned around.

Check Your Knowledge 11.3

True or false?

1. First-generation antipsychotics include medications like Haldol or Prolixin; second-generation antipsychotics include clozapine and olanzapine.
2. Second-generation antipsychotics produce more motor side effects than first-generation antipsychotics.
3. Cognitive behavior therapy, but not cognitive enhancement therapy, is effective for schizophrenia, if given along with medications.
4. One important focus of residential treatment programs is to help people with schizophrenia become employed.

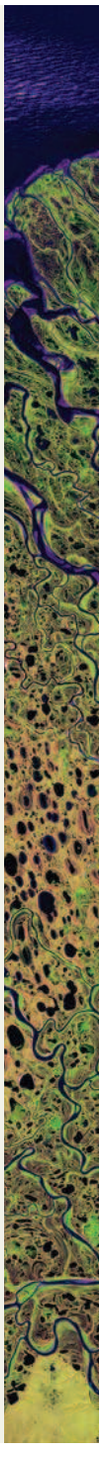
Summary

Clinical Description

- The symptoms of schizophrenia involve disturbances in several major areas, including thought, perception, and attention; motor behavior; affect; and life functioning. Symptoms are typically divided into positive, negative, and disorganized categories. Positive symptoms include excesses and distortions, such as delusions and hallucinations. Negative symptoms are behavioral deficits, which include flat affect, avolition, alogia, asociality, and anhedonia. Disorganized symptoms include disorganized speech and behavior. Other more rare symptoms include catatonia and inappropriate affect.
- The DSM-IV-TR includes several subtypes of schizophrenia, including disorganized, catatonic, and paranoid. These subtypes are based on the prominence of particular symptoms (e.g., delusions in the paranoid subtype) and reflect the variations in behavior found among people diagnosed with schizophrenia. However, the subtypes have little predictive validity.

Etiology

- The evidence for genetic transmission of schizophrenia is impressive. Family and twin studies suggest a genetic component; adoption studies show a strong relationship between having a parent with schizophrenia and the likelihood of developing the disorder, typically in early adulthood. Molecular genetics studies are still in need of replication. The most promising findings to date seem to indicate genes such as DTNBP1, NGR1, and COMT.
- The genetic predisposition to develop schizophrenia may involve neurotransmitters. It appears that increased sensitivity of dopamine receptors in the limbic area of the brain is related to the positive symptoms of schizophrenia. The negative symptoms may be due to dopamine underactivity in the prefrontal cortex. Other neurotransmitters, such as serotonin, glutamate, and GABA, may also be involved.



- The brains of some people with schizophrenia have enlarged ventricles and problems with the prefrontal cortex. Some of these structural abnormalities could result from maternal viral infection during the second trimester of pregnancy or from damage sustained during a difficult birth.
- The diagnosis of schizophrenia is most frequently applied to people of the lowest socioeconomic status, apparently because of downward social mobility created by the disorder. In addition, vague communications and conflicts are evident in the family life of people with schizophrenia, though it is less clear whether these contribute to their disorder. High levels of expressed emotion in families, as well as increases in general life stress, have been shown to be an important determinant of relapse. Developmental studies have identified problems in childhood that were there prior to the onset of schizophrenia, but these studies were not designed to predict schizophrenia, so it is difficult to interpret the findings. High-risk studies suggest that the causes of positive and negative symptoms may be different. Other studies have found cognitive problems in childhood to predict the onset of adult psychopathology, but not specifically schizophrenia.

Treatment

- Antipsychotic drugs, especially the phenothiazines, have been widely used to treat schizophrenia since the 1950s. Second-generation antipsychotic drugs, such as clozapine and risperidone, are also effective and produce fewer motoric side effects, though they have their own set of side effects. Drugs alone are not a completely effective treatment, though, as people with schizophrenia need to be (re)taught ways of dealing with the challenges of everyday life.
- The efficacy of psychoanalytic treatments has not been supported by evidence. In contrast, family therapy aimed at reducing high levels of expressed emotion has been shown to be valuable in preventing relapse. In addition, social skills training and various cognitive behavioral therapies have helped people with schizophrenia meet the inevitable stresses of family and community living. Recent efforts to change the thinking of people with schizophrenia with cognitive behavior therapy are showing promise as well.
- The most promising approaches to treatment today emphasize the importance of both pharmacological and psychosocial interventions. Unfortunately, such integrated treatments are not widely available.

Answers to Check Your Knowledge Questions

11.1 1. flat affect; 2. delusion or ideas of reference; 3. anhedonia (anticipatory); 4. disorganized thinking or derailment.

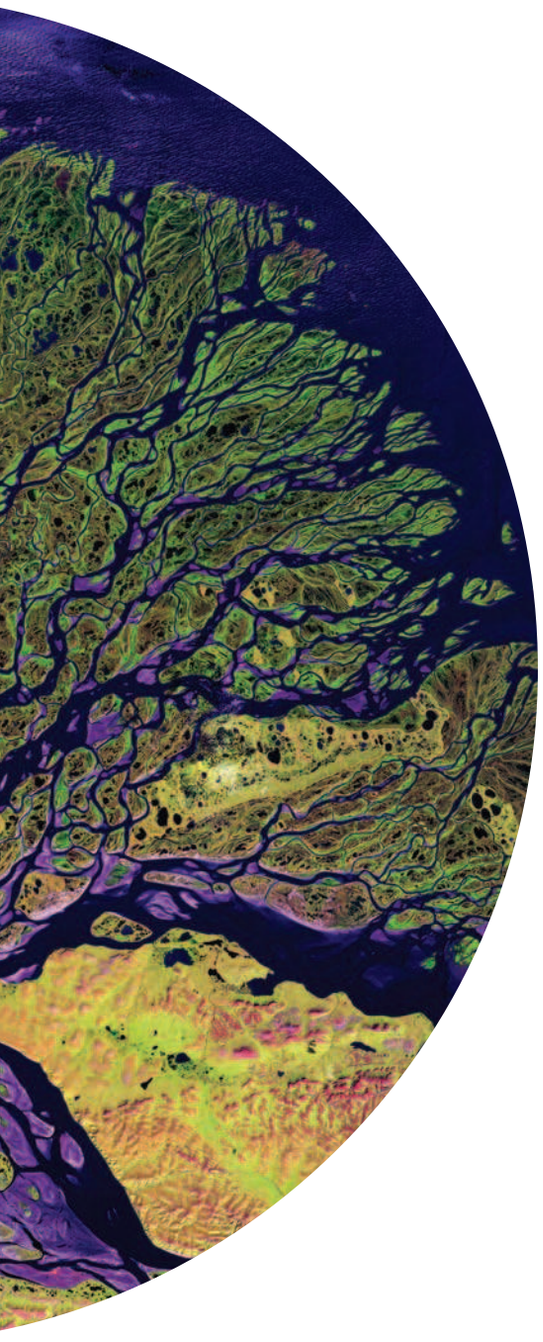
11.2 1. Family, adoption; 2. DTNBP1, NGR1; 3. prefrontal; 4. Hostility, critical comments, emotional overinvolvement.

11.3 1. T; 2. F; 3. F; 4. T

Key Terms

alogia
anhedonia
anticipatory pleasure
antipsychotic drugs
asociality
avolition
brief psychotic disorder
catatonia
catatonic immobility
catatonic schizophrenia
cognitive enhancement therapy (CET)
consummatory pleasure
delusional disorder
delusions
dementia praecox
disorganized behavior
disorganized schizophrenia
disorganized speech
disorganized symptoms
dopamine theory
expressed emotion (EE)
flat affect
grandiose delusions
hallucinations
ideas of reference
inappropriate affect
loose associations (derailment)
negative symptoms
paranoid schizophrenia
positive symptoms
prefrontal cortex
residual schizophrenia
schizoaffective disorder
schizophrenia
schizophreniform disorder
second-generation antipsychotic drugs
social selection theory
social skills training
sociogenic hypothesis
undifferentiated schizophrenia

12 Personality Disorders



LEARNING GOALS

1. Be able to explain the issues in classifying personality disorders and to describe alternative dimensional approaches to diagnosis.
2. Be able to define the key features of each personality disorder.
3. Be able to describe the genetic, neurobiological, social, and other risk factors for personality disorders, and be able to discuss problems in the research on etiology.
4. Be able to describe the available medication and psychological treatments of personality disorders.

Clinical Case: Mary

Mary was single and 26 years old when she was first admitted to a psychiatric hospital. She had been in outpatient treatment with a psychologist for several months when her persistent thoughts of cutting, burning, and killing herself led her therapist to conclude that she needed more than outpatient treatment.

Mary's first experience with psychotherapy occurred when she was an adolescent. Her grades declined sharply in the eleventh grade, and her parents suspected she was using drugs. She began to miss curfews and, occasionally, to stay out all night. She often skipped school. Family therapy was started, and it seemed to go well at first. Mary was enthusiastic about the therapist and asked for additional, private sessions with him.

During the private sessions, Mary revealed she had used drugs extensively, including "everything I can get my hands on." She had been promiscuous and had prostituted herself several times to get drug money. Her relationships with her peers were changeable, to say the least. There was a constant parade of new friends, whom Mary at first thought to be the greatest ever but who soon disappointed her and were cast aside, often in very unpleasant ways. Except for the one person with whom she was currently enamored, Mary had no friends. She said that she stayed away from others for fear that they would harm her in some way.

After several weeks of family therapy, Mary's parents noticed that Mary was angry and abusive toward the therapist. After a few more weeks had passed, Mary refused to attend any more sessions. In a subsequent conversation with the therapist, Mary's father learned that she had behaved seductively toward the

therapist during their private sessions and that her changed attitude coincided with his rejection of her advances, despite the therapist's attempt to mix firmness with warmth and empathy.

Mary managed to graduate from high school and enrolled in a local community college, but the old patterns returned. Poor grades, cutting classes, continuing drug use, and lack of interest in her studies finally led her to quit college in the middle of the first semester of her second year. After leaving school, Mary held a series of low-paying jobs. Most of them didn't last long, as her relationships with co-workers paralleled her relationships with her peers in high school. When Mary started a new job she would find someone she really liked, but something would come between them, and the relationship would end angrily. She was often suspicious of her co-workers and reported that she heard them plotting how to prevent her from getting ahead on the job. She was quick to find hidden meanings in their behavior, as when she interpreted being the last person asked to sign a birthday card to mean that she was the least liked person in the office. She indicated that she "received vibrations" from others and could tell when they really didn't like her even in the absence of any direct evidence.

Mary's frequent mood swings, with periods of depression and extreme irritability, led her to seek therapy several times. But after initial enthusiasm, her relationships with therapists always deteriorated, resulting in premature termination of therapy. By the time of her hospitalization, she had seen six therapists.

THE PERSONALITY DISORDERS ARE a heterogeneous group of disorders defined by long-standing, pervasive, and inflexible patterns of behavior and inner experience that deviate from the expectations of a person's culture. These problematic patterns are manifested in at least two of the following areas: cognition, emotions, relationships, and impulse control. Like all other DSM-IV-TR disorders, personality disorders are not diagnosed unless they cause distress or functional impairment.

As we examine the personality disorders, some might seem to fit people we know, not to mention ourselves! This seems a good time to remind readers about the medical student syndrome, so called because medical students (and psychology students) have a tendency to see themselves or their families and friends in descriptions of the disorders they study. For example, suppose you hear a loud burst of laughter just as you enter a crowded room, and this makes you feel that you are the target of some joke and that people are talking about you. Such concerns would qualify as symptoms of paranoid personality disorder only if they occurred often enough and intensely enough to prevent you from developing close personal relationships. This illustrates a general point: from time to time, we all behave, think, and feel in ways that look similar to symptoms of personality disorders, but an actual personality disorder is defined by the extreme, inflexible, and maladaptive ways in which these traits are expressed. The symptoms of personality disorders are pervasive and persistent.

In this chapter we begin by looking at how personality disorders are classified in the DSM, at issues related to the DSM diagnostic system for personality disorders, and at an alternative system of classification. Next, we turn to clinical descriptions of the personality disorders and to discussions of their etiology. We conclude with discussions of the treatment of personality disorders. Throughout, the extent of our coverage depends on how much is known about the specific personality disorder under consideration; for example, there have been few studies of histrionic personality disorder, but there is a vast literature on antisocial personality disorder.

Classifying Personality Disorders

There is considerable debate about the best way to classify personality disorders. We begin by providing an overview of the DSM-IV-TR approach, then turn to an alternate dimensional approach.

The DSM Approach to Classification

In DSM-IV-TR, the 10 different personality disorders are classified in three clusters, reflecting the idea that these disorders are characterized by odd or eccentric behavior (cluster A); dramatic, emotional, or erratic behavior (cluster B); or anxious or fearful behavior (cluster C). These clusters form a useful organizational framework for our discussions in this chapter. Table 12.1 presents the personality disorders, their key features, and their grouping in clusters.

Beginning with DSM-III, personality disorders were placed on a separate axis, Axis II, to ensure that clinicians would consider whether a personality disorder is also present. Typically, clients seek help for the symptoms of an Axis I disorder (such as panic disorder), without initially emphasizing symptoms of personality disorders. It is important to note, though, that many people with an Axis I disorder will also experience an Axis II disorder. When this comorbidity occurs, the personality disorder shapes the form of the Axis I symptoms. For example, a person diagnosed with an anxiety disorder on Axis I and obsessive-compulsive personality disorder on Axis II will express anxiety in perfectionistic and controlling ways. As one researcher put it, different personality disorders "evoke contrasting ways of perceiving and coping" with Axis I disorders, which means that clinicians should consider the "context of personality" when dealing with Axis I disorders (Millon, 1996, p. vii). Comorbid personality disorders are associated with more severe symptoms, poorer social functioning, and worse treatment outcomes for Axis I disorders (Clark, 2007). As a result, personality disorders are commonly encountered in treatment settings. See Table 12.2 for the rates of personality disorders in the general community as compared to treatment settings.

Diagnostic Reliability Before DSM-III, the diagnosis of personality disorders was very unreliable—one clinician might diagnose a flamboyant patient with narcissistic personality disorder, whereas another might diagnose the patient with histrionic personality disorder. DSM-III began a trend toward improved reliability by including specific diagnostic criteria for personality disorders, as it did for other disorders (Coolidge & Segal, 1998). Structured interviews were also developed to assess personality disorders, and these, too, helped improve diagnostic reliability.

Table 12.1 Key Features of the DSM-IV-TR Personality Disorders

Cluster A (odd/eccentric)	
Paranoid	Distrust and suspiciousness of others
Schizoid	Detachment from social relationships and restricted range of emotional expression
Schizotypal	Lack of capacity for close relationships, cognitive distortions, and eccentric behavior
Cluster B (dramatic/erratic)	
Antisocial	Disregard for and violation of the rights of others
Borderline	Instability of interpersonal relationships, self-image, and affect, as well as marked impulsivity
Histrionic	Excessive emotionality and attention seeking
Narcissistic	Grandiosity, need for admiration, and lack of empathy
Cluster C (anxious/fearful)	
Avoidant	Social inhibition, feelings of inadequacy, and hypersensitivity to negative evaluation
Dependent	Excessive need to be taken care of, submissive behavior, and fears of separation
Obsessive-compulsive	Preoccupation with order, perfection, and control

Table 12.2 Rates of DSM-IV Personality Disorders in the Community and in Treatment Settings

Disorder	Prevalence in the Community (%)	Prevalence in Treatment Settings (%)	Gender Ratio
Paranoid	0.7–5.1	4.2	Males > females
Schizoid	0.9–1.7	1.4	Males > females
Schizotypal	0.6–1.10	0.6	Males > females
Antisocial	1.2–4.1	3.6	Males > females
Borderline	0.5–3.9	9.3	Females > males
Histrionic	0.2–0.9	1.0	Females > males
Narcissistic	0.0–2.2	2.3	Males > females
Avoidant	1.8–6.4	14.7	Males = females
Dependent	0.1–0.8	1.4	Females > males
Obsessive-compulsive	4.7	8.7	Males > females

Source: Prevalence estimates for community settings are drawn from Crawford et al. (2005) and Samuels et al. (2002). Prevalence estimates for treatment settings are drawn from Zimmerman, Rothschild, & Chelminski (2005).

Table 12.3 shows interrater reliabilities from a study of the DSM-IV personality disorders using a structured diagnostic interview administered by experts (Zanarini et al., 2000). Although diagnoses of most personality disorders have adequate or good reliability when structured interviews are used, schizoid personality disorder is still characterized by relatively low interrater reliability. This may be because clinicians differ in their thresholds for seeing a behavior as pathological. Of concern, most clinicians do not use structured interviews to assess personality, so in real life, the reliability of personality diagnoses is likely to be relatively low (Heumann & Moreg, 1990).

When there is disagreement about how to apply diagnostic criteria, there is a potential for the personal biases of a clinician to influence decisions. Some have noted that clinicians tend to be more likely to decide that certain behaviors are pathological for women more than they are for men. (See Focus on Discovery 12.1 for discussion of gender biases in diagnosing personality disorders.)

One issue in assessing personality disorders is whether people can accurately describe their own personalities. When clients' reports of their personality disorder symptoms are compared

Table 12.3 Interrater Reliability for the Personality Disorders

Diagnosis	Interrater Reliability
Paranoid	.86
Schizoid	.69
Schizotypal	.91
Antisocial	.97
Borderline	.90
Histrionic	.83
Narcissistic	.88
Avoidant	.79
Dependent	.87
Obsessive-compulsive	.85

Source: Zanarini et al. (2000).

FOCUS ON DISCOVERY 12.1

Gender and Personality Disorders

For many personality disorders, prevalence varies a great deal by gender (see Table 12.2). For example, women are more likely than men to be diagnosed with borderline, histrionic, and dependent personality disorders, and men are more likely than women to be diagnosed with antisocial, narcissistic, and obsessive-compulsive personality disorders. Before the publication of DSM-IV, some researchers argued that certain of the diagnostic criteria for personality disorders pathologized feminine traits (Kaplan, 1983). For example, histrionic personality disorder included criteria for emotional lability, a focus on physical appearance, and sexual seductiveness. Are these traits more reinforced, and therefore more common, among women? In response to these types of criticisms, DSM-IV refined such criteria to make them more gender-neutral. For example, the criterion for a focus on physical appearance was modified to read as "consistently uses physical appearance to draw attention to self," and the text now includes descriptions of ways in which men might show macho behaviors that fit this criterion (Hartung & Widiger, 1998).

Despite these changes to the criteria, research has suggested that clinicians are still biased by gender stereotypes in the way they diagnose personality disorders. For example, clinicians might focus on different behaviors, depending on whether they are diagnosing a man or a woman. In a typical test of this issue, two different vignettes are written involving people with personality disorders. The versions are identical except that in one, the person in the vignette is named Joan, and in the other, the person is named John. Clinicians read the vignettes and provide the most likely diagnosis. In these types of studies, clinicians are more likely to diagnose the person as having histrionic personality disorder if the vignette is about a woman and more likely to diagnose the person as having antisocial personality disorder if the vignette is about a man (Garb, 1997). These findings highlight how important it is for clinicians to be aware of biases.

to the reports of friends and families, agreement tends to be low (Klonsky, Oltmanns, & Turkheimer, 2002). Intriguingly, it is not the case that people always downplay their difficulties; sometimes clients are more harsh than are their friends and family members, and sometimes they are less harsh in describing their personality symptoms. Nonetheless, having more than one perspective on personality disorders is important. Interviews with people who know the patient well improve the reliability of diagnosis (Bernstein et al., 1997). However, fewer than 10 percent of published studies of personality disorders gather data from people other than the person being diagnosed (Bornstein, 2003), even though the diagnostic criteria often specify that people with personality disorders tend to see themselves in distorted ways (Thomas, Turkheimer, & Oltmanns, 2003).

By definition, personality disorders are supposed to be more stable over time than episodic Axis I disorders like major depressive disorder. Therefore, studies of test–retest reliability—whether clients receive the same diagnosis at two assessments separated by some time interval—are an important test of the basic definition of the disorder. Figure 12.1 shows a summary of test–retest reliability (i.e., diagnostic stability) from one study (Shea et al., 2002). The figure indicates that diagnoses of personality disorders are much more stable than diagnoses for major depressive disorder; nevertheless, about half of the people initially diagnosed with a personality disorder did not receive the same personality disorder diagnosis when they were interviewed one and two years later. These results, then, indicate that many of the personality disorders may not be as enduring as the DSM asserts.

Even though the personality disorders do not have high diagnostic stability, there are several issues that are important to consider. First, many of the people in the study still had symptoms at the second interview, just not at the levels required for diagnosis. Second, even if people no longer meet the full criteria for personality disorder, there might be a sustained influence of personality disorders on functioning. In one study, people with and without personality disorders were reinterviewed at a 15-year follow-up; baseline diagnoses of personality disorders were a significant predictor of lower functioning 15 years later (Hong et al., 2005).

In sum, there are many issues to consider in obtaining reliable estimates of personality. Using structured interviews and multiple informants can improve reliability, but a core concern is that many diagnoses are not stable. As pointed out by Lee Anna Clark (2007), most laypeople know that understanding personality requires gathering data across multiple situations, over time, from many different perspectives. Perhaps it is not so surprising, then, that obtaining high-quality assessments of personality disorder would require careful assessments gathered from different informants at different time points.

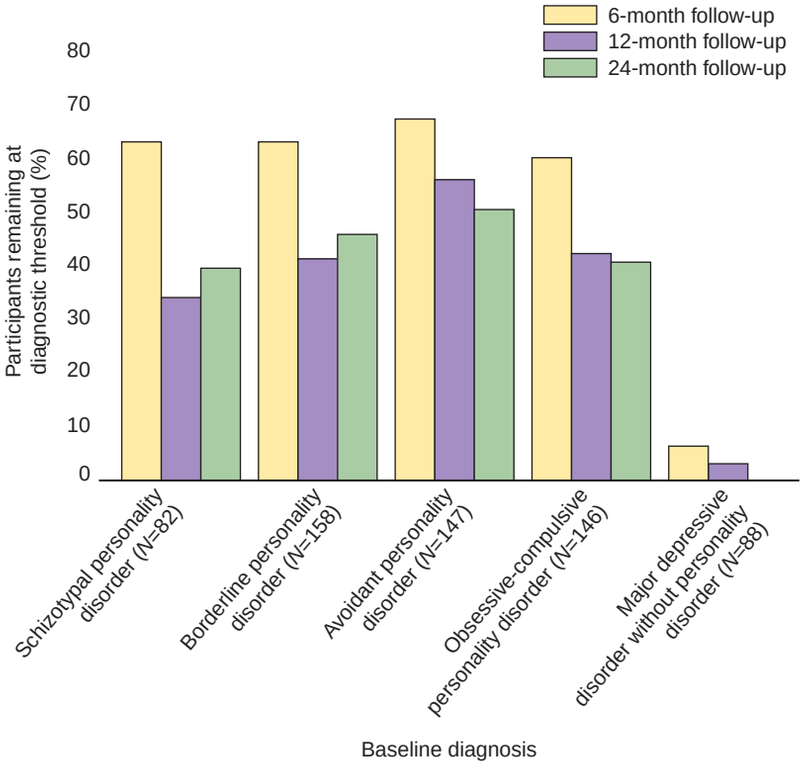


Figure 12.1 Test–retest stability for personality disorders and major depressive disorder across 6-, 12-, and 24-month follow-up interviews. Drawn from Grilo et al. (2004); Shea et al. (2002).

Comorbidity A major problem in classifying personality disorders arises from their comorbidity with Axis I disorders and with each other. The clinical case of Mary illustrates this issue: Mary met the diagnostic criteria not only for borderline personality disorder but also for paranoid personality disorder. More than 50 percent of people diagnosed with a personality disorder meet the diagnostic criteria for another personality disorder, and more than two-thirds meet lifetime criteria for an Axis I disorder (Lenzenweger et al., 2007). These facts are discouraging when we try to interpret the results of research that compares people who have a specific personality disorder with some control group. If, for example, we find that people with borderline personality disorder differ from healthy people, is our finding related to borderline personality disorder or to personality disorders in general, or perhaps even to comorbid Axis I disorders?

In sum, the categorical system of the DSM might not be ideal for classifying personality disorders, because of concerns about the lack of test–retest stability, the potential for gender bias, and the high rates of comorbidity. These types of concerns have led some authors to recommend shifting to a dimensional approach.

A Dimensional Approach to Personality: The Five-Factor Model

The personality traits used for classification form a continuum; that is, most of these traits are present in varying degrees across people (see p. 70 for a discussion of dimensional versus categorical systems). When people with a personality disorder take a personality inventory, they endorse more extreme personality traits than those seen in the general population (Clark & Livesley, 2002). Thus, personality disorders might be defined by extremes of characteristics we all possess. Given this, a dimensional approach to personality is being considered as one option for DSM-V.

There are a number of advantages of using a dimensional approach to personality. Most importantly, it handles the comorbidity problem, because comorbidity is a difficulty only in a categorical classification system like the one used in DSM-IV-TR. A dimensional system also links normal and abnormal personality, so general findings on personality traits become relevant to the study of personality disorders. Clinicians also report that they find a dimensional approach to personality to be more helpful than the current categorical system in describing clients and considering treatment options (Samuel & Widiger, 2006; Verheul, 2005).

Although there are many different models of personality, a major focus is on the **five-factor model** (McCrae & Costa, 1990), in which the five factors, or major dimensions, of personality are neuroticism, extraversion/introversion, openness to experience, agreeableness/antagonism, and conscientiousness. Table 12.4 presents questionnaire items that assess each of these dimensions; by reading the items, you can get a sense of what each dimension means. These dimensions of personality are moderately heritable (Jang et al., 2002), and the patterns of heritability for these dimensions are consistent across cultures (Yamagata et al., 2006). These personality traits prospectively predict important life outcomes, such as divorce, educational attainment, and occupational status (Roberts et al., 2007).

Several studies have shown that each of the different personality disorders can be explained using a set of these personality traits (Widiger & Costa, 1994). A meta-analysis shows that findings are fairly consistent across a range of studies that have mapped personality disorder diagnoses onto the dimensions of the five-factor model. Most personality disorders are characterized by high neuroticism and antagonism. High extraversion was tied to histrionic and narcissistic disorders (two disorders that involve dramatic behavior), whereas low extraversion was tied to disorders that involve social isolation, such as schizoid, schizotypal, and avoidant personality disorders (Saulsman & Page, 2004).

The five-factor model is not without its critics, however. In a study in which people with personality disorders completed a questionnaire to assess the five factors, the profiles of the various personality disorders turned out to be rather similar to one another (Morey et al., 2000). Some might say this is fine, and that fewer dimensions would simplify things. But proponents of the need to be more specific have responded to this difficulty by claiming that differentiating the personality disorders requires breaking down the five factors into their "facets" (Lynam

Table 12.4 Sample Items from the Revised NEO Personality Inventory Assessing the Five-Factor Model

Personality Trait	Sample Items
Neuroticism	I often feel tense or jittery.
Extraversion/introversion	I really like most people I meet.
Openness to experience	I have a very active imagination.
Agreeableness/antagonism	I tend to be cynical and skeptical of others' intentions (reverse scored).
Conscientiousness	I often come into situations without being prepared (reverse scored).

& Widiger, 2001). Each of the five factors has six facets, or components; for example, the extraversion factor includes the facets of warmth, gregariousness, assertiveness, activity, excitement seeking, and positive emotionality. Differentiating among the personality disorders might require a more detailed assessment that includes these specific personality facets.

Beyond the need to consider facets, it appears that some disorders, such as schizotypal personality disorder, are more distinct than being just extreme points along a dimension; statistical analyses suggest that people with these disorders tend to be qualitatively different from other people. For example, people with schizotypal personality disorder tend to experience perceptual oddities that others don't experience even in mild degrees (Haslam & Kim, 2002). The five-factor model is not a total solution to the problem of classifying personality disorders, but the important point is that a dimensional model has several distinct advantages compared to the current categorical system.

Problems with classifying personality disorders should not lead us to underestimate the importance of being able to identify them. Personality disorders are prevalent, and they cause severe impairments. We now turn to a review of the clinical description and etiology of the personality disorders in cluster A, cluster B, and cluster C.

Check Your Knowledge 12.1 (Answers are at the end of the chapter.)

True or false?

1. Most of the DSM-IV-TR personality disorders can be diagnosed with good interrater reliability.
2. Most people diagnosed with a personality disorder will still show that personality disorder one year later.
3. People who meet diagnostic criteria for a personality disorder are likely to meet diagnostic criteria for a second or third personality disorder as well.
4. Most studies of personality disorders include informants.
5. The seven-factor model is a popular approach to personality dimensions.

Odd/Eccentric Cluster

DSM-IV-TR Criteria for Paranoid Personality Disorder

Presence of four or more of the following signs of distrust and suspiciousness, beginning in early adulthood and shown in many contexts:

- Pervasive unjustified suspiciousness of being harmed, deceived, or exploited
- Unwarranted doubts about the loyalty or trustworthiness of friends or associates
- Reluctance to confide in others because of suspiciousness
- The tendency to read hidden meanings into the innocuous actions of others
- Bears grudges for perceived wrongs
- Angry reactions to perceived attacks on character or reputation
- Unwarranted suspiciousness of the fidelity of partner

The odd/eccentric cluster of personality disorders includes paranoid personality disorder, schizoid personality disorder, and schizotypal personality disorder. The symptoms of these three disorders bear some similarity to the types of bizarre thinking and experiences seen in schizophrenia. In personality disorders, though, the bizarre thinking and experiences are less severe than they are in schizophrenia.

Paranoid Personality Disorder

People with **paranoid personality disorder** are suspicious of others. This suspicion influences relationships with family, colleagues, and casual acquaintances. They expect to be mistreated or exploited and thus are secretive and continually on the lookout for signs of trickery and abuse. They are often hostile and react angrily to perceived insults. They might read hidden threatening messages into events.

This disorder is different from paranoid schizophrenia because other symptoms of schizophrenia, such as hallucinations, are not present and there is less impairment in social and occupational functioning. Also absent is the cognitive disorganization that is characteristic of schizophrenia. It differs from delusional disorder because full-blown delusions are not present. Paranoid personality disorder co-occurs most often with schizotypal, borderline, and avoidant personality disorders.

Schizoid Personality Disorder

Like Joe (see clinical case), people with **schizoid personality disorder** do not desire or enjoy social relationships and usually have no close friends. They appear dull, bland, and aloof and have no warm, tender feelings for other people. They rarely experience strong emotions, are not interested in sex, and have few pleasurable activities. Indifferent to praise, criticism, and the sentiments of

Clinical Case: Joe

Joe was a 53-year-old unmarried Vietnam veteran who was referred for treatment by his general practitioner, who was concerned about Joe's disconnection from life. Joe reluctantly agreed to see a therapist. He had not worked in several years and survived on a small disability pension from the Veterans Administration. He said that he found it unpleasant to shop for groceries because he didn't like having other people around him. The landlady at his boarding house persisted in trying to introduce him to women, even though he had declared his lack of interest in each and every one of the 10 women she had pestered him to meet. He stated that he did not like talking, and in treatment he was often silent for long periods. He did talk about his sense that he had little connection with life and that he experienced little emotion other than mild irritability. Indeed, he was unable to describe a single person or activity that made him happy. After six weeks of treatment, Joe announced that he didn't think that he was a person who was going to feel any better from talking about things and that he had decided to spend his remaining savings to purchase a small cabin in a remote section of Maine. He seemed content with his decision, stating that by living there, he could avoid most interactions with people. He moved the next week.

others, people with this disorder are loners who pursue solitary interests. Comorbidity is highest for schizotypal, avoidant, and paranoid personality disorders, most likely because of the similar diagnostic criteria for the four disorders (see the DSM-IV-TR diagnostic criteria).

DSM-IV-TR Criteria for Schizoid Personality Disorder

Presence of four or more of the following are present from early adulthood:

- Lack of desire for or enjoyment of close relationships
- Almost always prefers solitude to companionship
- Little interest in sex
- Few or no pleasurable activities
- Lack of friends
- Indifference to praise or criticism from others
- Flat affect, emotional detachment

Schizotypal Personality Disorder

People with **schizotypal personality disorder** are often socially isolated, like people with schizoid personality, but they also show other, more eccentric symptoms, which are milder versions of the symptoms that define schizophrenia. (See the DSM-IV-TR diagnostic criteria for schizotypal personality disorder.) People with this disorder might have odd beliefs or magical thinking—for instance, the belief that they can read other people's minds and see into the future. It is also common for them to have ideas of reference (the belief that events have a particular and unusual meaning for them personally) and to show suspiciousness and paranoid ideation. They might also have recurrent illusions (inaccurate sensory perceptions), such as sensing the presence of a force or a person that is not actually there. In their speech, they might use words in an unusual and unclear fashion—for example, they might say "not a very talkable person" to mean a person who is not easy to talk to. Their behavior and appearance might also be eccentric—for example, they might talk to themselves or wear dirty and disheveled clothing. Their affect appears constricted and flat. A study of the relative importance of these symptoms for diagnosis found that paranoid ideation, ideas of reference, and illusions were most telling (Widiger, Frances, & Trull, 1987).

Comorbidity with other personality disorders is particularly high, even given the generally high comorbidity among personality disorders; on average, people with schizotypal personality disorder meet the diagnostic criteria for at least two other personality disorders, the most likely being avoidant personality disorder and paranoid personality disorder, perhaps because of overlapping criteria (McGlashon et al., 2000).

DSM-IV-TR Criteria for Schizotypal Personality Disorder

Presence of five or more of the following in many contexts beginning in early adulthood:

- Ideas of reference
- Peculiar beliefs or magical thinking, e.g., belief in extrasensory perception
- Unusual perceptions, e.g., distorted feelings about one's body
- Peculiar patterns of thought and speech
- Suspiciousness or paranoia
- Inappropriate or restricted affect
- Odd or eccentric behavior or appearance
- Lack of close friends
- Anxiety around other people, which does not diminish with familiarity

Etiology of the Personality Disorders in the Odd/Eccentric Cluster

What causes the odd thinking, bizarre behavior, and interpersonal difficulties that appear in this cluster of personality disorders? Each of the cluster A personality disorders appears to be highly heritable (Kendler et al., 2007). Beyond this, researchers don't know much about the etiology of paranoid personality disorder or schizoid personality disorder—as you can imagine, people with these disorders aren't likely to be interested in completing lengthy research interviews.

The genes that increase risk for schizotypal personality disorder appear to overlap with the genes that increase risk for schizophrenia. That is, family studies have shown that the relatives of clients with schizophrenia are at increased risk for schizotypal personality disorder (Nigg & Goldsmith, 1994), as are adopted children of biological mothers with schizophrenia (Tienari et al., 2003). People with schizotypal personality disorder also have deficits in cognitive and

neuropsychological functioning that are similar to but milder than those seen in schizophrenia (Cadenhead et al., 2002; Lenzenweger, 2001). Furthermore, and again paralleling findings from schizophrenia research, people with schizotypal personality disorder have enlarged ventricles and less temporal lobe gray matter (Dickey, McCarley, & Shenton, 2002).

Quick Summary

Personality disorders are defined by long-standing and pervasive ways of being that cause distress and impairment through their influence on cognition, emotions, relationships, and impulse control. Most people with personality disorders experience comorbid Axis I conditions as well as other personality disorders. In DSM-IV-TR, personality disorders are classified in three clusters, reflecting the idea that these disorders are characterized by odd or eccentric behavior (cluster A); dramatic, emotional, or erratic behavior (cluster B); or anxious or fearful behavior (cluster C). Interrater reliability of personality disorder diagnoses, particularly when clinicians use structured interviews, is strong. But despite the idea that personality disorders are defined as long-standing, test–retest reliability is only modest. Concerns have also been raised about gender bias in diagnoses. Some have argued that we should be measuring personality traits as dimensions rather than attempting to classify people with personality disorders. A key issue is how many personality traits should be assessed to adequately differentiate the types of problems that are encountered in clinical settings, but much of current research focuses on five personality factors.

The odd/eccentric cluster of personality disorders (cluster A) includes paranoid personality disorder, schizoid personality disorder, and schizotypal personality disorder. People with paranoid personality disorder are suspicious of others, people with schizoid personality disorder are socially aloof, and people with schizotypal personality disorder are eccentric in their thoughts and behavior. Genetic studies indicate that schizotypal personality disorder and schizophrenia are related. Cluster A personality disorders appear to be highly heritable.

Dramatic/Erratic Cluster

DSM-IV-TR Criteria for Borderline Personality Disorder

Presence of five or more of the following in many contexts beginning in early adulthood:

- Frantic efforts to avoid abandonment
- Unstable interpersonal relationships in which others are either idealized or devalued
- Unstable sense of self
- Self-damaging, impulsive behaviors in at least two areas, such as spending, sex, substance abuse, reckless driving, binge eating
- Recurrent suicidal behavior, gestures, or self-injurious behavior (e.g., cutting self)
- Chronic feelings of emptiness
- Recurrent bouts of intense or poorly controlled anger
- During stress, a tendency to experience transient paranoid thoughts and dissociative symptoms

The disorders in the dramatic/erratic cluster—borderline personality disorder, histrionic personality disorder, narcissistic personality disorder, and antisocial personality disorder—are characterized by symptoms that range from highly inconsistent behavior to inflated self-esteem, exaggerated emotional displays, and rule-breaking behavior. More is known about the etiology of personality disorders in the dramatic/erratic cluster than those in the other clusters.

Borderline Personality Disorder

Borderline personality disorder (BPD) has been a major focus of interest for several reasons. Among these reasons, BPD is very common in clinical settings, very hard to treat, and associated with suicidality.

Clinical Description The core features of **borderline personality disorder** (BPD) are impulsivity and instability in relationships and mood. For example, attitudes and feelings toward other people might change drastically and inexplicably very quickly. Emotions are intense, erratic and can shift abruptly, particularly from passionate idealization to contemptuous anger. As in the clinical case of Mary, which opened this chapter, the intense anger of people with BPD often damages relationships. People with BPD are overly sensitive to small signs of emotions in others (Lynch et al., 2006). Their unpredictable, impulsive, and potentially self-damaging behavior might include gambling, reckless spending, indiscriminate sexual activity, and substance abuse. People with BPD often have not developed a clear and coherent sense of self—they sometimes experience major swings in such basic aspects of identity as their values, loyalties, and career choices. They cannot bear to be alone, have fears of abandonment, demand attention, and experience chronic feelings of depression and emptiness. They may experience transient psychotic and dissociative symptoms when stressed.

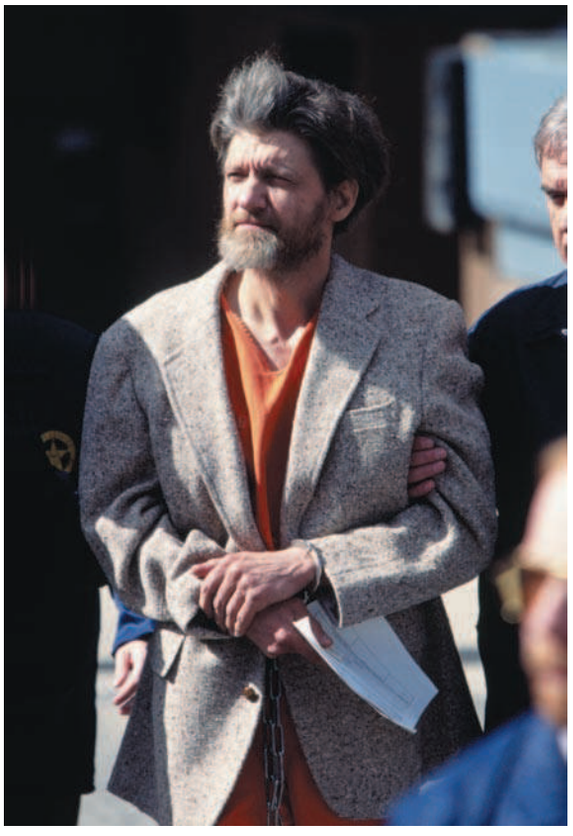
Suicidal behavior is a particular concern in BPD. One study found that, over a 20-year period, approximately 7.5 percent of people with BPD committed suicide (Linehan & Heard, 1999). In a study of 621 people with BPD, 15.5 percent were found to have engaged in at least one suicidal behavior within the previous year (Yen et al., 2003). People with BPD are also particularly likely to engage in *self-mutilating behavior*. For example, they might slice their legs with a razor blade or burn their arms with cigarettes—behaviors that are harmful but unlikely to cause death. At least two-thirds of people with BPD will engage in self-mutilation at some point during their lives (Stone, 1993).

Over a 10- or 15-year period, as many as three-quarters of people with BPD stabilize so that they no longer meet diagnostic criteria, and their functioning approximates that of the general population (Zanarini et al., 2006). Most people no longer meet the diagnostic criteria by age 40 (Paris, 2002). Symptoms of self-harm and suicidality diminish more quickly than do other symptoms, such as tendencies toward anger and impulsivity (Zanarini et al., 2006).

People with BPD are highly likely to have a comorbid Axis I anxiety disorder (especially posttraumatic stress disorder) or mood disorder (McGlashan et al., 2000). They are also at risk for comorbid substance-related disorders and eating disorders, as well as for other personality disorders from the odd/eccentric cluster (McGlashan et al., 2000). When present, comorbid Axis I conditions predict greater likelihood that BPD symptoms will be sustained over a 6-year period (Zanarini et al., 2004).

A colorful account by Jonathan Kellerman, a clinical psychologist and successful mystery writer, gives a good sense of what people with BPD are like.

> *They're the chronically depressed, the determinedly addictive, the compulsively divorced, living from one emotional disaster to the next. Bed hoppers, stomach pumpers, freeway jumpers, and sad-eyed bench-sitters with arms stitched up like footballs and psychic wounds that can never be sutured. Their egos are as fragile as spun sugar, their psyches irretrievably fragmented, like a jigsaw puzzle with crucial pieces missing. They play roles with alacrity, excel at being anyone but themselves, crave intimacy but repel it when they find it. Some of them gravitate toward stage or screen; others do their acting in more subtle ways. . . .*
>
> *Borderlines go from therapist to therapist, hoping to find a magic bullet for the crushing feelings of emptiness. They turn to chemical bullets, gobble tranquilizers and antidepressants, alcohol and cocaine. Embrace gurus and heaven-hucksters, any charismatic creep promising a quick fix of the pain. And they end up taking temporary vacations in psychiatric wards and prison cells, emerge looking good, raising everyone's hopes. Until the next letdown, real or imagined, the next excursion into self damage. (Kellerman, 1989, pp. 113–114)*



Ted Kaczynski, the "unibomber," is believed to have schizoid personality disorder; he has a long history of extreme detachment from interpersonal relationships. (Ralf-Finn Hestoft/Corbis Images.)

Fortunately, research on new treatments for BPD, discussed later in the chapter, indicates a more positive outlook than Kellerman offers.

Etiology of Borderline Personality Disorder There are several views concerning the causes of BPD. We discuss neurobiological factors, social factors, object relations theory, and Linehan's diathesis–stress theory.

Neurobiological Factors Both twin studies and family studies support a strong heritability for BPD. Genes account for more than 60 percent of the variance in the development of this disorder. To understand the neurobiology of BPD, it helps to separate two types of symptoms of BPD—emotion dysregulation and impulsivity. Deficits in sensitivity to the neurotransmitter serotonin are associated with impulsivity and emotion dysregulation. People with BPD demonstrate lower serotonin function than do controls (Soloff et al., 2000).

Beyond serotonin, separable aspects of genetic and neurobiological vulnerability may contribute to the components of emotion dysregulation or impulsivity, rather than to the disorder as a whole (Siever et al., 2000). Consistent with the idea that emotional dysregulation may be one of the components of this disorder, the parents of people with BPD have elevated rates of mood disorders (Shachnow et al., 1997). Hence some of the genetic vulnerability to BPD might overlap with genetic vulnerability to mood disorders.

Otto Kernberg, one of the leading object relations theorists, has been very influential in the study of borderline personality disorder. (Courtesy Dr. Otto Kernberg.)

Some neurobiological characteristics might be closely related to emotional dysregulation. For example, people with BPD show increased activation of the amygdala (Herpetz et al., 2001; Silbersweig et al., 2007). Amygdala activation appears to be correlated with several disorders that involve intense emotions, including mood disorders and anxiety disorders, so it might be relevant for understanding the emotion dysregulation of BPD.

The prefrontal cortex is thought to help control impulsiveness, and in some studies, people with BPD perform poorly on neuropsychological tests of frontal lobe functioning (Bazanis et al., 2002; Fertuck et al., 2006; Ruchsow et al., 2006). In brain-imaging studies, people with BPD show low levels of activity and structural changes in the prefrontal cortex (van Elst et al., 2001, van Elst, 2003).

Social Factors: Childhood Abuse People with BPD are much more likely to report a history of parental separation, verbal abuse, and emotional abuse during childhood than are people diagnosed with other Axis II disorders (Reich & Zanarini, 2001). Indeed, such abuse is believed to be more frequent among people with BPD than among people diagnosed with most other disorders (Herman, Perry, & van der Kolk, 1989), with the exception of dissociative identity disorder (see Chapter 6), which is also characterized by very high rates of childhood abuse. Given the frequency of dissociative symptoms in people with BPD, we can speculate that BPD and dissociative identity disorder might be related and that, in both, dissociation is caused by the extreme stress of child abuse. Indeed, one study found that people who dissociated after child abuse were more likely to develop symptoms of BPD (Ross et al., 1998). Two major psychological models build on these high rates of reported abuse to explain how a person might come to develop the symptoms of BPD. We review these theories in the next two sections.

Object Relations Theory Object relations theory (see Chapter 2) focuses on the way children internalize their images of the people who are important to them, such as their parents. In other words, the central focus is how children identify with people to whom they have strong emotional attachments. These internalized images (***object relations***) become part of the person's ego and influence how the person reacts to the world. But internalized values can come into conflict with the wishes and ideals of the adult—for example, when a college-age woman has internalized the idea that all relationships will be abusive but strives to relate to a warm and supportive partner without conveying mistrust and suspicion.

Otto Kernberg is a leading object relations theorist who has written extensively about BPD. Kernberg (1985) proposed that adverse childhood experiences—for example, having parents who provide love and attention inconsistently, perhaps praising achievements but being unable to offer emotional support and warmth—cause children to internalize disturbed object representations that fail to integrate the loving and unloving aspects of the people who are close to them. As a result of these disturbed object relations, they develop insecure egos, a major feature of BPD. People with BPD cope with their fragile sense of self by seeking almost continuous reassurance.

To avoid perceived relationship threats, people with BPD often use a defense mechanism called splitting—dichotomizing objects into all good or all bad and failing to integrate positive and negative aspects of another person or the self into a whole. This tendency causes extreme difficulty in regulating emotions because people with BPD see the world, including themselves, in black-and-white terms. One week, they might see their therapist as a perfect human being, capable of saving them from pain and turmoil, but then might become scathingly angry the next week if the therapist is unavailable for some reason.

Linehan's Diathesis–Stress Theory Marsha Linehan proposes that BPD develops when people who have difficulty controlling their emotions because of a biological diathesis (possibly genetic) are raised in a family environment that is invalidating. That is, a diathesis of emotional dysregulation interacts with experiences of invalidation to promote the development of BPD.

In an invalidating environment, the person's feelings are discounted and disrespected—that is, the person's efforts to communicate feelings are disregarded or even punished. An extreme form of invalidation is child abuse, either sexual or nonsexual, where the abusive parent claims to love the child and yet hurts the child.

The two main hypothesized factors—emotional dysregulation and invalidation—interact with each other in a dynamic fashion (see Figure 12.2). For example, the emotionally dysregulated child makes enormous demands on his or her family. The exasperated parents ignore or even punish the child's outbursts, which leads the child to suppress his or her emotions. The suppressed emotions build up to an explosion, which then gets the attention of the parents. Thus, the parents end up reinforcing the very behaviors that they find aversive. Many other patterns are possible, of course, but what they have in common is a vicious circle, a constant back-and-forth between dysregulation and invalidation.

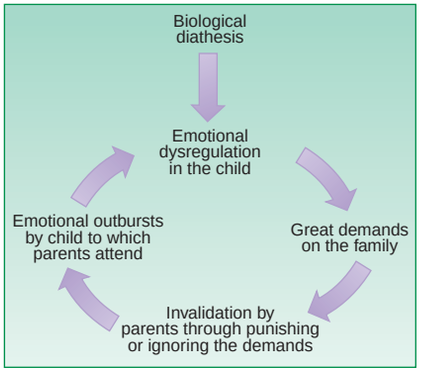


Figure 12.2 Marsha Linehan's diathesis–stress theory of borderline personality disorder.

Histrionic Personality Disorder

The key feature of **histrionic personality disorder** is overly dramatic and attention-seeking behavior. People with this disorder often use their physical appearance, such as unusual clothes, makeup, or hair color, to draw attention to themselves. Despite displaying extravagant and intense emotions, they are thought to be emotionally shallow. For example, someone with this disorder might gush about and call a person his or her best friend, only to have trouble remembering a conversation with that person the next day. They are self-centered, overly concerned with their physical attractiveness, and uncomfortable when not the center of attention. They can be inappropriately sexually provocative and seductive and are easily influenced by others. Their speech is often impressionistic and lacking in detail. For example, they might state a strong opinion yet be completely unable to support it. (*Patient:* "She was absolutely the greatest." *Interviewer:* "What did you like best about her?" *Patient:* "Gosh, I'm not sure I could describe that."). Histrionic personality disorder is highly comorbid with depression, borderline personality disorder, and medical problems (Nestadt et al., 1990).

DSM-IV-TR Criteria for Histrionic Personality Disorder

Presence of five or more of the following shown in many contexts by early adulthood:

- Strong need to be the center of attention
- Inappropriate sexually seductive behavior
- Rapidly shifting expression of emotions
- Use of physical appearance to draw attention to self
- Speech that is excessively impressionistic and lacking in detail
- Exaggerated, theatrical emotional expression
- Overly suggestible
- Misreads relationships as more intimate than they are

Etiology of Histrionic Personality Disorder Psychodyanmic theory proposes that the emotional display and seductiveness that are characteristic of this disorder are encouraged by parental seductiveness, especially a father's seductive behavior toward his daughter. The theory also proposes that people with this disorder were raised in a family environment in which parents talked about sex as something dirty yet behaved as though it was exciting and desirable. Such an upbringing might explain a preoccupation with sex, coupled with a fear of actually behaving sexually. Exaggerated displays of emotion are seen as symptoms of such underlying conflicts. Being the center of attention is seen as a way of defending against low self-esteem (Apt & Hurlbert, 1994). Unfortunately, this theory has not been tested.

Narcissistic Personality Disorder

People with **narcissistic personality disorder** have a grandiose view of their abilities and are preoccupied with fantasies of great success (as demonstrated by Bob in the clinical case below). They are more than a little self-centered—they require almost constant attention

Clinical Case: Bob

Bob, a 50-year-old college professor, sought treatment only after urging from his wife. During the interview, Bob's wife noted concerns that he seemed so focused on himself and his own advancement that he often belittled others. Bob was dismissive of these concerns, stating that he had never been the sort of person to tolerate fools, and he could see no reason why he should begin offering such tolerance now—in rapid fire, he described his supervisor, his students, his parents, and a set of former friends as lacking the intelligence to merit his friendship. He willingly acknowledged working long hours but stated that his research had the potential to change life for people and that other activities could not be allowed to interfere with his success.

DSM-IV-TR Criteria for Narcissistic Personality Disorder

Presence of five or more of the following shown by early adulthood in many contexts:

- Grandiose view of one's importance
- Preoccupation with one's success, brilliance, beauty
- Belief that one is special and can be understood only by other high-status people
- Extreme need for admiration
- Strong sense of entitlement
- Tendency to exploit others
- Lack of empathy
- Envious of others
- Arrogant behavior or attitudes

and excessive admiration. Their interpersonal relationships are disturbed by their lack of empathy, by their arrogance coupled with feelings of envy, by their habit of taking advantage of others, and by their feelings of entitlement—they expect others to do special favors for them. People with this disorder are extremely sensitive to criticism and might become enraged when others do not admire them. They tend to seek out high-status partners whom they idealize, but when, inevitably, these partners fall short of their unrealistic expectations, they become angry and rejecting (like those with borderline personality disorder). They are also likely to change partners if given an opportunity to be with a person of higher status. This disorder most often co-occurs with borderline personality disorder (Morey, 1988).

Etiology of Narcissistic Personality Disorder In this section, we discuss the two most influential models of the etiology of this disorder: the self-psychology model and the social-cognitive model. Both theories are attempts to understand how a person develops these traits.

Self-Psychology Model Heinz Kohut established a variant of psychoanalysis known as *self-psychology,* which he described in his two books, *The Analysis of the Self* (1971) and *The Restoration of the Self* (1977). Kohut noted that the person with narcissistic personality disorder projects remarkable self-importance, self-absorption, and fantasies of limitless success on the surface. But Kohut theorizes that these characteristics mask a very fragile self-esteem. People with narcissistic personality disorder strive to bolster their sense of self-worth through unending quests for respect from others.

Kohut described parenting styles that might contribute to the development of narcissism. When parents respond to a child with respect, warmth, and empathy, they endow the youngster with a normal sense of self-worth. Parental coldness may contribute to an insecure sense of self. Beyond this, Kohut described a pattern in which the child is valued as a means of fostering the parents' self-esteem, and the child's talents and abilities are overly emphasized. The child will experience a deep sense of shame over any of his or her shortcomings. Hence, Kohut hypothesized that two parenting dimensions would increase risk of narcissism: emotional coldness and an overemphasis on the child's achievements. Recent research indicates that people with high levels of narcissism report experiencing both of these parenting issues when they were children (Otway & Vignoles, 2006).

Narcissistic personality disorder draws its name from the Greek mythological figure Narcissus, who fell in love with his own reflection, was consumed by his own desire, and was transformed into a flower. (Museum Bojimans Van Beuningen, Rotterdam, Netherlands/Bridgeman Art Library/SuperStock, Inc.)

Social-Cognitive Model A model of narcissistic personality disorder developed by Carolyn Morf and Frederick Rhodewalt (2001) is built around two basic ideas: first, that people with this disorder have fragile self-esteem, in part because they are trying to maintain the belief that they are special and second, that interpersonal interactions are important to them for bolstering self-esteem, rather than for gaining closeness or warmth. In other words, they are captive to the goal of maintaining a grand vision of themselves, and this goal pervades their experiences. The work of Morf and Rhodewalt is impressive in that they have designed laboratory research studies aimed at elucidating the cognitive, emotional, and interpersonal processes associated with narcissistic personality disorder.

To assess the idea that people with narcissistic personality disorder are trying to maintain grandiose beliefs about themselves, they examine biases in how people with this disorder rate themselves in various settings. For example, in laboratory studies, people with narcissistic personality disorder overestimate their attractiveness to others and their contributions to group activities. ("Others must be jealous of me, I've been responsible for the lion-share of our progress here today.") In some studies, researchers have provided people with feedback that they were successful on a task (regardless of their actual performance), then asked participants to rate the reasons why they were successful. In these types of studies, people with narcissistic personality disorder attribute successes to their abilities rather than chance or luck. So, a set of studies suggest that people with narcissistic personality disorder show cognitive biases that would help maintain grandiose beliefs about the self.

To assess whether people with narcissistic personality disorder have fragile self-esteem, Morf and Rhodewalt review studies of how much self-esteem depends

on external feedback. For example, when falsely told they have done poorly on an IQ test, they show much more reactivity than others do; similarly, they show more reactivity to being told they have succeeded at something. Morf and Rhodewalt argue that this vulnerability of self-esteem to external feedback arises from the attempt to maintain an inflated self-view.

According to this theory, when people with narcissistic personality disorder interact with others, their primary goal is to bolster their own self-esteem. This goal influences how they act toward others in several ways. First, they tend to brag a lot; this often works well initially, but over time, repeated bragging comes to be perceived negatively by others (Paulhus, 1998). Second, when someone else performs better than they do on a task that is relevant to self-esteem, they will denigrate the other person, even if they have to do so to that person's face. That is, it is more important for them to be admired or to achieve competitive success than it is to have closeness with others. This framework makes it easy to understand why people with narcissistic personality disorder do things that alienate others; their sense of self depends on "winning," not in gaining or maintaining closeness (Campbell et al., 2007).

Check Your Knowledge 12.2

Answer the questions.

1. Which personality disorder is most related to schizophrenia in family history studies?
   - **a.** schizoid
   - **b.** schizotypal
   - **c.** antisocial
   - **d.** borderline
2. Which of the following factors play a central role in Linehan's model of BPD (choose all that apply)?
   - **a.** emotional dysregulation
   - **b.** parental invalidation
   - **c.** conflicts between introjected values and current needs
   - **d.** splitting as a defense mechanism
3. Which personality disorder is most common in clinical settings?
   - **a.** schizoid
   - **b.** schizotypal
   - **c.** antisocial
   - **d.** borderline

Antisocial Personality Disorder and Psychopathy

Informally, the terms *antisocial personality disorder* and *psychopathy* (sometimes referred to as *sociopathy*) often are used interchangeably. Antisocial behavior, such as breaking laws, is an important component of both, but there are important differences between the two disorders. One difference is that antisocial personality disorder is included in the DSM-IV-TR, whereas psychopathy is not. In this next section, we will review the definitions of these two highly related constructs, then discuss research on the etiology of these syndromes.

Clinical Case

A 19-year-old man with irregular breathing, a rapid pulse, and dilated pupils was brought to the hospital by a friend, who eventually admitted that they had been using a lot of cocaine before the symptoms began. The men didn't want to identify themselves, but eventually the medical team was able to get enough information to contact the patient's mother, who arrived at the hospital distraught and smelling of alcohol. When interviewed, she reported that her son had a long history of disobedience and disengagement from family activities. When she attempted to set rules, he became violently argumentative; he often stayed out all night. She said that the father was not present to help with parenting. She believed that her son was a good student and a star basketball player, but both of these beliefs turned out to be false. Later research revealed, though, that her son was deeply involved in drugs and in drag racing, and he bragged that he typically consumed a case of beer per day. He used various schemes to get money for drugs, including stealing car radios and taking money from his mother. He denied that he had any problems and ended his first interview with a therapist early. [Adapted from Spitzer et al. (1994).]

DSM-IV-TR Criteria for Antisocial Personality Disorder

- Age at least 18
- Evidence of conduct disorder before age 15
- Pervasive pattern of disregard for the rights of others since the age of 15 as shown by at least three of the following:
  1. Repeated law-breaking
  2. Deceitfulness, lying
  3. Impulsivity
  4. Irritability and aggressiveness
  5. Reckless disregard for own safety and that of others
  6. Irresponsibility as seen in unreliable employment or financial history
  7. Lack of remorse

Antisocial Personality Disorder: Clinical Description The DSM-IV-TR diagnostic criteria for **antisocial personality disorder** (APD) include two major components: (1) a pervasive pattern of disregard for the rights of others since the age of 15, and (2) the presence of a conduct disorder (see Chapter 14) before the age of 15. Truancy, running away from home, frequent lying, theft, arson, and deliberate destruction of property are major symptoms of conduct disorder. People with APD show irresponsible behavior such as working only inconsistently, breaking laws, being irritable and physically aggressive, defaulting on debts, being reckless and impulsive, and neglecting to plan ahead. They show little regard for truth and little remorse for their misdeeds.

The disorder is more common among people of low socioeconomic status, and there is evidence that culture influences whether or not people develop this disorder—for example, rates of APD are higher in the United States than in Scotland (Cooke & Michie, 1999). Rates are also higher among younger adults than among older adults, and some people seem to mature out of the symptoms. In one study, people who had been hospitalized for APD were followed up 16 to 45 years later. About one-quarter of them no longer had APD, and another third had improved (Black, Baumgard, & Bell, 1995). About three-quarters of people with APD meet the diagnostic criteria for another disorder, with substance abuse being the most common comorbid disorder (Newman et al., 1998). Not surprisingly, then, high rates of APD are observed in drug and alcohol rehabilitation facilities (Sutker & Adams, 2001).

Psychopathy: Clinical Description The concept of psychopathy predates the DSM-IV-TR diagnosis of antisocial personality disorder. In his classic book *The Mask of Sanity* (1941/1976), Hervey Cleckley drew on his clinical experience to formulate diagnostic criteria for psychopathy. Unlike the DSM diagnostic criteria for APD that focus on observable symptoms, Cleckley's criteria for psychopathy refer less to behavior per se and more to the person's thoughts and feelings.

In Cleckley's description, one of the key characteristics of psychopathy is poverty of emotions, both positive and negative: Psychopathic people have no sense of shame, and their seemingly positive feelings for others are merely an act. They are superficially charming and use that charm to manipulate others for personal gain. Their lack of anxiety might make it impossible for them to learn from their mistakes, and their lack of remorse leads them to behave irresponsibly and often cruelly toward others. Another key point in Cleckley's description is that the antisocial behavior of a person with psychopathy is performed impulsively, as much for thrills as for a reason such as financial gain.

The most commonly used scale to assess psychopathy is the Psychopathy Checklist–Revised (Hare, 2003). Raters using this scale conduct an extensive interview but also gather information from other sources, such as criminal records and social worker reports, to rate 20 items. Some of the items overlap with the criteria for APD, including juvenile delinquency, criminality, impulsivity, and irresponsibility. The scale also includes interpersonal items (such as superficial charm, pathological lying, and manipulativeness) and affective symptoms (such as lack of remorse, shallow affect, and lack of empathy) (Hare & Neumann, 2006).

As you can see, the criteria for APD and psychopathy differ a good deal. Note that the criteria for psychopathy do not require onset of symptoms before age 15. Some researchers criticize the APD criteria for relying on retrospective reports of people who may not describe their behavior accurately (Hare, Hart, & Harpur, 1991)

Because the criteria for psychopathy criteria cover a broader range of problems than do the criteria for APD, many of the people diagnosed with APD do not meet criteria for psychopathy. Indeed, only 20 percent of people diagnosed with APD obtain high scores on the Psychopathy Checklist (Rutherford, Cacciola, & Alterman, 1999). However, because the APD criteria emphasize observable behaviors, APD is three times as common in criminal settings as is psychopathy (Hare & Neumann, 2006). Both APD and psychopathy are observed much more frequently among men than women.

Etiology of Antisocial Personality Disorder and Psychopathy In this section, we consider the etiology of APD and psychopathy. As we review the research in this area, keep in mind two issues that make findings a little hard to integrate. First, research has been conducted

on persons diagnosed in different ways—some with APD and some with psychopathy. Second, most research on APD and psychopathy has been conducted on persons who have been convicted as criminals. Thus, the results of this research might not be applicable to psychopaths who are not criminals or who avoid arrest. Indeed, on cognitive and psychophysiological measures, psychopaths who have been convicted show more deficits than those who have not been caught (Ishikawa et al., 2001).

Three-quarters of convicted felons meet the DSM criteria for antisocial personality disorder. (Chris Steele-Perkins/Magnum Photos, Inc.)

Genetic Factors Adoption studies reveal a higher-than-normal prevalence of antisocial behavior in adopted children of biological parents with APD and substance abuse (Cadoret et al., 1995; Ge et al., 1996). Older studies suggested that criminality (Gottesman & Goldsmith, 1994), psychopathy (Taylor et al., 2003), and APD (Eley, Lichtenstein, & Moffitt, 2003) were moderately heritable, with heritability estimates of 40 to 50 percent. Remember, though, that poor reliability will limit validity and that test–retest and multiple informant reliability estimates for personality disorders can be low. Recent studies have addressed this by gathering repeated measures of symptoms (Burt et al., 2007), by gathering multiple indices of psychopathy (Larsson, Andershed, & Lichtenstein, 2006), or by gathering reports of antisocial symptoms from teachers, parents, and children (Baker et al., 2007). By combining multiple measures, one can obtain an index of psychopathy or antisocial behavior that is much more reliable. Each study using this type of approach has found much higher heritability estimates; in one case, it was estimated that heritability of antisocial behavior symptoms was .96 (Baker et al., 2007).

Genetic risk for APD, psychopathy, conduct disorder, and substance abuse appear to be related. A person might inherit a general vulnerability for these types of symptoms, and then environmental factors might shape which of the symptoms evolve (Kendler, Prescott, et al., 2003; Larsson et al., 2007). Some genetic risk, however, is very specific—for example, some genes might influence aggressive behavior within APD (Eley et al., 2003).

Adoption research has also shown that genetic, behavioral, and family influences are very hard to disentangle (Ge et al., 1996). That is, the genetically influenced antisocial behavior of the child can provoke harsh discipline and lack of warmth, even in adoptive parents, and these parental characteristics in turn exacerbate the child's antisocial tendencies.

Social Factors: Family Environment and Poverty Since much psychopathic behavior violates social norms, many investigators focus on the primary agent of socialization, the family, in their search for the explanation of such behavior. High negativity, low warmth, and parental inconsistency predict antisocial behavior (Marshall & Cooke, 1999; Reiss et al., 1995). The family environment might be particularly important when a child has an inherited tendency toward antisocial behavior. For example, in the adoption study referred to above (Cadoret et al., 1995), an adverse environment in the adoptive home (such as marital problems and substance abuse) was related to the development of APD, particularly when the biological parents had APD.

Outside of twin studies, there is substantial prospective research to show that social factors, including poverty and exposure to violence, predict antisocial behavior in children (Loeber & Hay, 1997), even when children are not genetically at risk for APD (Jaffee et al., 2002). Among adolescents with conduct disorder, those who are impoverished are twice as likely to develop APD as are those from higher socioeconomic status backgrounds (Lahey et al., 2005).

Emotion and Psychopathy There is a large body of work on the emotional components of psychopathy. In defining the psychopathic syndrome, Cleckley noted the inability of people with psychopathy to profit from experience or even from punishment; they seem to be unable to avoid the negative consequences of social misbehavior. Many are chronic lawbreakers despite their experiences with jail sentences. They seem immune to the anxiety or pangs of conscience

that keep most of us from breaking the law, lying, or injuring others, and they have difficulty curbing their impulses. In the terminology of learning theory, psychopaths do not learn to avoid certain behaviors because they are unresponsive to punishments for their antisocial behavior. Presumably, they do not experience conditioned fear responses when they encounter situations in which such responses would normally serve to inhibit antisocial behavior.

A classic study tested the idea that people with psychopathy have few inhibitions about committing antisocial acts because they experience little anxiety (Lykken, 1957). It is believed that anxiety mediates the ability to learn to avoid aversive stimuli, such as shocks. Lykken assessed how well people with psychopathy learned to avoid shock. Consistent with the idea that psychopathy is associated with low anxiety levels, people with psychopathy were poorer than controls at learning to avoid shock.

Studies of the activity of the autonomic nervous system have also yielded with supported the idea that psychopaths respond to fear-eliciting stimuli with less anxiety than other people. At rest, people with psychopathy have lower-than-normal levels of skin conductance, and their skin conductance is less reactive when they are confronted with or anticipate an aversive stimulus (Lorber, 2004). In one study, skin conductance reactivity to aversive stimuli (loud tones) at age 3 was found to predict psychopathy scores at age 28 (Glenn et al., 2007). Research using other methods of assessing emotion has confirmed these results. One study measured the eyeblink component of the startle response, a good nonverbal indicator of whether a person is in a negative emotional state. When people are anxious, they demonstrate a larger startle response in response to a sudden loud noise. People with psychopathy do not show increased startle while they are viewing negative stimuli, like a picture of a gun or a horrible accident (Levenston et al., 2000), confirming the idea that they do not experience anxiety in response to aversive stimuli.

In an interesting extension of this theory, researchers used brain activity as a way to examine what happens with classical conditioning in which an unconditioned stimulus (painful pressure) was repeatedly paired with a neutral picture (the conditioned stimuli). To measure responses to the CS after these repeated pairings, the researchers measured activity of the amgydala and other brain regions involved in emotion responsivity (Birbaumer et al., 2005). After conditioning, healthy control participants showed increases in amygdala activity when viewing the neutral pictures. People with psychopathy, though, did not show this expected increase in amgydala activity. These findings suggest that the people with psychopathy are failing to show classical conditioning to aversive stimuli at a very basic level.

The research we have described so far has been based on the idea that punishment does not arouse strong emotions in people with psychopathy and thus does not inhibit antisocial behavior. But some researchers believe that empathy, not punishment, is the critical agent of socialization. Empathy means being in tune with the emotional reactions of others; thus, empathizing with someone's distress could inhibit the tendency toward callous exploitation. From this perspective, one could argue that some features of psychopathy arise from a lack of empathy.

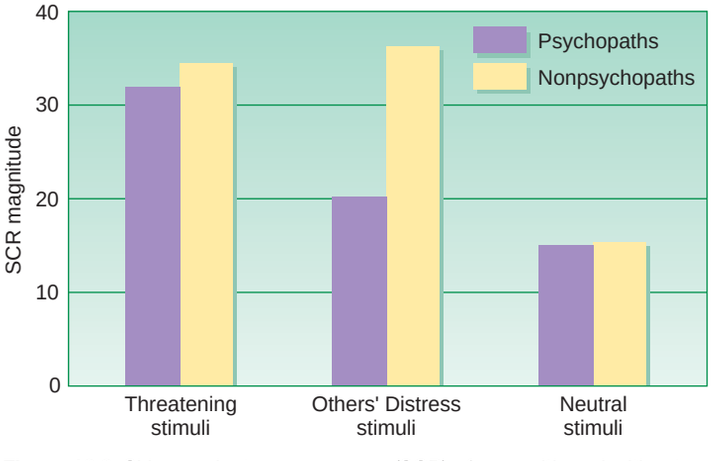


Figure 12.3 Skin-conductance response (SCR) of men with and without psychopathy to three types of stimuli. The men with psychopathy showed less responsiveness to the distress stimuli, indicating a deficit in empathy. (Blair et al.1997).

This idea has been tested by monitoring the skin conductance of men with and without psychopathy as they viewed slides showing three different types of pictures: threatening (e.g., gun, shark), neutral (e.g., book), and others' distress (e.g., a crying person). Unlike the results of the studies described above, the two groups did not differ in their responses to threatening stimuli, but the people with psychopathy were less responsive to the slides of others' distress (Blair et al., 1997)—that is, those with psychopathy indeed appeared to show less empathy (see Figure 12.3). Similarly, when asked to identify the emotion conveyed in pictures of various strangers, men with psychopathy did very poorly in recognizing others' fear, even though they recognized other emotions well (Marsh & Blair, 2008).

Response Modulation, Impulsivity, and Psychopathy Impulsivity is defined as the tendency to pursue potential rewards without attending to potential threats. Remember that the prefrontal cortex is involved in inhibiting impulsivity. More specifically, poor functioning of the

prefrontal cortex is related to the tendency to respond impulsively to immediate rewards and to the inability to learn to avoid punishment. Some researchers have suggested that deficits in the prefrontal cortex may drive psychopathy (Gorenstein & Newman, 1980). This idea is supported by studies showing that people with psychopathy have less gray matter in the prefrontal cortex than people without psychopathy (Raine & Yang, 2007).

People with psychopathy also show impulsivity when presented with a task designed to test the ability to modify responses depending on success or failure (Patterson & Newman, 1993). In one study demonstrating this phenomenon, participants viewed played a computerized card game (Newman, Patterson, & Kosson, 1987). If a face card appeared, the participant won five cents; if a nonface card appeared, the participant lost five cents. After each trial, the participant had the opportunity to continue or stop the game. The probability of losing was controlled by the experimenter and started at 10 percent. Thereafter, the probability of losing increased by 10 percent for every 10 cards played until it reached 100 percent. People with psychopathy continued to play the game much longer than did people without psychopathy. Nine of twelve people in the psychopathy group never quit, even though they had lost money on 19 of the last 20 trials. That is, they did not quit pursuing reward even though they were being punished.

The same game was played again with one variation—a 5-second waiting period was imposed after feedback, thus delaying the decision about whether to play again. This dramatically reduced the number of trials for which people with psychopathy played the game. It seems that enforcing a delay might lead people with psychopathy to reflect on negative feedback and behave less impulsively. Insensitivity to feedback of many forms (particularly without a pause for reflection) appears to be a feature of psychopathy (Newman, Schmitt, & Voss, 1997).

A card-guessing task that manipulates the odds of winning and losing was used to demonstrate psychopaths' impulsivity (Newman, Patterson, & Kosson, 1987). (Courtesy of Joseph Newman.)

Check Your Knowledge 12.3

True or false?

1. Psychopathy and borderline personality disorder are tied to impulsivity.
2. Psychopathy is tied to increased amygdala activation.
3. Psychopathy appears related to decreased emotional responsiveness.
4. Conduct disorder is not required for a DSM-IV-TR diagnosis of APD.

Quick Summary

The dramatic/erratic cluster (cluster B) includes borderline personality disorder, histrionic personality disorder, narcissistic personality disorder, and antisocial personality disorder. The key features of borderline personality disorder include intense emotionality, unstable identity, and impulsivity. Histrionic personality disorder is characterized by exaggerated emotional displays. Narcissistic personality disorder is characterized by highly inflated self-esteem but a deep need for admiration. Antisocial personality disorder is defined by violation of rules, and a disregard for others' feelings and social norms. Psychopathy is related to antisocial personality disorder but is not defined in the DSM. Psychopathy criteria focus on internal experiences as well as observable behavior.

There is evidence that BPD is inherited, and that heritability might be particularly related to the greater emotional dysregulation and impulsivity. Consistent with the symptoms of impulsivity, research indicates diminished activity in the prefrontal cortex among people with BPD. Consistent with the greater emotionality, people with BPD have also been found to demonstrate increased activity in the amygdala and decreased functioning of the serotonin system.

People with BPD report elevated rates of abuse. Both object relations theories and Linehan's model build on the high rates of abuse reported by people with BPD. Linehan's model also emphasizes the biological diathesis for emotional dysregulation. Object relations theory places an emphasis on conflicts between the internalized values drawn from major relationships and defense mechanisms such as splitting. Linehan's model focuses on emotional dysregulation coupled with parental invalidation.

Researchers know relatively little about the roots of histrionic personality disorder. This personality disorder is believed to be related to poor parenting.

According to the self-psychology theory of narcissistic personality disorder, parents who are inconsistent and focused on their own worth fail to help the child develop a stable sense of self-worth. Social-cognitive theory proposes that the behavior of the person with narcissistic personality disorder is shaped by the goal of maintaining specialness and the belief that that the purpose of interpersonal interactions is to bolster self-esteem.

When carefully measured, antisocial personality disorder and psychopathy are both highly heritable. Beyond genes, family environment and poverty seem to play a role in the development of this disorder.

People with psychopathy have little anxiety. Their callous treatment of others might also be linked to their lack of empathy. People with psychopathy are deficient in using negative feedback when pursuing reward—that is, they behave impulsively. This lack of anxiety and empathy, as well as their impulsivity, may drive misconduct without regret.

Anxious/Fearful Cluster

DSM-IV-TR Criteria for Avoidant Personality Disorder

A pervasive pattern of social inhibition, feelings of inadequacy, and hypersensitivity to criticism as shown by four or more of the following starting in early adulthood in many contexts:

- Avoidance of occupational activities that involve significant interpersonal contact, because of fears of criticism or disapproval
- Unwilling to get involved with people unless certain of being liked
- Restrained in intimate relationships because of the fear of being shamed or ridiculed
- Preoccupation with being criticized or rejected
- Inhibited in new interpersonal situations because of feelings of inadequacy
- Views self as socially inept or inferior
- Unusually reluctant to try new activities because they may prove embarrassing

The anxious/fearful cluster includes avoidant personality disorder, dependent personality disorder, and obsessive-compulsive personality disorder. People with these disorders are prone to worry and distress.

Avoidant Personality Disorder

People with **avoidant personality disorder** are so fearful of criticism, rejection, and disapproval that they will avoid jobs or relationships to protect themselves from negative feedback. In social situations they are restrained because of an extreme fear of saying something foolish, being embarrassed, blushing, or showing other signs of anxiety. They believe they are incompetent and inferior to others and are reluctant to take risks or try new activities.

About 80 percent of people with avoidant personality disorder have comorbid major depression, as Leon did in the clinical case. Other common comorbid conditions include borderline personality disorder, schizotypal personality disorder, and alcohol abuse (McGlashan et al., 2000). The very high rate of comorbidity with social phobia is probably a result of the fact that the diagnostic criteria for these two disorders are so similar; avoidant personality disorder might actually be a more chronic variant of social phobia (Alden et al., 2002). See Figure 5.1 (p. 0) for one way of thinking about these two disorders.

Both avoidant personality disorder and social phobia are related to a syndrome called taijin kyofusho that occurs in Japan (*taijin* means "interpersonal" and *kyofusho* means "fear"). Like people with avoidant personality disorder and social phobia, those with taijin kyofusho are overly sensitive in interpersonal situations and avoid interpersonal contact. But what they fear is somewhat different from the usual fears of those with the DSM diagnoses. People with taijin kyofusho tend to be anxious or ashamed about how they affect or appear to others—for example, they fear that they are ugly or have body odor (Ono et al., 1996).

Dependent Personality Disorder

The core features of **dependent personality disorder** are an overreliance on others and a lack of self-confidence. People with dependent personality disorder have an intense need to be taken care of, which often leads them to feel uncomfortable when alone. They subordinate their own

Clinical Case: Leon

Leon was a 45-year-old man who sought treatment for depression, which he claimed to have experienced almost continuously since the first grade. During the interview, Leon described feeling uncomfortable socially for as long as he could remember. By age five, he would experience intense anxiety with other children, and his mind would "go blank" if he had to speak in front of others. He grew up dreading birthday parties, teacher's classroom questions, and meeting new children. Although he was able to play with some of the children in his neighborhood, he never had a "best friend," and he never went out on a date. Although he did well academically through high school, his grades worsened during college. He took a job at the post office after graduation because it involved little social interaction. [Adapted from Spitzer et al. (1994).]

Clinical Case: Matthew

Matthew was a 34-year-old man who sought treatment after breaking up with a girlfriend. His mother, with whom he lived, had disapproved of his marriage plans because his girlfriend came from a different religious background. Matthew felt that he could not marry his girlfriend without his mother's approval because "blood is thicker than water." Although he canceled the engagement, he was angry with his mother and feared that she would never approve of anyone he wanted to marry. He said that he feared disagreeing with his mother because he did not want to have to "fend for himself." [Adapted from Spitzer et al. (2002).]

needs to ensure that they do not break up the protective relationships they have established. When a close relationship ends, they urgently seek another relationship to replace it. They see themselves as weak, and they turn to others for support and decision-making. The clinical case history of Matthew provides an example of dependent personality disorder.

The DSM diagnostic criteria for dependent personality disorder include some features that do not appear to be well supported by research. Specifically, the criteria portray people with dependent personality disorder as being very passive (e.g., having difficulty initiating projects or doing things on their own, not being able to disagree with others, allowing others to make decisions for them). Research indicates, however, that people with dependent personality disorder actually can do what is necessary to maintain a close relationship; this might involve being very deferential and passive, but it might involve taking active steps to preserve the relationship (Bornstein, 1997).

The prevalence of dependent personality disorder is higher in India and Japan than in the United States, perhaps because these societies encourage some behaviors that might be construed as dependent. Dependent personality disorder often co-occurs with borderline, schizoid, histrionic, schizotypal, and avoidant personality disorders, as well as with mood disorders, anxiety disorders, and bulimia.

DSM-IV-TR Criteria for Dependent Personality Disorder

An excessive need to be taken care of, as shown by the presence of at least five of the following beginning in early adulthood and shown in many contexts:

- Difficulty making decisions without excessive advice and reassurance from others
- Need for others to take responsibility for most major areas of life
- Difficulty disagreeing with others for fear of losing their support
- Difficulty doing things on own because of lack of self-confidence
- Doing unpleasant things as a way to obtain the approval and support of others
- Feelings of helplessness when alone because of lack of confidence in ability to handle things without others
- Urgently seeking new relationship when one ends
- Preoccupation with fears of having to take care of self

Obsessive-Compulsive Personality Disorder

The person with **obsessive-compulsive personality disorder** is a perfectionist, preoccupied with details, rules, and schedules. People with this disorder often pay so much attention to detail that they fail to finish projects. They are more oriented toward work than pleasure. They have inordinate difficulty making decisions (lest they err) and allocating time (lest they focus on the wrong thing). Their interpersonal relationships are often troubled because they demand that everything be done the right way—their way. They often become known as "control freaks." Generally, they are serious, rigid, formal, and inflexible, especially regarding moral issues. They are unable to discard worn-out and useless objects, even those with no sentimental value, and they are likely to be excessively frugal to a level that causes concern for those around them.

Obsessive-compulsive personality disorder is quite different from obsessive-compulsive disorder (OCD), despite the similarity in names. The personality disorder does not include the obsessions and compulsions that define the latter. Indeed, only a minority of people with OCD meet the diagnostic criteria for obsessive-compulsive personality disorder (Baer & Jenike, 1992). The disorder most frequently comorbid with obsessive-compulsive personality disorder is avoidant personality disorder (see DSM-IV-TR criteria on the next page).

Etiology of the Personality Disorders in the Anxious/Fearful Cluster

We briefly review ideas about the etiology of avoidant personality disorders, then obsessive-compulsive personality disorder, followed by dependent personality disorder. We begin by describing the evidence for heritability and then highlight social and psychological models.

DSM-IV-TR Criteria for Obsessive-Compulsive Personality Disorder

Intense need for order and control, as shown by the presence of at least four of the following beginning by early adulthood and evidenced in many contexts:

- Preoccupation with rules, details, and organization to the extent that the point of an activity is lost
- Extreme perfectionism interferes with task completion
- Excessive devotion to work to the exclusion of leisure and friendships
- Inflexibility about morals and values
- Difficulty discarding worthless items
- Reluctance to delegate unless others conform to one's standards
- Miserliness
- Rigidity and stubbornness

Very little research has been conducted to examine the heritability of cluster C personality disorders. Heritability appears to be about 27–35 percent for avoidant personality disorder (Reichborn-Kjennerud, Czajkowski, Neale et al., 2007; Torgersen et al., 2000). Although it is clear that genes influence the other personality disorders in cluster C, two available twin studies vary widely in their heritability estimates (Reichborn-Kjennerud, Czajkowski, Neale, et al., 2007; Torgersen et al., 2000).

For decades, theorists have suggested that the cluster C personality disorders relate to early childhood experiences. For example, avoidant personality disorder was thought to result when a child was taught, perhaps through modeling, to fear people and situations that others would regard as harmless.

Obsessive-compulsive personality traits were originally viewed by Freud as caused by fixation at the anal stage of psychosexual development. More contemporary psychodynamic theories emphasize a fear of loss of control, which is handled by overcompensation. For example, the man who is a compulsive workaholic might fear that his life will fall apart if he allows himself to relax and have fun.

Investigators have argued that dependent personality disorder may result from an overprotective and authoritarian parenting style that prevents the development of feelings of self-efficacy (Bornstein, 1997). Dependent personality disorder might also be related to "attachment" problems (Livesley, Schroeder, & Jackson, 1990). Developmental psychologists regard attachment as one of the major influences on personality development (see Chapter 2). In healthy development, infants become attached to an adult and use the adult as a secure base from which to explore and pursue other goals. Separation from the adult leads to anger and distress. As development proceeds, children become less dependent on the presence of the attachment figure for security. It is possible that the abnormal attachment behaviors seen in dependent personality disorder reflect something gone wrong in the usual developmental process, such as a disruption of the early parent–child relationship caused by death, neglect, rejection, or overprotectiveness. Persons with dependent personality disorder engage in a number of tactics, originally established to maintain their relationship with their parents, to keep their relationships with other people at any cost—for example, agreeing to do unpleasant tasks to keep others happy (Stone, 1993).

Check Your Knowledge 12.4

You are the director of human resources for a major corporation. You are asked to review a set of situations in which employees had interpersonal and task-focused problems that were severe and persistent enough to raise concerns in the workplace. Name the most likely personality disorder for each of the following.

1. José refuses to meet with his boss; he says that the boss is stupid and that only the top guns could understand the type of brilliant ideas he is generating. When asked to write his ideas down in a memo that could be shared, he refuses, stating that he doesn't have time for such petty exercises. When you sit down to meet with him, his first question is whether you are in a position of power to help him negotiate a higher salary.
2. Mariana refuses to meet with customers. She states that she is terrified that they will see that she does not know much. It turns out that she has called in sick the last three times her boss scheduled an appointment with her, and her colleagues barely know her name. When asked, she says that meeting with any of these people makes her feel horribly nervous about potential rejection of her ideas. She asks for a position that would involve little social contact.
3. Sheila has had three subordinate employees request transfers from her department. They each stated that she was too controlling, picked on small mistakes, and would not listen to any new ideas for solving problems. At the interview, she brought in a typed, 15-page chart of the goals she would like to execute for the company. Despite having an inordinate number of goals, she has failed to complete a single project during her first year with the company.
4. Seth, a 52-year-old man who has worked in the mailroom for 10 years, has been the subject of complaints from many other staff members. They say that he seems cold and indifferent, even though they attempt to include him in conversations. Other mailroom staff say they can't get him to talk. When you meet with Seth, he explains that he really has no interest in having friends or joining parties; socializing is just not part of his life in general. He is completely unenthusiastic about his colleagues, but he does his work without any other problems.
5. Police contact you to let you know that they have arrested Sam, one of your employees. He was caught at a bank trying to cash a $10,000 company check on which he had forged the signature. You learn that Sam had previously defrauded three other companies. When you meet with Sam, he laughs about how easy it was to get access to the checkbook, and he does not seem the least bit sorry.

Treatment of Personality Disorders

It is important to bear in mind that many people with personality disorders enter treatment because of an Axis I disorder rather than a personality disorder. For example, a person with antisocial personality disorder might seek treatment of substance-abuse problems; a person with avoidant personality disorder might seek treatment for social phobia; and a patient with obsessive-compulsive personality disorder might seek help for depression. In this connection, it can be mentioned that people with Axis I disorders and personality disorders usually do not improve as much from various forms of psychotherapy as do people with Axis I disorders alone (Crits-Christoph & Barber, 2002). The reason seems pretty clear: people with both types of disorders are more seriously disturbed than are those with only Axis I disorders and therefore might require treatment that is both more intensive (because of the long-standing nature of personality disorders) and more extensive (i.e., focused on a broad range of psychological problems).

Medications are often used to treat personality disorders (Koenigsberg, Woo-Ming, & Siever, 2002), the choice of drug being determined by the Axis I problem that the personality disorder resembles. For example, clients with avoidant personality disorder can be prescribed antidepressants in hopes of reducing their social anxieties. Given the connections noted earlier between schizophrenia and schizotypal personality disorder, it is not surprising that antipsychotic drugs (e.g., risperidone, trade name Risperdal) have shown some effectiveness with schizotypal personality disorder (Koenigsberg et al., 2003).

People with serious symptoms of personality disorders might attend a day treatment program that offers psychotherapy, in both group and individual formats, for several hours per day. Typically, psychotherapy sessions are interspersed with social and occupational therapy. The length of such programs varies, but some last several months. Programs tend to vary in their treatment approaches, with some offering psychodynamic approaches, others offering supportive approaches, and still others offering cognitive behavioral treatments. The early findings suggest that day treatment programs lead to improvements in symptoms and social functioning (Ogrodniczuk & Piper, 2001). Beyond day treatment programs, many clients are seen in individual outpatient psychological treatment. A review of 15 studies suggested that 52 percent of clients recovered within about 15 months of treatment (Perry, Banon, & Ianni, 1999). Most of these studies of the effectiveness of either day treatment or psychotherapy, though, do not include a control group but rather compare clients to those receiving standard care. This is of concern—Remember that half of personality disorders seem to dissipate over time naturally (see Figure 12.1). Given this, psychotherapy studies comparing active treatment to a control treatment are needed.

Psychodynamic therapists aim to alter the patient's present-day views of the childhood problems assumed to underlie the personality disorder. For example, they might guide a man with obsessive-compulsive personality disorder to the realization that his childhood quest to win his parents' love by being perfect does not need be carried into adulthood—that he does not need to be perfect to win the approval of others and that it is possible to make mistakes without being abandoned by those whose love he seeks. Studies of psychodynamic treatment often include a broad range of different personality disorders. In one trial that focused on more specific personality disorders, brief psychodynamic treatment was shown to be helpful in reducing symptoms of histrionic personality disorder and of personality disorders in the anxious/fearful cluster (Winston et al., 1994).

Cognitive behavioral therapists tend to break a personality disorder down into a set of separate problems. For example, a person diagnosed as having a paranoid personality disorder or avoidant personality disorder is extremely sensitive to criticism. This sensitivity might be treated by social skills training in how to address criticism, by systematic desensitization, or by cognitive therapy (Renneberg et al., 1990). Since the argumentativeness of people with paranoid personality disorder provokes counterattacks from others, the behavior therapist might help the person learn less antagonizing ways of relating to other people. Social skills training in a support group might encourage people with avoidant personality disorder to be more assertive with other people; one controlled study confirmed that this is a promising strategy (Alden, 1989).

Table 12.5 Examples of Maladaptive Cognitions Hypothesized to Be Associated with Each Personality Disorder

Personality Disorder	Maladaptive Cognitions
Avoidant	If people *know* the real me, they will reject me.
Dependent	I need people to survive, and I need constant encouragement and reassurance.
Obsessive-compulsive	I know what's best.
	People *should* do better and try harder.
Paranoid	Don't trust anyone.
	Be on guard.
Antisocial	I am entitled to *break* rules.
	Others are exploitative.
Narcissistic	Since I am special, I *deserve* special rules.
	I am better than others.
Histrionic	People are there to serve or admire me.
Schizoid	Others are unrewarding.
	Relationships are messy and undesirable.

Source: Beck & Freeman (1990).

Children normally go through a phase in which separation from a parent is distressing. People with dependent personality disorder might be experiencing a similar phenomenon in their adult relationships. (Mary Kate Denny/PhotoEdit.)

In cognitive therapy for personality disorders, Aaron Beck and colleagues (1990) apply the same kind of analysis used in the treatment of depression (see p. 238). Each disorder is analyzed in terms of negative cognitive beliefs that could help explain the pattern of symptoms (see Table 12.5). For example, cognitive therapy for a perfectionistic person with obsessive-compulsive personality disorder entails first persuading the patient to accept the essence of the cognitive model—that feelings and behaviors are primarily a function of thoughts. Biases in thinking are then explored, such as when the patient concludes that he or she cannot do anything right because of failing in one particular endeavor. The therapist also looks for dysfunctional assumptions or schemata that might underlie the person's thoughts and feelings—for example, the belief that it is critical for every decision to be correct. Beyond challenging cognitions, Beck's approach to personality disorders incorporates a variety of other cognitive behavioral techniques.

The traits that characterize the personality disorders are probably too ingrained to change thoroughly. Instead, the therapist—regardless of theoretical orientation—might find it more realistic to change a disorder into a style or a more adaptive way of approaching life (Millon, 1996).

Treatment of Borderline Personality Disorder

Few clients pose a greater challenge to treatment than do those with borderline personality disorder, regardless of the type of treatment being used. Clients with borderline personality disorder tend to show their interpersonal problems in the therapeutic relationship as much as they do in other relationships. Because these clients find it inordinately difficult to trust others, therapists find it inordinately difficult to develop and maintain the therapeutic relationship. The patient alternately idealizes and vilifies the therapist, demanding special attention and consideration one moment—such as therapy sessions at odd hours and countless phone calls during periods of particular crisis—and refusing to keep appointments the next; they beg the therapist for understanding and support but insist that certain topics are off-limits.