Co-occurring Substance Abuse and Mental Disorder

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Chapter Three: Co-occurring Substance Abuse and Mental Disorder

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Chapter Objectives

- To describe the diagnostic criteria and causal factors associated with various subtypes of disruptive behavior disorders.
- To examine relationships among mental disorder, criminal activity, and substance abuse during adolescence.
- To describe correlates and moderating factors involved in the profiles of attention deficit/hyperactivity disorder, oppositional defiant disorder, conduct disorder, anger, personality disorder, and post-traumatic stress disorder.
- To discuss the effectiveness of CBT in treatment of post-traumatic stress disorder.
- To present guidelines for treating co-occurring substance abuse and mental disorder.
- To describe psychotherapeutic medications used with children and adolescents in terms of mechanisms of action, side effects, and FDA approval.

THE SCOPE OF ADOLESCENT MENTAL HEALTH ISSUES

Most individuals go through adolescence without extreme duress. Some, however, encounter major psychological, psychosocial, and behavioral difficulties. Problems such as depression, antisocial behavior and conduct disorder, substance abuse, crime, and delinquency characterize this minority. These individuals may be unable to form or maintain close relationships; have negative attitudes toward themselves, their parents, or society; and be without the necessary skills and abilities to navigate through school and other productive activities. While these difficulties are not the norm for adolescents, statistics documenting them are of serious concern to communities and the broader society.

Of particular concern are youth affected by these difficulties who must endure the added difficulty of involvement with the juvenile justice system, a system that focuses on punishment and isolation. Paradoxically, some authors have noted a "backdoor" approach to mental health, whereby youth may enter the juvenile justice system because it is the only place they can receive treatment (Frabutt, Di Luca, & Graves, 2008).

The Department of Health and Human Services found that more than one in five children have a diagnosable mental health disorder (New Freedom Commission on Mental Health, 2003). This prevalence rate jumps, however, when juvenile offenders are studied. Up to 70% of youth in contact with juvenile justice systems suffer from one or more mental health disorder, with at least 20% experiencing disorders so severe that their ability to function is significantly impaired (Skowyra & Cocozza, 2007). Additionally, "as many as 50% of offending children have co-occurring substance abuse problems" (Frabutt et al., 2008, p. 114). An appreciation of the range of mental health issues that may beset juvenile offenders is important in the provision of effective treatment services, and an ideal criminal justice system would incorporate mental health as a primary consideration. Psychosocial problems and mental health difficulties in adolescence are generally divided into three broad categories of emotional-behavioral disorder: internalizing, externalizing, and substance abuse (Steinberg, 2011).

Internalizing Disorders

These disorders, such as depression, anxiety, and phobia, involve distress in the emotional and cognitive domains. Self-destructive behaviors often emerge in the forms of self-hatred and suicide (Laufer, 1995), as well as self-mutilation and tattooing (M. Friedman, Glasser, Laufer, Laufer, & Wohl, 1996). There also appears to be comorbidity (co-occurrence) among a variety of internalizing disorders. For example, depression frequently correlates with anxiety, phobic and panic disorders, obsessive and eating disorders, suicidal tendencies, and physical distress that has psychological origins, i.e., psychosomatic disorders (Steinberg, 2011). The co-occurrence of these internalizing distress symptoms may be indicative of a syndrome labeled "overcontrolled," or colloquially as "stuffing," while clustering of externalizing behaviors has been labeled "undercontrolled," otherwise referred to as "acting out" (R. W. Robins, John, Caspi, Moffitt, & Stouthamer-Loeber, 1996).

A co-occurrence of internalizing behaviors is reflective of a more general negative affect (Steinberg, 2011). Some individuals seem to become distressed more easily than others, and the negative affectivity that underlies this tendency predicts greater probabilities of depression, anxiety, and other internalizing disorders (Bardone, Moffitt, Caspi, Dickson, & Silva, 1996).

Externalizing Disorders

"Acting out" behaviors such as truancy, aggression, and delinquency are directed outside of the self in the form of a wide range of behavioral disorders characterized by an antisocial orientation to others and society. Adolescent delinquency and crime, aggression, and other forms of disorderly conduct fall under the category of externalizing behaviors and are believed to derive from a general propensity toward antisocial behavior. The association of juvenile delinquency and crime with this more generalized tendency toward antisocial behavior (such as lying, indifference toward the feelings of others, etc.) has led to a definition of *antisocial behavior* in this context as acts that "inflict physical or mental harm or property loss or other damage on others" (Loeber cited in Tolan & Loeber, 1993, p. 308).

Substance Disorders

These disorders involve the (nonexperimental) abuse of a substance or a wide range of substances, from prescription drugs (such as stimulants or sedatives), to street drugs (such as marijuana and cocaine), to legal substances (such as nicotine and alcohol). Substance disorders are characterized separately because they are

just as likely to accompany behavioral (externalizing) problems as they are depressions and other internalizing problems (Steinberg, 2011). Although substance abuse often appears alongside other difficulties (i.e., comorbidity; B. Henry et al., 1993), it may also appear alone, without other behavioral or affective problems. This is another reason for viewing substance abuse as a separate realm of disorder (Steinberg, 2011). In 2004, it was estimated that over 1.4 million youth were in need of substance abuse treatment—and fewer than 10% of those who could have benefited from it received specialty care (SAMHSA, 2005).

A comprehensive discussion of the assessment of substance use disorders (SUD) is presented in Chapter 12, including several approaches to determining the presence of a substance use problem, such as the *DSM-4-TR* and *DSM-5* diagnostic criteria.

Co-occurring Disorders

Comorbidity can encompass the presence of both externalizing and internalizing disorders within the same individual. For example, many adolescents who engage in delinquent behavior are also depressed (Hinden, Compas, Howell, & Achenbach, 1997). The most common co-occurring diagnoses involve the presence of conduct disorders, mood disorders, and attention deficit/hyperactivity disorder (Grella, Hser, Joshi, & Rounds-Bryant, 2001). The National Center for Mental Health and Juvenile Justice (NCMHJJ) study on youth involved with the juvenile justice system found that "of those youth who were diagnosed with a mental health disorder, 79.1 percent met criteria for at least one other mental health diagnosis" (cited in Skowyra & Cocozza, 2007, p. 3).

Among those youth with at least one mental health diagnosis, approximately 60% also met the criteria for a substance use disorder. Co-occurring substance use disorders were most common for youth with a diagnosis of disruptive behavior disorder. However, "significant proportions of youth with anxiety disorders (52.3%) and mood disorders (61.3%) also had a co-occurring substance use disorder" (Skowyra & Cocozza, 2007, p. 3). Hills (2007) identifies differences between adolescents with substance use disorders only and those with co-occurring disorders. Those with a mental disorder co-occurring with substance abuse

- "have an earlier onset of substance abuse;
- use substances more frequently;
- use substances over a longer period;
- have greater rates of family, school, and legal problems; and
- [have] early life issues" (pp. 3–4).

Some researchers have examined processes involved in other pathological forms of behavior that appear to have their origins during adolescence, such as suicide and self-mutilation. M. Friedman et al. (1996) argue that the capacity for aggression directed toward the self rests upon and emerges alongside rapid developmental changes in mental function during adolescence. Identifying the specific variables that render some juveniles able to negotiate adolescence without major difficulty while others develop self-destructive or antisocial-aggressive lifestyles is of key importance.

Note: Diagnostic criteria for the range of adolescent mental disorders discussed in this chapter are derived from *DSM-4-TR* (American Psychiatric Association, 2000) and the current *DSM-5* development proposal (American Psychiatric Association, 2010). Although some minor changes may occur following publication, the general diagnostic criteria as stated below are valid indicators for the major mental disorders that occur during adolescence.

DISRUPTIVE BEHAVIOR DISORDERS AND DIAGNOSTIC CRITERIA

All of the subtypes of disruptive behavior disorders (attention deficit disorder, oppositional defiant disorder, and conduct disorder) are more common among boys than among girls. Children who are diagnosed with these disorders experience difficulty in controlling their behavior and often develop adjustment problems that persist into adulthood.

Oppositional Defiant Disorder (ODD)

Children with oppositional defiant disorder (ODD) display a pattern of negativity, defiance, and opposition that leads to problems with teachers, parents, siblings, and peers. They vehemently resist restrictions or (limits) on behavior despite the "reasonableness" of the request. For example, they may refuse to wear a coat when it is snowing or they may have prolonged and exaggerated temper tantrums. These children have a constant tendency to "test the limits" by either ignoring or questioning what they are asked to do and by contradicting and provoking others. Aggression-related happiness may become manifest in

pleasure derived from disturbing, annoying, teasing, or irritating others. From an early age, these children seem to derive pleasure (i.e., they appear happy and joyous) when engaged in taunting or fighting with adults or their peers (Arsenio, Cooperman, & Lover, 2000). They typically lack tolerance and patience. Frustration may result in temper tantrums, prolonged arguments, and explosive verbal outbursts. When confronted with the harmfulness of their actions, children with ODD often shift the blame to others whom they perceive as abusive, unreasonable, unfair, or mean. The prevalence of ODD is estimated to be about 2% during the course of childhood (Seligman, Walker, & Rosenhan, 2001).

Table 3.1 presents the diagnostic criteria for ODD. These criteria describe behaviors that are common during the course of adolescence. This presents a challenge for accurate diagnosis: Where is the line between expected teenage defiance and mental disorder? The answer is usually determined by frequency, degree of severity, and duration of the disruptive behavior pattern.

Table 3.1 Oppositional Defiant Disorder: *DSM-5* Development Diagnostic Criteria

A. A persistent pattern of angry and irritable mood along with defiant and vindictive behavior as evidenced by four (or more) of the following symptoms being displayed with one or more persons other than siblings:

Angry/Irritable Mood

(1) Loses temper.

(2) Is touchy or easily annoyed by others.

(3) Is angry and resentful.

Defiant/Headstrong Behavior

(4) Argues with adults.

(5) Actively defies or refuses to comply with adults' requests or rules.

(6) Deliberately annoys people.

(7) Blames others for his or her mistakes or misbehaviors.

Vindictiveness

(8) Has been spiteful or vindictive at least twice within the last 6 months.

B. (Note: Under consideration) The persistence and frequency of these behaviors should be used to distinguish a behavior that is within normal limits from a behavior that is symptomatic to determine if they should be considered a symptom of the disorder. For children under 5 years of age, the behavior must occur on most days for a period of at least six months unless otherwise noted (see symptom #8). For individuals 5 years or older, the behavior must occur at least once per week for at least six months, unless otherwise noted (see symptom #8). While these frequency criteria provide a minimal level of frequency to define symptoms, other factors should also be considered such as whether the frequency and intensity of the behaviors are nonnormative given the person's developmental level, gender, and culture.

C. The disturbance in behavior causes clinically significant impairment in social, educational, or vocational activities.

D. The behaviors may be confined to only one setting or in more severe cases present in multiple settings.

Source: Adapted from American Psychiatric Association. (2011). DSM-5 *development.* Retrieved from http://www.dsm5.org/ProposedRevision/Pages/Default.aspx.

Conduct Disorder (CD)

Issues regarding mental health and mental illness in children and adolescents are fraught with controversy. Some question whether terms such as *psychopathology, criminal conduct,* and *psychopathy* can be aptly applied to youth, given their early (incomplete) stage of emotional and cognitive development and the harmful effects of labeling. Yet mental health issues must be addressed, as the vast majority of adults diagnosed with antisocial personality disorder displayed major conduct disruptions in childhood (L. N. Robins, 1978). Currently, the assessment of serious antisocial tendencies during childhood cluster in a syndrome known as conduct disorder (CD). The Psychopathy Screening Device has been used to assess the extent of cruelty and vindictiveness in people aged 2 to 12 years, elevated profiles of whom may indicate severe CD (Frick, Barry, & Bodin, 2000).

Most children, at one time or another, transgress societal norms for good behavior. In a study of 1,425 British boys, 13–16 years of age, 98% admitted to keeping something that did not belong to them, although in only 40% of the instances were the goods worth more than US$2 (Belson, 1975). For the most part, these are isolated instances and apparently a "normal" aspect of growing up. Conduct-disordered youth, however, persistently violate the rights of others, are habitually aggressive and cruel, and may repeatedly lie and cheat. CD often has its origins in ODD beginning in early and middle childhood (Dumas & Nilsen, 2003; Steiner & Remsing, 2007) A primary difference between ODD and CD is the scope and consequences of the disruptive behaviors. During adolescence, physical and sexual maturation creates increased opportunities for disruptive and antisocial behavior. CD is characterized by fights, threats, and intimidation that are frequent at home and at school; callousness and cruelty to people and animals; and theft, vandalism, and willful destruction of property. Children with CD are not only perpetrators but also frequent victims of violence such as aggravated assault, rape, and murder. The diagnosis is 3 times higher in boys, with a range of 6% to 16% of the general population, compared to a range of 2% to 9% of girls qualifying for the diagnosis. Girls are less likely to manifest physical aggression but are more likely to lie and be truant (Dumas & Nilsen).

The patterns of CD change with age. In early or middle childhood, there is likely to be a high rate of lying, fighting, and aggression toward animals. During adolescence, the severity of problems and the rate of CD increase dramatically, with youth becoming involved in such violent acts as muggings, armed robberies, or rapes. Children with CD are at increased risk for a diagnosis of antisocial personality disorder (the presence of a conduct disorder is one of the diagnostic criteria for antisocial personality disorder) when they reach adulthood (Langbehn, Cadoret, Yates, Troughton, & Stewart, 1998). Table 3.2 shows the *DSM-4-TR* criteria for the diagnosis of conduct disorder (American Psychiatric Association, 2000).

Table 3.2 Conduct Disorder: *DSM-4-TR* Diagnostic Criteria

A. A repetitive and persistent pattern of behavior in which the basic rights of others or major age-appropriate societal norms or rules are violated and manifested by the presence of three (or more) of the following criteria in the past 12 months, with at least one criterion present in the past 6 months.

Aggression to people and animals

(1) Often bullies, threatens, or intimidates others.

(2) Often initiates physical fights.

(3) Has used a weapon that can cause serious physical harm to others (e.g., a bat, brick, broken bottle, knife, gun).

(4) Has been physically cruel to people.

(5) Has been physically cruel to animals.

(6) Has stolen while confronting a victim (e.g., mugging, purse snatching, extortion, armed robbery).

(7) Has forced someone into sexual activity.

Destruction of property

(8) Has deliberately engaged in fire setting with the intention of causing serious damage.

(9) Has deliberately destroyed others' property (other than by fire setting).

Deceitfulness or theft

(10) Has broken into someone else's house or car.

(11) Often lies to obtain goods or favors or to avoid obligations (i.e., "cons" others).

(12) Has stolen items of nontrivial value without confronting a victim (e.g., shoplifting, but without breaking and entering; forgery).

Serious violations of rules

(13) Often stays out at night despite parental prohibitions, beginning before age 13 years.

(14) Has run away from home overnight at least twice while living in parental or parental surrogate home (or once without returning for a lengthy period).

(15) Is often truant from school, beginning before age 13 years.

B. The disturbance in behavior causes clinically significant impairment in social, academic, or occupational functioning.

C. If the individual is age 18 years of older, criteria are not met for Antisocial Personality Disorder.

Source: Reprinted with permission from the *Diagnostic and Statistical Manual for Mental Disorders*, Fourth Edition, Text Revision (Copyright © 2000). American Psychiatric Association.

In the forthcoming fifth edition of the *DSM*, the following additional criteria for "Callous and Unemotional Traits in Conduct Disorder" have been proposed:

1. Meets full criteria for Conduct Disorder.

2. Shows 2 or more of the following characteristics persistently over at least 12 months and in more than one relationship or setting. The clinician should consider multiple sources of information to determine the presence of these traits, such as whether the person self-reports them as being characteristic of him or herself and if they are reported by others (e.g., parents, other family members, teachers, peers) who have known the person for significant periods of time.

- **Lack of remorse or guilt.** Does not feel bad or guilty when he/she does something wrong (except if expressing remorse when caught and/or facing punishment).
- **Callous—lack of empathy.** Disregards and is unconcerned about the feelings of others.
- **Unconcerned about performance.** Does not show concern about poor/problematic performance at school, at work, or in other important activities.
- **Shallow or deficient affect.** Does not express feelings or show emotions to others, except in ways that seem shallow or superficial (e.g., emotions are not consistent with actions; can turn emotions "on" or "off" quickly) or when they are used for gain (e.g., to manipulate or intimidate others).

Source: American Psychiatric Association. (2010). DSM-5 *development.* http://www.dsm5.org/ProposedRevision/Pages/Default.aspx.

Psychosocial Correlates of Conduct Disorder

Children and adolescents are referred to mental health systems for a wide range of conduct difficulties. Though these various behaviors are generally subsumed under the rubric "conduct disorder," children in this group are diverse in the underlying causes, correlates, and developmental trajectories of their problem behaviors (Frick et al., 2000; McMahon & Frick, 2007). Risk factors and correlates of conduct disorder span a wide range (Burke, Loeber, & Birmaher, 2002; Hinshaw, Lahey, & Hart, 1993)—from individual, genetic, and neurochemical factors (Lahey, McBurnett, Loeber, & Hart, 1995) to the psychosocial and environmental domains (Holmes et al., 2001; Kazdin, 1996).

Psychosocial and environmental correlates of conduct disorder include the following:

- School failure (Burke et al., 2002; Maguin & Loeber, 1996; Mandel, 1997).
- Peer rejection (Burke et al.; Olson, 1992).
- Families characterized by parental psychopathology (Burke et al.; J. M. Halperin et al., 1997).
- Parental aggression (Burke et al.; Widom, 1997).
- Child abuse and neglect (Burke et al.; Widom).

Other problem behaviors that are frequently found in these juveniles include the following:

- Attention deficit/hyperactivity disorder (Burke et al., 2002).
- Depressive and anxiety disorders (Biederman, Newcorn, & Sprich, 1991; McMahon & Frick, 2007).
- Oppositional defiant behavioral style (Burke et al.; Loeber, Burke, Lahey, Winters, & Zera, 2000).
- Aggression (a frequent correlate of antisocial behavior, especially in childhood; Coie & Dodge, 1997; McMahon & Frick).

Furthermore, CD has been found to be one of the strongest predictors of progression from experimentation with drugs to the development of a substance-use disorder (Whitmore & Riggs, 2006).

Biological Correlates of Conduct Disorder

Biological factors may contribute to the development of CD and its related symptoms. For example, low levels of serotonin have been implicated in the development of attention deficit/hyperactivity disorder, juvenile aggression, and suicide (e.g., Burke et al., 2002; J. M. Halperin et al., 1997). Prenatal and perinatal problems have also been implicated; for example, maternal smoking during pregnancy has been found to predict CD in boys (Burke et al.). Low salivary cortisol levels have been associated with ODD, as well as with both child CD and parent antisocial personality disorder (Burke et al.). Genetic factors may also be involved; for example, the dopamine-transporter gene may contribute to the development of attention deficit disorder (attention deficit/hyperactivity disorder without the presence of hyperactivity; E. H. Cook et al., 1995). Differences in temperament may also link to child and adolescent behavioral disruptions (Caspi, Henry, McGee, Moffitt, & Silva, 1995). Effective treatment rests upon consideration of biological as well as psychosocial conditions.

Recognizing early indications of conduct difficulties (such as childhood aggression and other maladaptive responses) may provide a window for intervention that can halt the progression into full-blown CD and antisocial personality disorders (Holmes et al., 2001). Most studies suggest that the earlier the intervention, the better the prognosis (Fox & Levin, 2001).

DSM *Diagnosis of Conduct Disorder and Judicial System's Definition of "Adult Offender"*

The *DSM* diagnostics criteria clearly state that an individual under the age of 18 cannot be given a diagnosis of antisocial personality disorder (APD). The authors have argued that all offenders are antisocial (when engaged in consistent behavior that has gone against society) and that the majority of offenders can be classified as APD (Milkman & Wanberg, 2005; Wanberg & Milkman, 1998, 2008). As mentioned earlier, judicial systems and the treatment community see juvenile offenders as being different from adult offenders because they are in the formative stages of emotional and cognitive development. Some go so far as to conclude that juvenile offenders should not be labeled as "criminals" or as having engaged in criminal conduct and should not be labeled as antisocial. The *DSM* supports this position by using conduct disorder (versus antisocial disorder) for those under age 18.

Thus, tension exists between the diagnostic community and judicial jurisdictions that classify 16- or 17-year-olds as adult offenders. Since the judicial treatment community holds that many, if not most, offenders would meet APD criteria, that all have a history of antisocial behavior, and that the treatment

of CD can differ from the treatment of APD, those jurisdictions that use age 16 or 17 to define the adult offender will have to shift the treatment approach for these youth from methods that address CD to those that address antisocial patterns or APD.

Treating the juvenile offender as different from the adult offender is also problematic in that it minimizes the reality that juvenile justice clients, except possibly for status offenders (e.g., runaways), have engaged in criminal conduct and have committed crimes. Treating juveniles differently may downplay the importance of holding juvenile offenders responsible for their criminal activities. Although differences need to be recognized, treatment approaches for addressing CDs are simply not sufficient for many juvenile offenders.

Distinctions Between ODD and CD

The distinction between ODD and CD is based on violations of legal statutes and social mores. Children with ODD do not typically engage in repeated physical assault, destruction of property, or deceit. On average, ODD-type behaviors appear 2 to 3 years earlier, and "the diagnosis implies more circumscribed disturbances of lesser severity than CD" (Steiner & Remsing, 2007, p. 128).

The two disorders, however, tend to occur in sequence, with a high frequency of children who are diagnosed with ODD gradually developing CD during adolescence. Both disorders reflect deficits in the ability to solve interpersonal problems (Matthys, Cuperus, & van Engeland, 1999), and both are associated with increased risk for antisocial behavior during adulthood.

Regarding causation, research suggests similar factors at work in both CD and ODD. Youth with both tend to come from unstable homes, with parental discipline characterized by inconsistency, harsh punishment, and less involvement in the child's activities (Frick, Christian, & Wooton, 1999). Youth who are diagnosed with ODD or CD show reductions in indicators of serotonin activity (Steiner & Remsing, 2007; van Goozen, Matthys, Cohen-Kettenis, Westenberg, & van Engeland, 1999). Given the many similarities, treatment for both disorders has generally relied on behavioral principles as well as cognitive theories concerning the misinterpretation of events (Barkley, Edwards, & Robin, 1999; Christopherson & Finney, 1999).

However, a study by Connor and Doerfler (2007) has brought these similarities into question. These researchers studied a large sample of children with attention deficit/hyperactivity disorder (ADHD), some of whom had also been diagnosed with either ODD or CD. Splitting the children into three groups (ADHD + CD, ADHD + ODD, and only ADHD), the researchers found that "on parent-reported measures of delinquency, aggression, and ADHD symptom severity, significant differences between ODD and CD emerged . . . with ADHD having the least severity, ADHD + ODD being intermediate, and ADHD + CD being the most severe" (pp. 131–132). Accordingly, Connor and Doerfler suggest that clinicians consider the diagnoses of ODD and CD separately and not merge them into a general category of disruptive behavioral disorders.

A useful strategy for sorting through these similarities and differences may be the categorization of various conduct problems. One method for doing this identifies two bipolar dimensions: the overt-covert dimension and the destructive-nondestructive dimension (McMahon & Frick, 2007). Overt behavior is directly confrontational (e.g., aggression, defiance), whereas covert behavior is nonconfrontational (e.g., stealing, lying). Each of these poles can then be split into destructive and nondestructive behaviors. For example, oppositional behaviors are classified as overt-nondestructive, and property violations are covert-destructive.

CD, Criminal Behavior, and Antisocial Personality Disorder

Empirical research regarding "psychopathy" in youth ages 3 to 17 (using the Hare Psychopathy Checklist–Revised; Hare, 1991) reveals correlations among CD, other psychological disorders, and adolescent participation in crime (Forth & Mailloux, 2000). The symptoms of CD as defined in the *DSM-4* are found to correlate with engagement in criminal behavior during adolescence (Kjelsberg, 2002a). In a study of youth in juvenile detention facilities, 31.7% were provisionally diagnosed with CD (Wasserman, Ko, & Reynolds, 2004). The correlation between as few as 3 of 14 symptoms of CD (per the *DSM-4*) and possession of a criminal record reached .9 in males and was slightly lower in females. Theft was the strongest indicator of both general crime and violence in males, while running away was most strongly related to general crime and violent criminality in females. Forcing another into sexual activity strongly indicated the probability of sex offending later in life. Of the entire sample (11- to 18-year-olds) who displayed symptoms of CD, 48% had a criminal record of some kind (Kjelsberg).

The term *fledgling psychopath* (Lynam, 1996) aptly describes a subset of early-onset, conduct-disordered

adolescents who manifest insensitivity, harshness, and lack of remorse combined with callous and unemotional personality characteristics such as a disconcerting lack of empathy and respect for others. They may justify cruelty to animals by saying they were "just having fun" or they "enjoyed hurting them." This yet to be classified subset is the target of increasing attention from researchers and clinicians because the quality of parenting does not appear to modify their callousness and lack of remorse. This is not true for a majority of children with CD (Wootton, Frick, Shelton, & Silverthorn, 1997). Further, their psychological profile seems to correspond with that of adults who have been diagnosed with antisocial personality disorder (Blair, Colledge, Murray, & Mitchell, 2001; Frick & Ellis, 1999). Antisocial personality disorder cannot be diagnosed before the age of 18 because it is viewed as a chronic and pervasive personality style not present in childhood or adolescence.

A number of biologically relevant factors have been found to be closely associated with the development of antisocial personality disorder. These results have generally been interpreted in terms of interactional processes between biological and environmental factors (Magnusson, 1996; Mason & Frick, 1994). For example, some researchers have found that style of parental discipline (the use of coercion and punishment) combines with features of a child's personality that may have biological roots (such as impulsiveness and anxiety) to predict antisocial behavior and delinquency in adolescence (Tremblay, 1995). Other theorists suggest a strictly social development model, which interprets antisocial disorder as largely the result of powerful social influences (R. F. Catalano & Hawkins, 1996).

A study designed to explore the biological correlates of antisocial personality disorder compared three groups of males (nonoffenders, adolescence-limited offenders, and offenders whose antisocial behavior persisted through age 30) for difference in baseline levels of autonomic activity (Magnusson, 1996). When physiological reactivity was operationalized in terms of levels of adrenaline excreted from the adrenal medulla, the following was found:

- A strong association between persistent antisocial behavior and low levels of autonomic reactivity (low adrenaline excretion).
- No such relationship within the adolescence-limited offender group (Magnusson).

Neuropsychological deficits appear to correlate with antisocial behavior in early-onset offenders but not among those whose criminal conduct comes and goes during adolescence (A. R. Piquero, 2001). These observations support the distinction between life-course-persistent antisocial behavior and adolescence-limited antisocial behavior, which likely emanates from the powerful social pressures of those years (Moffitt et al., 2002; Patterson, 1995). Low levels of autonomic activity and other physical characteristics may have an underlying genetic derivation (Mason & Frick, 1994), which interacts with environmental experience in the development of antisocial behavior (Magnusson, 1996). Antisocial personality traits may exacerbate the drug-violence relationship (Kaplan & Damphousse, 1995).

Treatment Considerations for Adolescents With CD

Of children who manifest symptoms of CD or the less severe ODD, only 23% are referred for treatment (J. C. Anderson, Williams, McGee, & Silva, 1987). This is unfortunate in light of the fact that research increasingly demonstrates improved outcomes for treated youth (Brestan & Eyberg, 1998; Rhode, Clarke, Mace, Jorgensen, & Seeley, 2004). Successful interventions, generally derived from social learning theory, include the following goals:

- Help the client identify situations that trigger aggressive or antisocial behavior.
- Teach the child how to take the perspective of others and care about this perspective.
- Reduce the aggressive child's tendency to attribute hostility to others.
- Train the child in adaptive ways of solving conflicts with others.

Each of these goals is achieved through modeling, observational learning, positive reinforcement for the attainment of the desired behavior, and punishment or negative consequences for the continuation of negative patterns. Positive outcomes appear to be related to early involvement in treatment (soon after the child begins to exhibit antisocial behavior) combined with successful engagement of the family in the overall treatment design. Interventions that use multiple strategies and target a variety of risk domains are most effective (Burke et al., 2002; Frick, 1998). Theoretical and research perspectives along with efficacious models for treating conduct-disordered youth are covered in Section II, "Foundational Treatment Models: Evidence-Based Approaches."

Attention Deficit/Hyperactivity Disorder (ADHD)

Diagnosis of attention deficit/hyperactivity disorder is predicated upon symptom onset before the age of 7, persistence of symptoms for a minimum of 6 months, and symptoms being evident in multiple settings. Large-scale epidemiological studies conducted in multiple countries during the past 30 years show prevalence ranges for ADHD in the general population of 4.2% to 6.3%, with some estimates (based on *DSM-4* criteria) slightly higher. Szatmari, Boyle, and Offord (1989) report that between the ages of 6 and 12, ADHD affects approximately 6% to 9% of boys and 2% to 3% of girls, whereas in adolescence, the disorder affects 3% of boys and 1% of girls. Biederman et al. (2002) found that girls with the disorder were (a) twice as likely as boys to have the predominantly inattentive subtype of ADHD; (b) less likely than boys to have ODD, CD, and major depressive disorder; (c) less likely than boys to have learning or school problems; and (d) at greater risk than boys for drug use and abuse problems.

As shown in Table 3.3, the *DSM-5* development model lists symptoms of the disorder in two distinct groups: inattention and hyperactivity-impulsivity.

ADHD and Criminal Conduct

Clinical-syndrome hyperactivity has been operationalized as a combination of poor concentration skills and motor restlessness (Magnusson, 1996). Hyperactivity, low impulse control, attention deficits, and behavioral

Table 3.3 Attention Deficit/Hyperactivity Disorder: *DSM-5* Development Diagnostic Criteria

A. Either (1) or (2):

(1) Six (or more) of the following symptoms of inattention have persisted for at least 6 months to a degree that is inconsistent with developmental level and that impacts directly on social and academic/occupational activities.

Note: For older adolescents and adults (ages 17 and older), only four symptoms are required. The symptoms are not due to oppositional behavior, defiance, hostility, or a failure to understand tasks or instructions.

Inattention

(a) Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (for example, overlooks or misses details, work is inaccurate).

(b) Often has difficulty sustaining attention in tasks or play activities (for example, has difficulty remaining focused during lectures, conversations, or reading lengthy writings).

(c) Often does not seem to listen when spoken to directly (mind seems elsewhere, even in the absence of any obvious distraction).

(d) Frequently does not follow through on instructions (starts tasks but quickly loses focus and is easily sidetracked; fails to finish schoolwork, household chores, or tasks in the workplace) (not due to oppositional behavior or failure to understand instructions).

(e) Often has difficulty organizing tasks and activities (has difficulty managing sequential tasks and keeping materials and belongings in order, work is messy and disorganized, has poor time management, and tends to fail to meet deadlines).

(f) Characteristically avoids, dislikes, and is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework or, for older adolescents and adults, preparing reports, completing forms, or reviewing lengthy papers).

(g) Frequently loses things necessary for tasks or activities (e.g., school assignments, pencils, books, tools, wallets, keys, paperwork, eyeglasses, or mobile telephones).

(Continued)

Table 3.3 (Continued)

(h) Often easily distracted by extraneous stimuli (for older adolescents and adults may include unrelated thoughts).

(i) Is often forgetful in daily activities, chores, and running errands (for older adolescents and adults, returning calls, paying bills, and keeping appointments).

(2) Six or more of the following symptoms of hyperactivity-impulsivity have persisted for a least 6 months to a degree that inconsistent with developmental level and that impacts directly on social and academic/occupational activities.

Note: For older adolescents and adults (ages 17 and older), only four symptoms are required. The symptoms are not due to oppositional behavior, defiance, hostility, or a failure to understand tasks or instructions.

Hyperactivity and Impulsivity

(a) Often fidgets with hands or feet or squirms in seat.

(b) Often leaves seat in classroom or in other situations in which remaining seated is expected.

(c) Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness).

(d) Is often excessively loud or noisy during play, leisure, or social activities.

(e) Is often "on the go" or often acts as if "driven by a motor."

(f) Often talks excessively.

(g) Often blurts out answers before questions have been completed. Older adolescents or adults may complete people's sentences and "jump the gun" in conversations.

(h) Often has difficulty awaiting turn.

(i) Often interrupts or intrudes on others.

(j) Tends to act without thinking, such as starting tasks without adequate preparation or avoiding reading or listening to instructions. May speak out without considering consequences or make important decisions on the spur of the moment, such as impulsively buying items, suddenly quitting a job, or breaking up with a friend.

(k) Is often impatient, as shown by feeling restless when waiting for others and wanting to move faster than others, wanting people to get to the point, speeding while driving, and cutting into traffic to go faster than others.

(l) Is uncomfortable doing things slowly and systematically and often rushes through activities or tasks.

(m) Finds it difficult to resist temptations or opportunities, even if it means taking risks (a child may grab toys off a store shelf or play with dangerous objects; adults may commit to a relationship after only a brief acquaintance or take a job or enter into a business arrangement without doing due diligence).

B. Several noticeable inattentive or hyperactive-impulsive symptoms were present by age 12.

C. Some impairment from the symptoms is present in two or more settings (e.g., at school [or work] and at home).

D. There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning.

E. The symptoms do not occur exclusively during the course of a Pervasive Developmental Disorder, Schizophrenia, or other Psychotic Disorder and are not better accounted for by another mental disorder (e.g., Mood Disorder, Anxiety Disorder, Dissociative Disorder, or a Personality Disorder).

Specify Based on Current Presentation

- *Combined Presentation:* If both Criterion A1 (Inattention) and Criterion A2 (Hyperactivity-Impulsivity) are met for the past 6 months.
- *Predominately Inattentive Presentation:* If Criterion A1 (Inattention) is met but Criterion A2 (Hyperactivity-Impulsivity) is not met *and* three or more symptoms from Criterion A2 have been present for the past 6 months.
- *Predominately Hyperactive/Impulsive Presentation:* If Criterion A2 (Hyperactivity-Impulsivity) is met and Criterion A1 (Inattention) is not met for the past 6 months.
- *Inattentive Presentation (Restrictive):* If Criterion A1 (Inattention) is met but no more than two symptoms from Criterion A2 (Hyperactivity-Impulsivity) have been present for the past 6 months.

Source: Adapted from American Psychiatric Association. (2011). DSM-5 *development*. Retrieved from http://www.dsm5.org/ProposedRevision/Pages/Default.aspx.

difficulties, when combined, may serve as an early indicator of developing CD (Loeber, Green, Keenan, & Lahey, 1995). Some researchers suggest that hyperactivity, especially in concert with attention deficits and other childhood problems, may act as a catalyst for the development of antisocial behavior and substance abuse. It has been found that the onset of CD is particularly early in boys with ADHD (Loeber et al., 2000).

The combination of ADHD and CD is considered a major risk factor for later engagement in criminal conduct. One study also found that the joint occurrence of CD with ADHD, and not hyperactivity/ADHD alone, is the major risk factor for drug use by young adulthood (Barkley, Fischer, Smallish, & Fletcher, 2004). Hyperactivity and conduct problems from ages 8 to10 are correlated with persistent offending in adolescence (Mannuzza, Klein, Bessler, Malloy, & LaPadula, 1993). The development of later conduct problems and delinquency was worsened when early defiance was accompanied by aggression. A combination of ODD and physical aggression was shown to predict later CD, and one study found that attention deficit/hyperactivity disorder (ADHD) alone was sufficient to predict antisocial personality disorder in adulthood (Loeber et al., 1995; Mannuzza et al.).

Farrington, Loeber, and Van Kammen (1990) concluded that hyperactivity alone predicted an early onset of criminal conviction (between ages 10 and 13) better than did conduct problems alone. However, it is not yet certain whether hyperactivity as a single factor is associated with later CD and delinquency or whether its function is purely catalytic in the presence of other factors, as noted above. Hyperactivity may be a catalyst that in the presence of attention deficits, low levels of impulse control, disobedience, and/or aggressiveness may facilitate the development of serious CD (Loeber et al., 1995; Mannuzza et al., 1993). It is likely that hyperactivity initiates the onset of behaviors that manifest as defiance, opposition to rules, and other conduct difficulties. Punitive responses to these behaviors may initiate identification with deviance and delinquency.

A longitudinal study of later conviction for a criminal offense was carried out with adolescents who had been referred to psychiatric services for behavioral or emotional problems as children (Elander, Simonoff, Pickles, Holmshaw, & Rutter, 2000). The various symptoms associated with hyperactivity correlated with subsequent convictions (ages 17 to 21 years), with compound offending (five or more separate convictions), and with the incidence of incarceration following these convictions. Additional diagnosis of CD during childhood added little to the above predictions regarding later criminality.

Barkley and colleagues (2004) conducted a follow-up study of a large sample of young adults (ages 20 to 21 years) who had been diagnosed as either hyperactive or "control" children. These researchers found that

> a greater proportion of hyperactive children, by young adulthood, had committed a variety of antisocial activities at least once compared to the control children, encompassing theft of property, disorderly conduct, assault with fists, carrying a concealed weapon, and running away from home. (p. 207)

The study also found a strong correlation of hyperactivity with drug-related antisocial behavior, stating that severity of ADHD may be the principal risk factor for determining the frequency of such behavior committed by young adulthood.

Treatment of ADHD

In addition to the burdens on parents, teachers, schools, and neighborhood associates, perhaps the most problematic aspect of ADHD during childhood and adolescence is its interference with academic performance and peer relationships, thus setting the stage for "failure identity," rejection, or social isolation. Sadness and feelings of low self-worth are often profound, indicating the need for clinical intervention. The two most prominent approaches to treatment are medication and behavior therapy.

Drug and/or Behavioral Therapy

Paradoxically, many children who suffer from ADHD respond to tranquilizing medications by becoming more active. Conversely, they typically improve their capacity for attention and task focus when treated with stimulants. The most commonly prescribed stimulant is an amphetamine called methylphenidate (trade name Ritalin). Methylphenidate is a dopamine agonist; that is, it increases the levels of activity in brain systems that rely on dopamine as their neurotransmitter. Another stimulant used to treat ADHD is premoline (trade name Cylert). Like Ritalin, Cylert has been found to increase interpersonal responsiveness and goal-directed efforts along with decreasing activity level and disruptive behavior. Other drugs prescribed for ADHD are Concerta (a long-lasting capsule form of methylphenidate), Dexedrine (dextroamphetamine), and Adderall (a mixture of amphetamines). The mechanism of action of all these drugs involves stimulating the frontal parts of the brain that "filter out" distractions. These medications are neither tranquilizers nor sedatives and work similarly to caffeine. Youth appear "calmer" because they are more focused. In this more focused state, they have increased capacity to respond to behavior-modification interventions.

Contrary to earlier thought, these effects are not unique to ADHD children; normal youth also increase their focus and goal-directed activity when under the influence of these drugs (Seligman et al., 2001). It is widely known that high school and college students obtain these drugs to improve concentration during intense study periods.

B. Smith, Barkley, and Shapiro (2006) found that "stimulants provide a clear benefit in managing the disorder in the short term, and some continuing benefit in symptomatic management (but not necessarily academic achievement) in the long term" (p. 84). Indeed, "both overt and covert aggressive behavior are often reduced by stimulant treatment of children with ADHD who demonstrate abnormally high levels of pretreatment aggressiveness, though the effect on overt aggression may be somewhat less if CD is present" (p. 86). Overall, the results of research on stimulants "indicate overwhelmingly that these medications are quite effective for the management of ADHD symptoms in most children" (p. 84).

In terms of required dosage, there is significant between-subject variability, with some children showing most improvement at low to moderate dosage, while others are most improved at higher doses. There is also variability in the "domains that respond to medication. For instance, some children may improve in one domain (e.g., behavior) when treated with stimulants, but may show no change or even deteriorate in other domains (e.g., academic performance)" (B. Smith et al., 2006, p. 87).

Behavioral treatments are the main alternative to medication for ADHD, though these treatments are not mutually exclusive. Typically, operant conditioning provides incremental rewards for reducing the frequency of behaviors such as distracting others or being inattentive. These programs have been found to be effective in treating overactivity and attention deficits, particularly in the short run (Barkley, 1998). However, some authors have pointed out the unlikelihood of behavioral techniques implemented in the clinic or laboratory carrying over into home or school settings without formal programming for such generalization. As a result, "there has been no further research interest shown in the direct training of children with ADHD via behavioral means in clinical or laboratory settings" (B. Smith et al., 2006, p. 97). Instead, efforts have expanded to include training parents in child behavior management methods as well as training teachers in classroom behavior management (B. Smith et al.).

A critical question is whether behavioral therapies are as effective as medication or are more useful when used in combination with medication. One of the first things to consider is that among children who are already stimulant responsive, "it is not clear to what extent intensive psychosocial treatments provide added benefit" (B. Smith et al., 2006, p. 119). On the other hand, "medication is neither necessary nor

always sufficient for treating ADHD" because some children do not respond positively to pharmacological treatment, while some show only partial responses and need additional intervention to achieve clinically significant improvement (p. 119). Also important to consider is the fact that some issues, such as specific skill deficits, simply cannot be improved with medication alone. It is easy to imagine, therefore, many situations in which a combined treatment is necessary and appropriate. Indeed, at least two studies (the New York-Montreal Multimodal Treatment Study and the National Institute of Mental Health's Multimodal Treatment Study of Children with ADHD) have shown that combined treatments are superior to unimodal treatment on some measures in some subsets of children (cited in B. Smith et al.).

Table 3.4 shows the relative benefits and liabilities of the two approaches to treatment used separately and in combination.

Anger Disorders

Anger can play a vital role in adolescent problem behavior. According to general strain theory (Agnew, 2011), negative treatment or adversity leads to negative affect (anger), which in turn creates pressure for corrective action, often taking the form of crime or delinquency. Anger can "energize" the strained individual to action, lowering inhibitions and increasing felt injury. Building on this theory, Brezina (2010) notes the relative contributions of affective and cognitive processes to "angry aggression" as well as the interrelationship between the two processes. He writes that

> in addition to having physiological and psychological components, anger can be viewed as a social construction and as a "transitory social role" that individuals adopt. Viewed as such, anger typically involves a constellation of meanings and associated cognitive processes that can be difficult to disentangle from the raw emotional experience of "anger." (p. 188)

Anger frequently occurs "when a social norm has been violated and the individual believes that he or she has been 'wronged'—for example, a promise is broken or one's trust is betrayed" (Brezina, 2010, pp. 188–189). Indeed, angry individuals often come to feel that their targets are not only blameworthy but also untrustworthy. Furthermore, anger involves asserting a personally held belief or perspective, one that is assumed to be valid. This sense of validity empowers the angry person to rely on his or her own judgments and inclinations (Brezina). These judgments, in turn, are infused by negative affect, for "while in an angry state, individuals tend to adopt attitudes and beliefs that are consistent with their feelings" (Brezina, p. 189). Anger in youth is most frequently manifested in "non-stranger interpersonal contexts, with aggressive behavior being directed towards authority figures

Table 3.4 Medications and Behavioral Treatment for ADHD

	Stimulants	*Antidepressants*	*Behavior Therapy*	*Combined Treatment*
Improvement	About 80% at least moderately improved	About 50% moderately improved	About 40% moderately improved	Slightly better than stimulants alone
Relapse	High	High	Low to moderate	Moderate
Side effects	Mild to moderate	Mild to moderate	Low to moderate	Moderate
Cost	Inexpensive	Inexpensive	Expensive	Expensive
Time scale	Weeks/months	Months	Weeks/months	Months
Overall	Good	Useful	Marginal	Good

Sources: M. Campbell and Cueva, 1995; Greenhill, 1998; Hinshaw, Klein, and Abikoff, 1998; revised with MTA cooperative group, 1999. Adapted from Seligman, M. E. P., Walker, E. F., & Rosenhan, D. L. (2001). *Abnormal psychology* (4th ed.). New York, NY: W. W. Norton, p. 365.

such as parents and teachers, peers and family members, particularly siblings" (Down, Willner, Watts, & Griffiths, 2010/2011, p. 34).

Ordinary incidents involving anger are ultimately resolved once the perceived wrong has been in some way addressed. Chronic anger, on the other hand, can manifest if disturbed relationships have not been (cannot be) renegotiated and if trust has not been (cannot be) restored. A state of chronic anger "may lead individuals to see dangers and risks in the social world that others do not see," for instance, to attribute hostile motives to people they have not met before (Brezina, 2010, p. 190). Chronically angry individuals tend to view the world as a relatively dangerous place and the majority of the people around them as untrustworthy; as a result, such persons will tend to view aggression as appropriate or justifiable. Severe negative experiences such as physical abuse or sexual assault can contribute to the development of such a state of chronic anger.

In theoretical models of offending, affective and cognitive processes are often treated as distinct, but the results of the Brezina (2010) study lend support to their integration, consistent with the tenets of general strain theory. The study found that, with adolescent males, "aggression is a function of both emotional and attitudinal factors" (p. 199). The two dimensions do not contribute in equal measures, however. Anger does play a larger role than attitudes, but the experience of chronic anger can shape or distort attitudes in a manner conducive to aggressive behavior. Specifically, "an increase in anger is associated with the strengthening of aggressive attitudes" (p. 199). Thus, anger's effect on aggression is not limited to a direct, purely emotional influence; it also indirectly influences aggression by altering cognitive processes.

One of the most common manifestations of anger in youth is distrust of authority figures. As a result, efforts to treat anger-affected youth may be severely impaired before they even begin, especially if the treatment involves one-on-one counseling. Increasingly, theorists and clinicians have turned to alternative methods for reducing anger in adolescents, namely peer education and group counseling. These programs seek to use direct youth involvement to promote healthy behaviors. Typical programs are structured on a classroom model, with a set script and planned group interactions. In the realm of peer education, these activities are facilitated by a peer educator, with the underlying assumption that youth will "respond better to someone they perceive as similar both in age, experience, and outlook" (Puskar, Stark, Northcut, Williams, & Haley, 2010, p. 6). This method is inexpensive and even benefits the peer educators themselves, who are able to grow in confidence and teaching skills. However, peer education also demands a good deal of planning and structure, with particular emphasis on the training, retaining, and monitoring of the peer educators.

Group interventions, without peer educators, are a viable option for anger management in youth. Down and colleagues (2010/2011) studied the relative efficacy of personal development (PD) and cognitive-behavioral therapy (CBT) anger management group interventions in comparison to a waiting list control group. The PD group focused on the following:

- Establishing a realistic, neither depressive nor arrogant, sense of self-esteem (as both extremes have been associated with aggression).
- Enhancing motivation by establishing a future focus and a more pro-social identity.
- Discussing relationships, particularly parent-child difficulties.
- Using games extensively as well as playful projective and oblique exercises (e.g., drawing exercises for discussion of family conflict).

The CBT group, alternatively, used the following:

- Psycho-education about anger.
- Self-monitoring to identify patterns of response to provocation.
- Teaching and practicing cognitive and behavioral self-management skills.
- Extensive group problem solving and role-playing.

Both groups emphasized an authoritative, caring role for the facilitators; better recognition of others' emotions; and peer support. The authors found that both treatment groups produced statistically significant positive outcomes. However, some differences did emerge concerning the age of participants. They found that, generally, "adolescents below the age of 14 benefited most from the PD group and those aged 14 or above benefited most from the CBT group" (Down et al., 2010/2011, p. 47). This is likely because CBT demands a higher level of social and emotional maturity than PD. CBT is more structured and requires participants to be more open with the group and thus more vulnerable; the PD group, on the other hand, used "more projective and oblique, therefore less overtly 'personal' techniques to encourage processing of personal material and to foster trust"

(p. 47). These findings will be helpful in future studies, but from a practical perspective, both methods were found to be effective in reducing anger.

Kassinove and Tafrate (2002) note that there is no formal diagnosis for anger, and they argue for officially recognizing anger "as a disorder of the emotions, along with anxiety and depression," noting that "each of these three human problems has self-report, biophysical, and behavioral components and, given what we already know, there is little reason to ignore anger" (p. 69). O'Neill (1999) provides a list of suitability inclusion and exclusion criteria for referring clients into anger management programs:

- Aggression to objects or others that is fed by anger.
- Being upset because anger caused a loss of freedom or loss of objects or relationships.
- Getting easily upset by external events or triggers.
- Impatience and impulsivity that lead to reacting to triggers with anger.
- Low self-esteem.
- Feeling motivated to get help and wanting treatment.

Here are additional factors to consider:

- Person is impulsive and irrationally reacts to external frustrating events.
- There is a pattern of repeated blowups.
- The person is aware that angry episodes are irrational.
- The person is unable to recall the reasons or events that preceded past anger and only remembers getting angry.
- Anger results in negative and harmful outcomes.

O'Neill (1999) suggests that a person who displays the following *may not* be a candidate for more concentrated anger management treatment:

- Shows deliberate and planned, instrumental aggression rather than angry aggression.
- Does not want to change the anger pattern and in fact perceive benefits from getting angry.
- Is involved in current and consistent use of drugs.
- Shows signs of psychosis, memory problems, or language functioning that does not allow for self-instruction.

Aggression and Violence Prevention

It is important to distinguish between the treatment of anger and the treatment of aggression and violence. With respect to anger, we utilize the concepts of management and control. With respect to aggression and violence, we refer to prevention. Thus, we *manage* anger and *prevent* aggression and violence.

A number of programs address the management of anger and the prevention of aggression. A widely used program and approach are found in Aggression Replacement Training (ART; Goldstein & Glick, 1987; Goldstein, Glick, & Gibbs, 1998). We present this program as an example of programs in this genre.

ART is a violence prevention program designed to replace aggressive behavior with socially acceptable responses (Goldstein et al., 1998). Based on reinforcement and social learning theory, it is a cognitive-behavioral approach. Although originally developed for at-risk youth, it has been adapted for use in adult corrections.

The component of social skills training (behavioral component) teaches interpersonal skills to deal with anger-provoking events. It is based on the assumption that aggressive and violent youth have skills deficits that are related to their offending behavior. The anger control training (affective component) teaches youth skills to reduce their affective impulses to act with anger by increasing their self-control competencies. Youth learn to identify those factors that create their anger and role-play ways to use self-control techniques. Moral reasoning (cognitive component) is a set of procedures designed to raise participants' sense of fairness, justice, and concern with the needs and rights of others.

The Wilder Research Center conducted an evaluation of ART involving 295 youth (Hosley, 2005). Outcome findings were as follows:

- 77% had an offense during the year prior to entering ART and 31% in the year after participating. The latter figure was comparable to the offense rate among all youth in the jurisdiction from which the treatment sample was drawn.
- 80% to 90% were still in school 3 months after ART.
- 80% reported that ART had made a positive difference in their lives, with improvement noted in understanding other people's anger, managing anger and interpersonal conflict, looking for alternatives other than fighting, and avoiding situations that portend trouble.

PERSONALITY DISORDERS

A longitudinal study by Johnson and colleagues (2000) of inner-city youth, from age 5 through their early 20s, and their mothers showed that personality disorders during adolescence correlate with an increased incidence of violent behavior during adolescence and early adulthood. The study also revealed that the more personality disorder symptoms a juvenile displays in early adolescence, the more likely that youth is to be involved in such criminal conduct as physical assault and fighting, robbery, arson, and generally threatening behavior. Youth who met diagnostic criteria for narcissistic, passive-aggressive, and paranoid personality disorders showed increased risk for violent and criminal conduct, even after the study controlled for factors such as parental psychopathology, socioeconomic stress, sex, and comorbid psychiatric distress.

Johnson and colleagues' (2000) research also found links between specific personality disorders in adolescence and violent behavior during early adulthood. Although the study could not formally apply the diagnosis of APD to those under age 18 because of *DSM* criteria, its childhood precursor CD was clearly linked to a marked increase in violent behavior during early adulthood. The study also focused on other personality disorders that had not been previously investigated. The two disturbances that were particularly associated with risk for violent acts and criminal behavior during early adulthood were narcissistic and passive-aggressive personality disorders.

Johnson and colleagues (2000) describe youth with narcissistic personality disorder as lacking empathy and being easily irritated when other people do not respond to their self-centered demands for special attention. They become verbally and physically abusive and often become associated with crimes involving arson and vandalism, threats to inflict harm with a weapon, initiation of fights, assault, and overall escalation of violent actions.

The passive-aggressive disorder was also linked to crime and violence. This disorder is statistically infrequent (1% to 2% of the adolescent or early adult population), but people who are diagnosed as passive-aggressive are also likely to be actively aggressive. Contrary to popular belief, passive-aggressive youth are not merely "quiet saboteurs" who procrastinate, come late, don't appear when they are supposed to, or launch a litany of complaints against their supervisors or teachers. Similar to those with narcissistic personality disorder, passive-aggressive youth showed a high risk for committing vandalism and arson, threatening to injure people with a weapon, and initiating fights and for overall increased levels of violence during early adulthood.

Johnson and colleagues (2000) also found paranoid personality disorder to be associated with teenage crime and violence. Individuals with this disorder tend to be extremely suspicious and mistrustful and share little personal information about themselves. They typically have difficulty with people they work with or with whom they become romantically involved and are at substantially greater risk for initiating physical fights.

POST-TRAUMATIC STRESS DISORDER (PTSD)

Briere & Lanktree (2008, 2011) developed the *Integrative Treatment of Complex Trauma for Adolescents (ITCT-A): A Guide for the Treatment of Multiply Traumatized Youth.* This manual is designed to

> assist clinicians in the evaluation and treatment of adolescents who have experienced multiple forms of psychological trauma, typically in the context of negative living conditions such as poverty, deprivation, and social discrimination. Socially marginalized, multiply traumatized adolescents often suffer from the intersect of two injurious phenomena: sustained exposure to an invalidating social environment, and the cumulative effects of repeated maltreatment—in some cases early psychological neglect and usually multiple instances of interpersonal victimization. (2008, p. 2).

Challenged by life-shattering events, trauma survivors have a natural inclination to avoid thoughts, feelings, and memories about horrific circumstances. Trauma may propel a victim toward chronic suppression of thoughts, feelings, and memories and evoke such behaviors as substance abuse or inflicting harm on the self or others. These responses often result in further anguish, since they not only produce additional problems but decrease the extent to which pain is effectively managed (Briere & Langtree, 2011). The Briere and Lanktree *Guide* is an invaluable resource for providers as they face the nearly inevitable circumstance of providing treatment services for trauma-affected youth.

According to *DSM-4-TR*, diagnosis of PTSD is predicated upon the individual having experienced

a threat to his or her own life or physical integrity to which he or she responded with intense fear, horror, or helplessness (American Psychiatric Association, 2000).

A number of traumatic events are viewed as precipitants of PTSD, including

- Natural and man-made disasters such as floods.
- Violent crimes such as kidnapping, rape, or murder of a parent.
- Sniper fire and school shootings.
- Motor vehicle accidents such as car and plane crashes.
- Severe burns.
- Exposure to community violence.
- War.
- Peer suicide.
- Sexual and physical abuse.

Three factors have been shown to increase the likelihood that children will develop PTSD (Hamblen & Barnett, 2010): (a) severity of the traumatic event, (b) parental reaction to the event, and (c) physical proximity to the event. Children with greater family support and less parental distress will show less severe symptoms of PTSD. The type of trauma experienced will also affect the likelihood of developing PTSD; for example, interpersonal traumas such as rape and assault are more likely to result in PTSD than other types of traumas.

Very young children, who may present with relatively few PTSD symptoms, report more generalized fears such as stranger anxiety, avoidance of situations, and preoccupation with words or symbols (which may or may not be directly related to the event). Elementary school–aged children experience time skew (i.e., improperly sequencing traumatic events when recalling the memory) and omen formation (i.e., believing that warning signs predicted the trauma; Hamblen & Barnett, 2010).

Adolescent responses to trauma, however, appear similar to adult PTSD with a few notable exceptions. While children are likely to exhibit post-traumatic play, which is a literal representation of the harmful event through compulsive repetition of some aspect of it (e.g., playing more shooting games after exposure to a school shooting), adolescents are likely to manifest post-traumatic reenactment, in which the individual behaviorally re-creates some aspect of the trauma (e.g., carrying a weapon after exposure to violence). Further, adolescents are more likely than adults to exhibit aggressive and impulsive patterns of behavior (Birmaher & Brent, 2007).

As shown in Table 3.5, key characteristics of the disorder include intrusive symptoms, avoidance symptoms, and hyperarousal.

Table 3.5 Key Characteristics of Post-Traumatic Stress Disorder

Intrusive symptoms:

Intrusive symptoms consist of "recurrent and intrusive distressing recollections of the event, including images, thoughts or perceptions" and, in young children, repetitive play that reenacts some aspect of the trauma (APA, 2000). These repetitive images have the power to continuously retraumatize youth even when they are safe; for example, a 15-year-old rape victim may relive the scene of her victimization every time she closes her eyes or a 4-year-old child may compulsively "beat her dolls to death" as she relives emotions connected to witnessing the repetitive and brutal beating of her mother. Intrusive symptoms may also include nightmares or flashbacks in which the youth may relive the event, often in a state of panic.

Avoidance symptoms:

A primary symptom of PTSD is the deliberate avoidance of thoughts, people, places, and events that are reminiscent of the trauma. Adolescents, more so than younger children, may also exhibit partial or total loss of memory about the traumatic event. Additionally, there is typically a loss of interest in people and activities that were previously sources of comfort and pleasure. Adolescents who are afflicted with PTSD are characteristically emotionally flat, showing limited affect and unable to experience the same range of ups and downs as their peers. Specifically, victims of repeated sexual abuse may give the impression that

(Continued)

Table 3.5 (Continued)

they are suffering from "emotional anesthesia" in that they can't seem to come into contact with their emotional selves. There is often an accompanying sense of "foreshortened" or limited future in the sense of not being able to make plans beyond the moment in connection with an unpredictable and shattering worldview. The general personality constellation of adolescents who suffer from PTSD is characterized by low self-esteem, guilt feelings, and pessimism; these are attributed to a world viewed as unpredictable, dangerous, and difficult to control with limited or no respite from untrustworthy adults.

Hyperarousal:

PTSD is also associated with symptoms of hyperarousal, which may include difficulty falling or staying asleep, heightened irritability, limited capacity to maintain attention and concentration, hypervigilance to danger or threats, and being startled easily (i.e., an exaggerated reaction to sudden noises or unexpected events).

Source: Dumas, J. E., & Nilsen, W. J. (2003). *Abnormal child and adolescent psychology*. Boston, MA: Allyn & Bacon, pp. 286–288.

PTSD and Associated Patterns of Problem Behavior

Post-traumatic stress disorder is found with high frequency among juveniles involved in problem behavior, and it is most often caused by a criminal act, such as violent and/or sexual assault during childhood (Saigh, Yasik, Sack, & Koplewicz, 1999). More specifically, "having seen or heard someone get hurt very badly or killed" was found in one study to be the most frequent precipitating trauma for PTSD among detained adolescent males who had been diagnosed (Abram et al., 2004). Among females, the most frequent precipitating trauma for PTSD was "thinking you or someone close to you was going to be hurt very badly or die" (Abram et al.).

A history of trauma increases risk of arrest by 59% and of committing a violent crime by 30% (Frabutt et al., 2008). Some estimates indicate that 84%–94% of juvenile offenders report a history of trauma, with girls being more likely to meet criteria for PTSD than boys. PTSD itself affects at least 1 in 10 youths in detention facilities (Abram et al., 2007). PTSD has also been found to be a reliable predictor of comorbidity among youth. In a study of juvenile offenders (Abram et al.), 93% of participants with PTSD had at least one comorbid psychiatric disorder, whereas only 64% of participants without PTSD had at least one comorbid disorder. Moreover, 54% of the juvenile detainees with PTSD had two or more types of comorbid disorders (affective, anxiety, behavioral, or substance use).

In a study of risk factors associated with adolescent substance abuse and dependence, teenagers who had been physically or sexually assaulted, who had witnessed violence, or who had parents with AOD problems were at increased risk for substance abuse and dependence. The presence of PTSD increased risk for marijuana dependence or hard drug use and dependence (Kilpatrick et al., 2000). Similarly, Abram et al. (2007) found that juvenile offenders with PTSD had "significantly greater odds of having a substance use disorder, alcohol use disorder, and both alcohol and drug use disorders than those without PTSD" (p. 1313). In a longitudinal study of the relationship between childhood trauma and substance abuse, children who were maltreated were at one-third greater risk for using drugs as teenagers (Kelley, Thornberry, & Smith, 1997). This, along with the elevated risk of trauma among girls, may explain the increase in arrests for drug abuse violations among adolescent females (Frabutt et al., 2008).

In another study, adolescents who reported that they had been sexually abused also reported that they began using drugs at a younger age and tended to be heavier users of drugs and alcohol as early as the eighth grade (Bensley, Spieker, Van Eenwyk, & Schoder, 1999). Further, the probability of being arrested for an AOD-related offense is about 39% higher for abused children than for comparison subjects (Ireland & Widom, 1994). In addition to substance abuse and the associated symptoms of PTSD, a number of psychiatric disorders are commonly found in children who have experienced trauma. The disorder of depression is often co-occurring, as are anxiety disorders such as separation anxiety, panic disorder, and generalized

anxiety disorder. Externalizing disorders such as ODD, CD, and ADHD are also quite common (Abram et al., 2004; Birmaher & Brent, 2007).

In summary, the problems most likely to be associated with childhood trauma are PTSD and other forms of anxiety, grief and depression, aggressive and defiant behavior, physical symptoms, lowered self-esteem, substance abuse, and social and academic difficulties. Moreover, childhood trauma is a common event in some communities. The Project on Human Development in Chicago Neighborhoods (Molnar, Buka, Brennan, Holton, & Earls, 2003) studied self-reported exposure to violence among urban youth:

- 88% had witnessed someone physically striking another person during their lifetimes.
- 3% reported they had been sexually assaulted during the last year.
- 23% to 30% had seen a shooting or someone being killed or shot at.
- 66% had heard live gunfire.
- 8% had been shot in the past year.
- 15% had been attacked with a weapon.
- 31% had been hit.
- 14% had been sexually assaulted during their lifetimes.

PTSD Treatment Implications

The implications of these statistics are far-reaching. Educational campaigns and exclusive reliance on criminal justice sanctions, without carefully targeted mental health services, are unlikely to affect positively this cognitively, behaviorally, and emotionally damaged population. Because of the above-mentioned gender differences and the unique precursors to violence among girls, "programs should be cognizant that trauma-sensitive and gender-specific treatment models are needed to prevent future offending behaviors" (Frabutt et al., 2008, p. 115).

It is believed that CBT is the most effective means for helping children to decrease the consequences of childhood trauma. CBT generally includes the child's directly discussing the traumatic event (exposure), anxiety management techniques (e.g., relaxation training and assertiveness training), and assistance in correcting or modifying inaccurate or distorted thoughts that emanate from the traumatic experience (e.g., "I am always unsafe, wherever I am."). Although there is some controversy regarding the wisdom of re-exposing children to the events that frightened them, exposure-based treatments are indicated when memories or reminders of the trauma are constant sources of distress (Briere & Lanktree, 2008).

Children are taught relaxation skills and learn to relax while recalling their experiences. Through gradual exposure, in the context of successful relaxation training, traumatized children can learn that they do not have to respond with fear to their memories. CBT also involves challenging and correcting distorted views, such as "the world is totally unsafe," or "nobody can be trusted." CBT with children and adolescents is often accompanied by parental involvement in psychoeducation regarding the symptoms and effects of PTSD. The better parents are able to cope with the trauma, the more they can support their children, and the more treatment outcomes will improve. It is therefore suggested that parents seek treatment for themselves to improve their capacity to assist their children. Special interventions may be required for children who manifest extreme and persistent PTSD-related symptoms (e.g., inappropriate sexual behavior or extreme behavioral problems).

Evaluation of PTSD Treatment Efficacy

McNally, Bryant, and Ehlers (2003) conducted a comprehensive review of interventions designed to mitigate acute distress and prevent long-term psychopathology associated with acute stress disorder (ASD) and PTSD. In consideration of the fact that the vast majority of trauma survivors recover from initial post-trauma reactions without professional help, McNally and colleagues emphasize the need for controlled evaluation of commonly used interventions.

Psychological debriefing, the most widely used method for early intervention, has shown disappointing results. "Although the majority of debriefed survivors describe the experience as helpful, there is no convincing evidence that debriefing reduces the incidence of PTSD and some controlled studies suggest that it may impede natural recovery from trauma" (McNally et al., 2003, p. 45). The most recent recommendations are that crisis intervention workers carefully assess trauma survivors' needs, offering support as necessary, without forcing disclosure of personal feelings and thoughts about the event. Providing information about the event and its consequences is also considered important.

Cognitive-behavioral treatments for PTSD differs from debriefing in that it is delivered weeks or months after the traumatic event, whereas crisis intervention methods are delivered within a few hours or days.

They are not designed to prevent disorder but rather to help individuals whose symptoms remain problematic several weeks post-trauma. Several controlled studies on the efficacy of CBT for trauma survivors show promising results. Severity of early post-trauma symptoms from about 1 to 2 weeks after the trauma seems to be the best indicator of need for treatment (Halligan, Michael, Clark, & Ehlers, 2003). CBT may be effective in accelerating recovery and reducing the risk of long-term PTSD (see reviews by Ehlers & Clark, 2003; Litz, Gray, Bryant, & Adler 2002). Following their extensive study of early interventions for PTSD, McNally et al. (2003) found that certain cognitive-behavioral methods may reduce the incidence of PTSD among people exposed to traumatic events: "These methods are more effective than either supportive counseling or no intervention" (p. 45).

CBT can be tailored specifically to youth. The goals and procedures are very much the same as in adults but with the added element of incorporating parents into the therapy. Support and skills are provided to nonoffending parents to help them cope effectively with their own emotional distress, as well as to respond optimally to and support their children (J. Cohen et al., 2007). The treatment also maintains its effectiveness for the children themselves, with studies showing that "more than 80% of children show marked improvement in symptoms within 12 to 16 sessions (using one 60- to 90-minute session per week)" (p. 6).

Foa, Hearst-Ikeda, and Perry (1995) evaluated a cognitive-behavioral protocol for treating the trauma of rape within several weeks of occurrence. The intervention was comprised of four weekly 2-hour sessions that proceeded in the following sequence: education about trauma symptoms, detailed reliving of the traumatic event in memory, real-life exposure to avoided situations associated with the assault, cognitive restructuring designed to modify maladaptive beliefs, and training in relaxation and breathing skills. A description of the treatment procedure follows:

1. **First session.** The therapist educated the patient about typical acute responses to trauma and assembled a list of objectively safe situations that the patient had been avoiding since the event.
2. **Second session.** The therapist provided information and rationale for exposure therapy, explaining that many symptoms may persist because the patient had not adequately processed the trauma. After learning techniques for deep muscle relaxation and controlled breathing skills, patients were asked to close their eyes and describe the assault in the present tense as if it were recurring (imaginal exposure). As the trauma was retold, the therapist noted any cognitive distortions on the part of the patient regarding the dangerousness of the world or about the victim's perceptions of personal incompetence. Both the relaxation procedure and imaginal reliving were audiotaped, and patients were asked to listen to the tapes as homework practice. They were encouraged to confront avoided situations and activities (exposure in vivo), and they participated in a therapist-initiated discussion of the irrational beliefs presented by the patient during the imaginal reliving.
3. **Third session.** This began with 45 minutes of imaginal exposure, followed by further cognitive therapy targeted at distorted thoughts involving patients' beliefs about the unpredictability, danger, and uncontrollability of the world and extremely negative beliefs about the self. After the therapist helped patients to identify these problematic beliefs, homework involved addressing negative thinking in daily life.
4. **Fourth session.** This session included imaginal exposure, cognitive restructuring, and a review of skills mastered by the patients in the program.

At 2 months post-intervention, when compared to patients who did not receive CBT, fewer of those who received the CBT intervention met the criteria for PTSD (10% vs. 70%). Relative to untreated patients, the CBT group reported significantly fewer re-experiencing and arousal symptoms. However, at a 5.5-month assessment, there were no significant differences in measures of PTSD between treated and untreated patients. The study suggests that although CBT may accelerate recovery, natural healing also occurs, albeit at a slower rate.

TREATMENT GUIDELINES FOR CO-OCCURRING SUBSTANCE ABUSE AND MENTAL DISORDER

Recognizing that comorbidity is the rule rather than the exception among adolescents in treatment for substance use disorders (SUD), Whitmore, Sakai, and Riggs (2010) developed guiding principles for integrated assessment and treatment of these youth. Their approach recommends concurrent treatment as opposed to sequential treatment because "substance

use disorders are often chronic and relapsing, and co-occurring untreated mental health disorders may impact the ability to remain substance free" (p. 12). These interactions make a sequential treatment approach much more prone to failure.

The authors begin by calling attention to the importance of assessment. Successful treatment hinges on proper initial assessment and diagnosis, particularly in youth with co-occurring disorders. Symptom patterns that can overlap, mimic, or mask each other increase the complexity of diagnosis. Whitmore and colleagues (2010) stress that a "thorough multidimensional assessment is the foundation of integrated treatment and the development of a targeted treatment plan" (p. 7). They recommend assessing personal, family, cultural, and neighborhood factors, essentially leaving no stone unturned. In terms of assessment strategies or tools, the authors point to the importance of structured interviews. They recommend using instruments that cover both psychiatric and substance use disorders. They also stress the importance of using self- and collateral-reported substance use data combined with drug testing to determine accurate substance histories. Comprehensive guidelines for the screening and differential assessment of juvenile justice clients are presented in Chapter 12: Assessment Strategies for High-Risk Youth. While developing an alliance and engaging the adolescent is required for proper assessment, it is also the first goal of treatment (Whitmore et al.). Providers are urged to elicit treatment goals and expectations from the adolescent as well as the parents. It is also recommended that they be mindful of the impact that symptoms of co-occuring mental disorders may have on initial clinical presentation and treatment motivation (e.g., cognitive distortions, tearfulness, irritability, poor concentration).

Having the same clinician provide therapy for SUD as well as co-occurring disorders is "ideal and provides a seamless approach" (Whitmore et al., 2010, p. 13). However, separate funding streams for mental health and substance abuse, as well as the cost of physician-conducted therapy, make this ideal somewhat unrealistic, so integration and coordination of care are needed among providers. For example, there should be direct and consistent communication among personnel who prescribe and manage psychotropic medications for a co-occurring disorder client and those providing direct mental health and substance abuse treatment to that client. This would include issues related to attendance, response to treatment, interactions between ongoing drug use and medication or apparent side effects/interactions, and other important issues related to client care. Substance abuse treatment providers should be aware of the specific mental disorder diagnosis, medications being prescribed, what side effects might be expected, rationale for the medication, and nonresponding target symptoms in their clients. To streamline this process, integrated treatment requires extra training and ongoing education for both addictions counselors and mental health providers in each other's area of expertise.

With regard to the role of medications in integrated treatment, Whitmore et al. (2010) take the position that "abstinence should not be a requirement before evaluation and treatment is begun" (p. 22) and that although little is known regarding the interaction between medications and drugs of abuse, abstinence is "often not a realistic goal for adolescents" (p. 16). They do state that "abstinence is ideal before initiating medication for comorbidity, and the psychiatrist and/or treatment staff should support reduction in substance abuse or abstinence while starting a new medication" (p. 16). With respect to the use of alcohol by the underage client and the use of any illicit drug, regardless of the treatment setting or the diagnostic condition (e.g., substance abuse, co-occurring disorders), treatment providers must take the position of total abstinence. In every state, the possession or use of alcohol by a minor is illegal, and the possession of illegal drugs by minors or adults is illegal. In essence, abstinence from alcohol or other illegal drugs must be the clearly stated position of providers of treatment of minors.

The position of the authors of *PSDC* is that abstinence from alcohol is the goal for underage clients, not only during treatment but also as long as clients are in the legal status of being a minor. As for illegal drugs, the goal is lifetime abstinence.

From a treatment perspective, this goal does have some qualifications:

- Prescribing physicians may decide that a psychotropic drug regimen is necessary for a certain mental condition, such as depression or a psychotic disorder, before the client has achieved abstinence from alcohol or other illicit drugs or these drugs have cleared the system. This is the Whitmore et al. (2010) position.
- The treatment of certain drug withdrawal syndromes may require the use of certain medications to effect safe withdrawal from a drug.
- Treatment should be continued for adolescent clients who relapse into alcohol or other drug use, but the treatment regimen must be adjusted to address and manage the relapse.

The issue of abstinence for juvenile judicial clients becomes compounded by their legal status. Not only is alcohol or other illegal drug use by minors illegal, it may also be a violation of the terms of a judicial or court order. An example would be an adolescent who is convicted of drug possession and placed on probation. Continued use would result in violation of the terms of probation and in revocation and incarceration. Any indication on the part of treatment providers of juvenile justice clients that alcohol or illegal drug use is acceptable contributes to the violation of the client's judicial requirements.

According to Whitmore et al. (2010), treatment effectiveness is enhanced when the treatment of the SUD is integrated with treatment of the co-occurring disorder by identifying "interventions, guiding principles, and evidence-based practices that can be adopted by agencies and providers with fidelity to the original models" (p. 21). Furthermore, to begin to implement integrated care, "there must be strong and high-level leadership . . . as well as a belief by all staff that this is the best approach" (p. 22). Accordingly, training and education of staff are required. If possible, comprehensive treatment strategies should be developed that ensure that all necessary elements are available under one roof. If that is not possible, as is often the case for juvenile justice clients, a system whereby clients have seamless access to both substance and mental health treatment concurrently would be the next best option. In sum, it is very important that "clients not have to wait to receive, or be successful in, one type of service before they can receive the other" (p. 22). To achieve this, agencies/providers are encouraged to include as wide a variety of treatment providers as possible to encompass a more comprehensive overall knowledge base and range of clinical skills.

PSYCHOTHERAPEUTIC MEDICATIONS FOR CHILDREN AND ADOLESCENTS

Epidemiological studies report that 10% to 20% of American children suffer from some form of mental disorder, with 5% to 8% experiencing extreme emotional distress (Costello, 1999; Costello et al., 1996; M. Friedman et al., 1996; Powers, Hauser, & Kilner, 1989; Roberts, Attkisson, & Rosenblatt, 1998; Shaffer et al., 1996). Children between the ages of 5 and 19 have at least a 7.5% chance of being diagnosed with ADHD (approximately 5 million youth), with others receiving diagnosis and medication for obsessive-compulsive disorder, social anxiety disorder, PTSD, pathological impulsiveness, sleeplessness, and depression. Table 3.6 summarizes mechanisms of action, side effects, and treatment indications for psychiatric medications commonly used for children and adolescents.

Table 3.6 Psychiatric Medications Commonly Used for Children and Adolescents

Name	*How It Works*	*Side Effects*	*Tested/Approved*
Adderall	A once-a-day amphetamine, inhibits areas of the brain responsible for organizing thoughts.	Rapid heartbeat, high blood pressure, in rare cases overstimulation, sometimes addictive	Approved to treat ADHD in children 3 and older.
Concerta	Keeps high levels of norepinephrine and dopamine, which reduce hyperactivity and inattention.	Headache, stomach pain, sleeplessness, in rare cases overstimulation	Approved to treat ADHD in children 6 and older.
Daytrana	Patch form of methylphenidate, delivers continuous low doses through the skin.	Similar to those for Ritalin	Approved to treat ADHD in children 6 and older.
Depakote	Antiseizure medication is effective for grandiose, hyperagitated state of mania.	Liver and white blood cell abnormalities, headache, nausea, drowsiness	Approved to treat seizures in children 2 and up; also prescribed for bipolar mania for adults.

Name	*How It Works*	*Side Effects*	*Tested/Approved*
Effexor	Targets serotonin and norepinephrine to regulate mood.	Nausea, constipation, nervousness, loss of appetite, drowsiness	Not approved for children; based on adult data is prescribed for depression.
Lithium	Stabilizes episodes of elated, intensely joyous mood associated with mania.	Seizures, loss of coordination, excessive thirst, slurred speech, hallucinations, itching/rash	Not approved for children; prescribed for childhood bipolar mania.
Paxil	Elevates levels of serotonin (similar to Prozac and Zoloft).	Nausea, drowsiness, insomnia	Not approved for children; based on adult data is prescribed for depression, anxiety, OCD, and others.
Prozac	Approved in 1987, was first antidepressant aimed at regulating serotonin.	Insomnia, anxiety, nervousness, weight loss, mania	Approved to treat depression and OCD in children 8 and up.
Ritalin	Active agent is methylphenidate; stimulates the brain to filter and prioritize incoming information.	Headache, lack of appetite, irritability, nervousness, insomnia	Approved to treat ADHD in children 6 and older.
Strattera	First nonstimulant for ADHD, enhances norepinephrine levels in the brain.	Decreased appetite, fatigue, nausea, stomach pain	Approved to treat ADHD in children 6 and older.
Zoloft	Enhances levels of serotonin to maintain feelings of satisfaction and stability.	Upset stomach, dry mouth, agitation, decreased appetite	Approved to treat OCD *only* in children 6 and up.
Zyprexa	Mood stabilizer is designed to balance brain levels of serotonin and dopamine.	Weight gain, drowsiness, dry mouth, seizures	Not approved for children; prescribed for bipolar mania and schizophrenia.

Source: National Institute of Mental Health. (2008). *Mental health medications* (NIH Publication No. 08-3929). Washington, DC: U.S. Department of Health and Human Services.

CHAPTER REVIEW

This chapter begins with a reminder that most adolescents manage the teen years without extreme difficulty. It then goes on to describe a subset of adolescents who manifest symptoms of psychological distress or dysfunction and who make up a sizeable percentage of adolescents who become involved in criminal activity and other problem behavior. Depression, conduct disorders, antisocial personality disorder, post-traumatic stress disorder, and substance abuse disorders are among these patterns of adolescent disturbance. Internalizing disorders (e.g., depression), externalizing disorders (e.g., conduct disorder), and substance abuse can—and often do—occur in the same individual concurrently.

Disruptive behavior disorders, including attention deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and conduct disorder (CD), are more common among males during childhood and adolescence. These share common difficulties in controlling behavior with adjustment problems that often persist into adulthood. These disorders may be found in juvenile justice clients with substance use and abuse problems.

Children with ODD display a pattern of negativity, defiance, and opposition that leads to problems with teachers, parents, siblings, and peers. CD is distinguished from ODD based on violations of legal statutes and social mores. Children with ODD do not typically engage in repeated physical assault, destruction of property, or deceit. During adolescence, the severity of problems and the rate of CD increases dramatically, with youth becoming involved in such violent acts as muggings, armed robberies, or rapes. The term *fledgling psychopath* aptly describes a subset of early-onset

conduct-disordered adolescents who manifest insensitivity, harshness, and lack of remorse combined with callous and unemotional personality characteristics such as a disconcerting lack of empathy and respect for others. Disruptive behavior disorders may have an underlying genetic derivation that interacts with environmental experience in the development of antisocial behavior. The presence of certain types of personality disorders may exacerbate the drug-violence relationship.

A relatively small percentage (23%) of children who manifest symptoms of CD or the less severe ODD are referred for treatment. This is unfortunate in light of the fact that research shows improved outcomes for treated youth. Successful interventions, generally derived from social learning theory, include the following goals:

- Helping the client identify situations that trigger aggressive or antisocial behavior.
- Teaching the child how to take the perspective of others and care about this perspective.
- Reducing the aggressive child's tendency to attribute hostility to others.
- Training the child in adaptive ways of solving conflicts with others.

Each of these goals is achieved through modeling, observational learning, and positive reinforcement for the attainment of the desired behavior and punishment or negative consequences for the continuation of negative patterns.

Clinical-syndrome hyperactivity is diagnosed on the basis of poor concentration skills and motor restlessness. Hyperactivity, low impulse control, attention deficits, and behavioral difficulties, when combined, may serve as an early indicator of developing CD. It is likely that hyperactivity initiates the onset of behaviors, which manifest as defiance, opposition to rules, and other conduct difficulties. Punitive responses (by parents, caretakers, and teachers) to these behaviors may initiate identification with deviance and delinquency. A critical question is whether behavioral therapies and medication are equally effective individually or more useful when used in combination. Studies that compare the two approaches show that medication is more effective in treating the symptoms of ADHD; however, a combination of drug and behavioral therapy is most effective in reducing the conduct problems that often accompany ADHD.

Other personality disorders tend to correlate with an increased incidence of violent behavior during adolescence and early adulthood. Youth who meet diagnostic criteria for narcissistic, passive-aggressive, and paranoid personality disorders show an independent association with increased risk for violent and criminal conduct, even after factors such as parental psychopathology, socioeconomic stress, sex, and comorbid psychiatric distress are controlled.

A diagnosis of post-traumatic stress disorder (PTSD) is predicated upon the individual having experienced a threat to his or her own life or physical integrity to which he or she responded with intense fear, horror, or helplessness. Children who were maltreated are at greater risk for using drugs as teenagers, and those who report sexual abuse say they began heavy drug use at a younger age. Further, the probability of being arrested for an AOD-related offense is higher for abused children. The problems most likely to be associated with childhood trauma are PTSD and other forms of anxiety, grief and depression, aggressive and defiant behavior, physical symptoms, lowered self-esteem, and social and academic difficulties. These findings strongly suggest that educational campaigns and exclusive reliance on criminal justice sanctions, without carefully targeted mental health services, are unlikely to affect positively this cognitively, behaviorally, and emotionally damaged population. Cognitive-behavioral therapy (CBT) shows promise as the treatment of choice for PTSD.

Research points toward use of an integrated treatment approach that synthesizes behavioral, biological, and psychological information. Prediction is enhanced through the addition of social factors, such as family dynamics, experiences with physical/sexual trauma, and other information about the specific adolescent's problem behavior. Treatment outcomes may be enhanced by attending to personality issues that vary according to offense type.

When indicated, an array of psychotherapeutic medications have become strong allies, as neuroscience and psychology have become increasingly effective at targeting specific patterns of cognition, affect, and behavioral disturbance in adolescents who struggle with mental disorder. Overall, this chapter highlights the importance for the juvenile justice system of considering and incorporating mental health treatment. While "most people become conventional adults as they gain experience in responsible institutional roles at work, in the family, and through key community networks," those youth involved with the juvenile justice system do not have access to these same roles (Frabutt et al., 2008, p. 109). That is why it is imperative for the juvenile justice system "to cultivate youth competencies across cognitive, social, moral, emotional and behavioral domains" (p. 109).

Substance Abuse and the Adolescent Brain

4

Chapter Four:
Substance Abuse and the Adolescent Brain

Chapter Outline

The Human Brain: A Fast Idiot

- The joy of dopamine

The Adolescent Brain

- Brain development during adolescence
- Implications for drug abuse and other risky behavior

Alcohol

- Neurochemistry 301: Alcohol and neurotransmission
- Neurotransmitter regulation and dysfunction
- Alcohol and the adolescent brain
- Learning and memory: Alcohol and adolescence
- The dangers of binge drinking
- Summary of alcohol's effects

Methamphetamine: Need a Sudafed?

Cocaine in the Brain

- Crack: Faster and stronger
- Cocaine high
- Health effects of cocaine
- "Crack babies" revisited
- Cocaine and neuronal growth
- Summary of cocaine's effects

Marijuana: "Reefer Madness" Revisited

- Medical marijuana and the "benefits" of pot: Why do so many people smoke?
- Marijuana's effects on the brain
- Withdrawal
- Marijuana's effects on cognition
- Marijuana and the endocrine system
- Marijuana and the immune system
- Marijuana's long-term effects on health

Opiates: Everyone Makes Them

- Opiates and the brain
- Heroin: The ultimate pipe dream
- Summary of heroin's effects

Ecstasy: Let's Party

- Health effects of Ecstasy
- Summary of Ecstasy's effects

Inhalants: How Stupid Can You Get?

- Nitrites: Nonprescription Viagra
- Inhalants and the brain
- Summary of inhalants' effects

Hallucinogenic Drugs: Chemical Vision

- Hoffmann's nightmare
- Effects of LSD
- Other mind-altering drugs
- Summary of hallucinogenic drugs' effects

Tobacco: The Ultimate Drug

- Tobacco's effects on the brain
- Other health effects of smoking
- Summary of tobacco's effects

Chapter Review

Chapter Objectives

- To understand how the human brain works.
- To understand how alcohol and other drugs affect the body, with emphasis on the adolescent brain.

THE HUMAN BRAIN: A FAST IDIOT

The experience of pleasure is derived from stimuli, originating outside or inside the body, that increase the concentration of dopamine in the nucleus accumbens, the primary reward center of the human brain (Milkman & Sunderwirth, 2010).

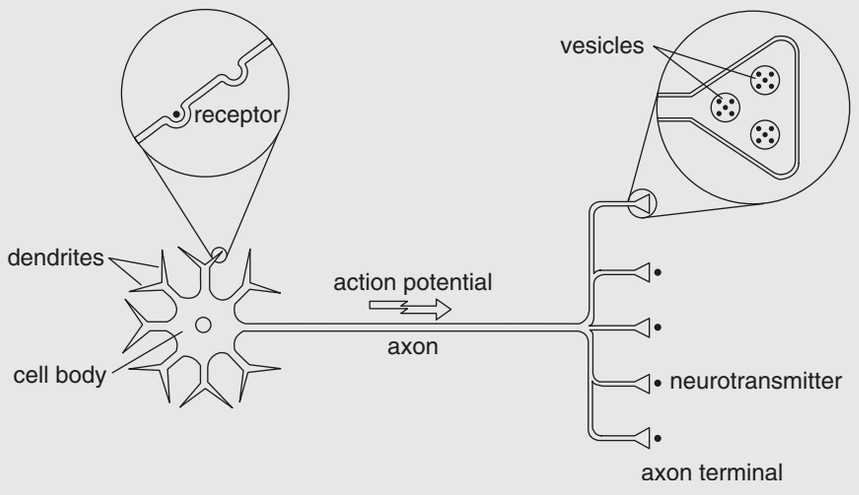
In Chapter 1: Adolescent Development and Pathways to Problem Behavior, risk-taking and judgment during adolescence were discussed in the context of the relatively strong influence (compared to that in adults) of the emotional region of the brain, or amygdala. Because of the enormous impact of drugs on the brain's primary reward center, or nucleus accumbens, adolescents are likely to have even more powerful emotional ties to both the pleasurable and emotional-escape aspects of the drug experience. In recognition that adolescents are biologically primed to appreciate the novelty and risk associated with altered states of consciousness (Dobbs, 2011), this chapter presents a detailed analysis of how substance abuse interacts with the still-emerging teenage brain,

Before discussing the powerful effects of drugs on the mind and body, we take some time to explain the basic design of the brain, which may be described as an electrochemical ecosystem that is the most complex in the entire known universe (Milkman & Sunderwirth, 2010). Indeed, the brain is a giant pharmaceutical factory constantly manufacturing chemicals that result in moods such as fear, anger, shame, despair, joy, depression, mania, and any other mood to which the human species is subjected. However, in this chapter we are interested in how drugs manufactured *outside the brain* (possibly in your neighbor's SUV) affect mood and behavior. To comprehend how these external chemicals affect the internal chemistry of the brain, we need to understand how the brain itself works. So prepare yourself for Neurochemistry 101.

Although the metaphor is not perfect, it is helpful to consider the brain as an electrochemical computer as well as a chemical factory (Milkman & Sunderwirth, 2010). Its 100 billion or so nerve cells, which constitute the brain's "hardware," are able to store more information than all the libraries in the world combined. Each of these nerve cells, or neurons, is in turn composed of three basic elements (Figure 4.1).

The nucleus of the cell (cell body) constitutes a "miniature brain" within the larger brain. It is the cell body that "decides" to transmit a message (an electrical impulse) from one nerve cell to the next; this transmission is called "firing." Or the cell body may decide to ignore the message (i.e., not "fire"). This is the only decision the cell body needs to make, but it needs to make that decision very quickly. For example, you don't want to wait 5 minutes to remove the hand you unwittingly placed on a hot stove while each neuron takes its time deciding to transmit the message to the next neuron and ultimately to the brain. Like a computer, the cell body is "a fast idiot." It has to make one of only two possible decisions, to fire or not to fire.

Figure 4.1 The Neuron. Neurons are made up of a cell body, an axon that transmits electrical impulses called action potentials, dendrites with receptors that respond to chemical signals (neurotransmitters, left blowup), and axon terminals that store molecules of neurotransmitter in vesicles (membrane enclosed sacs, right blowup).



Connected to the cell body is a long fiber, the axon, through which the message must travel on its way to the next neuron. The message is transferred from one of the many branches at the end of the axon of the sending neuron to one of a number of branches on the receiving cell. These branches are called dendrites; each neuron may have up to 10,000 dendrites. If we consider the possibilities of interaction between the 100 billion neurons found in the human brain with 10,000 dendrites per neuron, we have the possibility of quadrillions of connections, each a different way to send messages to different "receivers," with different results. Clearly, the brain really is the most complex entity in this universe.

Incredibly, this process of communication between neuron and neuron is carried out without any direct physical contact between the two cells—as if it were taking place in a city of trillions of people, all talking to each other on cell phones! Neurons are separated by a gap known as the synapse or synaptic junction. The message is carried from one neuron to the next by molecules known as neurotransmitters, which in our computer analogy may be considered the "software" of the brain. Chemical changes that occur in these neuronal spaces determine how we respond to each message. This process of communication between neurons, known as neurotransmission, is largely responsible for the brain functions that determine who we are as individuals, including our personalities, intellect, and character. It is precisely because the neurons are separated by a synapse—in other words, they are not "hardwired"—that the brain ends up with nearly limitless options for neurotransmission, which results in the limitless complexity of the human species.

We are our neurotransmission. Who we are as human beings is reflected in the way our neurons communicate and form new pathways as well as utilize old ones. Francis Crick (1995) summarizes the relationship between self and neurotransmission as follows:

> The astonishing hypothesis is that you, your joys, and your sorrows, your memories and ambitions, your sense of personal identity and free will, are in fact no more than the behavior of a vast assembly of nerve cells and their associated molecules. As Lewis Carroll's Alice might have phrased it, "You're nothing but a pack of neurons." (p. 3)

In order for us to understand the effect of drugs on the brain, we need to know how the brain works and especially the role of neurotransmitters. Let us consider a very important neurotransmitter, norepinephrine (NE), which is found in a part of the brain known as the locus coeruleus (Figure 4.2). One of NE's primary functions is to produce arousal and excitability, including the fight-or-flight phenomenon associated with the release of adrenaline. The ability of NE to stimulate the fight-or-flight response is an evolutionary survival mechanism. A rise in NE levels in times of danger or stress results in an increase in adrenaline, which raises blood pressure and increases heart rate. This forces more oxygen-carrying blood into the muscles, which in turn enabled our prehistoric ancestors to fight if the attacker was a small bear or run like hell if it was a sabertooth tiger. To understand how NE, as well as other neurotransmitters, is involved in communication between neurons, let us continue in Neurochemistry 101.

As we have said, the language of the brain is chemistry, and therefore the flow of information (impulse) from one neuron to the next must be chemical. This action is illustrated in Figure 4.3, which indicates what occurs at a single synaptic junction between two neurons during the sabertooth tiger episode. Chemical messages flow from the axon on the top neuron (presynaptic neuron) across the synapse to the dendrite of the postsynaptic neuron on the bottom and then on to the cell body of the postsynaptic neuron. As the impulse reaches the presynaptic terminal, specific channels open in the membrane of this neuron, allowing doubly charged calcium atoms (ions) to enter the cell. This in turn stimulates the release of the neurotransmitter—in this case, NE (illustrated by curve-shaped molecules)—into the synapse. NE moves across the synapse, carrying the message to the postsynaptic neuron. Embedded in the outer membrane of this neuron are hundreds of complex chemicals (proteins), which act as receptors for NE. These receptors have specific shapes that exactly complement the shape of NE, and the molecules of NE attach themselves to these receptors in much the same way that a key fits into a lock. In fact, the key must not only fit the lock perfectly but must also open the door. Just as many Cadillac keys will fit the ignitions of Buicks but will not start the engines, the same is true of neurotransmitters and receptors.

Norepinephrine not only fits the locks but also opens the doors (ion channels) of the postsynaptic cell. Opening these cell doors allows certain ions (potassium, sodium, and chloride) to go in and out of this cell. If enough channels (doors) are opened and enough ions go in and out, the electrical nature of the cell's outer membrane is altered (depolarized). This

Figure 4.2 Cross Section of the Human Brain. The frontal cortex and major components of the limbic system are shown.

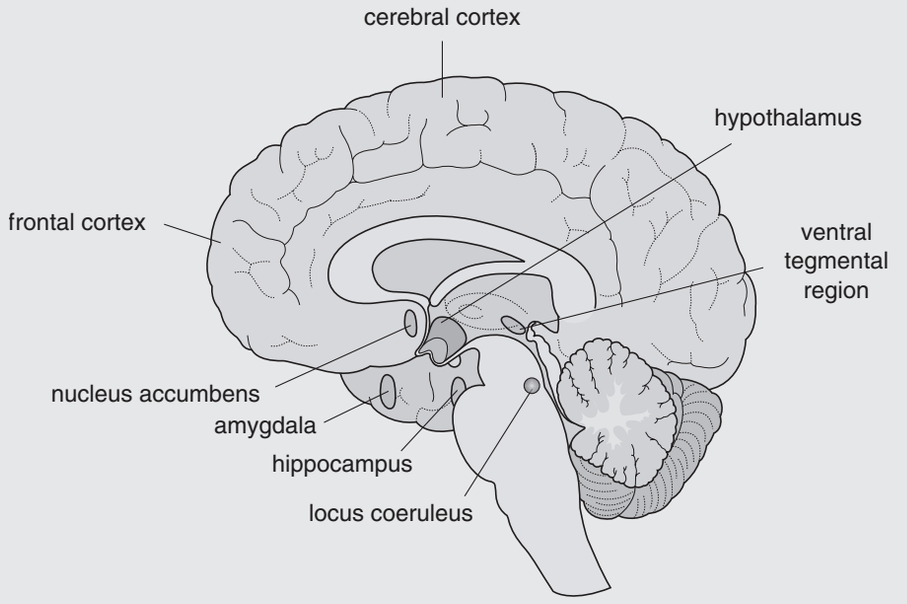
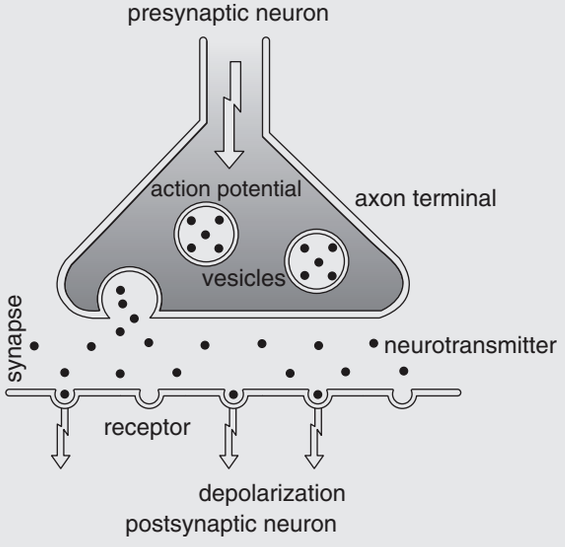


Figure 4.3 Mechanism of Neurotransmission. Signals are transmitted from presynaptic to postsynaptic neurons by neurotransmitters. An action potential in the presynaptic neuron causes vesicles to migrate to the cell membrane and release their neurotransmitter into the synapse (the space between adjacent neurons). The neurotransmitters diffuse across the synapse and combine with receptors on the postsynaptic membrane; this can open channels that permit ions (charged particles) to flow across the membrane. The postsynaptic neuron is said to be depolarized when positive ions enter the cell; if a sufficient amount of depolarization occurs, it will generate an action potential (see Figure 4.1).



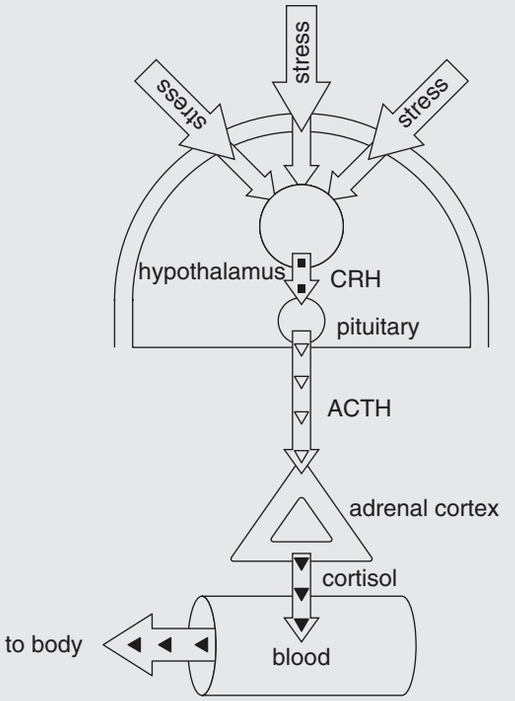
enables the message to be sent to the cell body of the postsynaptic cell, where it is processed along with input from thousands of other cells, all sending messages the same way.

Before the membrane of the postsynaptic cell can fire (become depolarized and send its impulse to the cell body), a critical number of the many receptor sites must be occupied by NE. The more molecules of this neurotransmitter (NE) that we can shove into the synapse, the quicker this critical number of sites will be occupied. Imagine trying to fill the holes of an egg carton by dropping ping-pong balls from 10 feet. Many of the balls will not land in the holes of the egg carton. If we want to fill the carton quickly, we need to drop more ping-pong balls in a given period of time. In the case of neurotransmission, the more molecules of neurotransmitter are released into the synapse, the sooner these receptor sites are occupied—and the more rapidly the neurons will fire. If the neurotransmitter is NE, the more aroused you will be and the faster you can run from the sabertooth tiger or your abusive boss [joke]. Just exactly how does an increase in NE neurotransmission bring this about?

The increased level of NE signals an organ in the brain known as the hypothalamus (H) to send messages to another organ in the brain, the pituitary gland (P), which in turn causes the adrenal glands (A) sitting on top of the kidneys to produce adrenaline. The activation of this system, known as the HPA axis (Figure 4.4), accelerates the heart rate, bringing oxygen and other nutrients to the various parts of the body, increasing strength, and decreasing reflex time. Following the escape from the tiger, or your boss, you are unable to sleep for many hours because the chemicals (NE) produced by this episode cascade back and forth across the synapse, keeping the rate of neurotransmission high, your eyes wide awake, and your brain active.

What makes neurotransmission so remarkable is the speed at which this seemingly cumbersome and

Figure 4.4 Hypothalamic-Pituitary-Adrenal (HPA) Axis. In response to stress, the hypothalamus releases corticotropin-releasing hormone (CRH) into a specialized blood supply that transports it to the pituitary gland, where it stimulates the release of adrenocorticotropic hormone (ACTH) into the general circulation. ACTH, in turn, stimulates the adrenal cortex to release cortisol into the general circulation. Cortisol is a steroid hormone that decreases inflammation and mobilizes sources of energy for the body.



complex process occurs. It is like running a marathon race in which there are a thousand streams to cross. At each stream, the runner must gather rocks (neurotransmitters) from the first shore (presynaptic terminal) to build stepping-stones to the next shore (postsynaptic terminal). The encounter with the tiger (boss) increases the number of "neuronal" rocks that are available on the shore where the runner arrives (presynaptic neuron); the more rocks available, the more rapidly will the runner be able to build a path to cross over the stream.

Of course, most activities in which we engage do not alter our consciousness to the level of arousal brought on by the attack of the tiger or serious confrontation with our boss. The tiger scenario should, however, give you some idea of how the mind and body can be energized, how mood can dramatically shift, and how the moment can be seized—all through the power of brain chemistry. It should be noted that this elevation of neurotransmission (i.e., mood) is brought about without resorting to stimulant drugs such as cocaine or methamphetamine. In today's society, we may be tempted to alter our mood by the use of drugs, which as we shall see, can increase neurotransmission in certain parts of the brain and result in pleasurable experiences.

Let us now turn our attention to the effect of drugs on the brain (Neurochemistry 102). It turns out that most of the mood alterations brought about by drugs are due to the role of a neurotransmitter known as dopamine (DA).

The Joy of Dopamine

> The most pleasure that life has to offer is an adequate flow of dopamine into the nucleus accumbens.
>
> *—S. G. Sunderwirth, cited in Milkman & Sunderwirth (2010, p. 35)*

Understanding the joyful feelings evoked by brain chemistry begins with a search for the site in the brain responsible for this pleasure. The presence of a "pleasure center" in the brain was demonstrated by Olds and Milner (1954) at McGill University. They found that a rat with an electrode implanted in a certain region of the brain would continually press a lever in order to receive electrical stimulation. Routtenberg (1978) of Northwestern University later showed that, given a choice between a lever that delivered food and one delivering brain stimulation, rats would forgo food in favor of the "reward" of brain stimulation. In other words, they chose ecstasy over survival. Rats, it seems, may become as addicted to an artificial (and ultimately fatal) paradise as humans.

In these experiments, the preference for "prolonged ecstasy" occurred only if the electrode was placed in a very small part of the brain, which Routtenberg referred to as the "reward center." In recent years, the search for the specific site in the brain that regulates mood has led scientists to a complex array of neuronal clusters known as the limbic system (Figure 4.2). This region of the brain is believed to control emotions and is often referred to as the "reptilian brain," since we share this primordial brain with other living creatures.

Blum (1991) proposes a model for reward (pleasure) involving the interaction of several neurotransmitters with the various parts of the limbic system that compose the reward center. Blum posits that the release of dopamine into the nucleus accumbens, an important reward site, plays a major role in mediating our moods. (Although there are other reward sites in the limbic system, for simplicity we will limit our discussion to the action of dopamine on the nucleus accumbens.) In Blum's model, which he calls the "reward cascade," feelings of well-being, as well as the absence of craving and anxiety, depend on an adequate supply of dopamine flowing into the nucleus accumbens. In humans, an imbalance that would lead to a deficit of dopamine would produce anxiety and a craving for substances (alcohol, cocaine, heroin, amphetamine, etc.) or activities (e.g., gambling, crime, promiscuous sex, hang gliding, etc.) that would temporarily restore this deficit.

A modified version of the reward cascade (Figure 4.5) by Milkman and Sunderwirth (2010) helps us to understand this complex interaction of neurotransmitters. Let's start with serotonin, that ubiquitous neurotransmitter about which thousands of articles have been written. The introduction of Prozac and other selective serotonin reuptake inhibitors (SSRIs) has made *serotonin* (5-hydroxytryptamine or 5-HT) a household word. In the hypothalamus, serotonin neurons stimulate the release of methionine enkephalin (or simply enkephalin), which in turn inhibits the release of GABA (gamma-aminobutyric acid) in the limbic system. (It seems that we have one more chemical to consider.) What is GABA? The brain must have synapses that retard neurotransmission as well as increase it; otherwise we would be in an even more constant state of emotional turmoil than we are. GABA is the neurotransmitter utilized by these inhibitory synapses; it's our own internal "Valium," regulating our

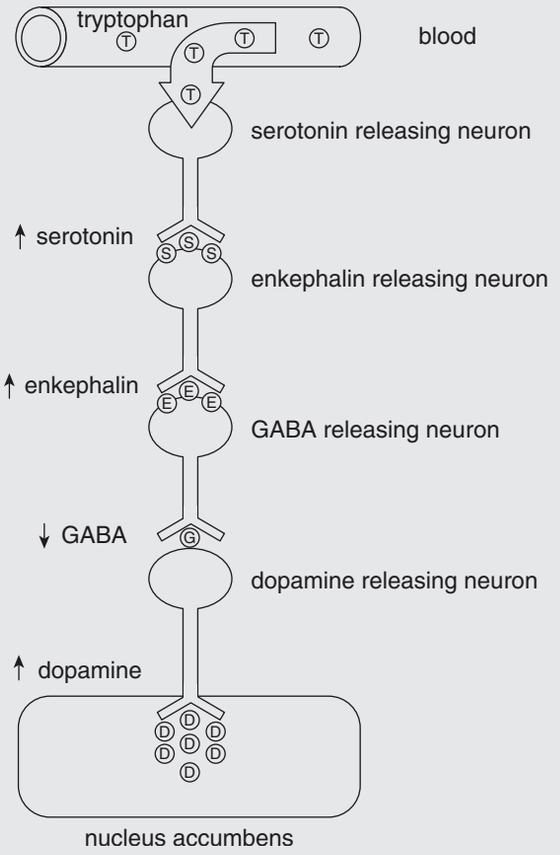
mood through inhibition of the release of neurotransmitters such as dopamine and norepinephrine.

Now that we have struggled through these technical terms, let's see what they really mean in terms of our emotional state. As we follow the reward cascade, the most important concept to keep in mind is that an adequate supply of dopamine in the nucleus accumbens is necessary for feelings of well-being. Studies have shown that increased levels of dopamine in the nucleus accumbens can lead to increased pleasure and reward as well as decreased anxiety. Most drugs of abuse as well as certain activities increase the supply of DA in the nucleus accumbens.

How does the reward cascade work to produce this flow of DA into the nucleus accumbens? As we have said, the process is initiated by the neurotransmitter serotonin, or 5-HT, which is produced in the brain from the amino acid tryptophan and is enhanced by antidepressants such as Prozac. Once we have a supply of serotonin, what does it do for us? How does it help us not only to sleep but in general to feel less anxiety and craving?

In the hypothalamus, serotonin-releasing neurons impinge on enkephalin neurons, enhancing the release of enkephalin. In Figure 4.5, the up and down arrows indicate an increase or decrease, respectively, of the appropriate neurotransmitter molecules. The primary function of enkephalin neurons in the brain is to inhibit the release of neurotransmitters from any neuron with which they interact; the more enkephalin released from these neurons, the more inhibition they exert on neurons on which they impinge.

Figure 4.5 The Reward Cascade. Serotonin neurons stimulate the release of enkephalin, which in turn inhibits the release of GABA (gamma-aminobutyric acid) in the limbic system. As GABA decreases, we can expect the release of dopamine to increase. In other words, the enkephalin has inhibited the inhibitor (GABA).



Source: Milkman, H. B., & Sunderwirth, S. G. (2010). *Craving for Ecstasy and natural highs: A positive approach to mood alteration.* Thousand Oaks, CA: Sage.

Now, how does GABA fit into this neurochemical puzzle? Conveniently, GABA-releasing neurons, as well as other neurons, have receptor sites for enkephalin molecules. As the number of these GABA receptor sites occupied with enkephalin molecules increases, the release of GABA decreases. But GABA keeps the release of dopamine in check through another inhibitory synapse. Therefore, as GABA decreases, due to either enkephalin increase or opiate ingestion, we can expect the release of dopamine to increase. In other words, the enkephalin has inhibited the inhibitor (GABA). This process works with the logic of a double negative and results in a positive increase in dopamine at the nucleus accumbens, which brings about a decrease in feelings of restlessness and anxiety as well as a general increase in feelings of well-being. Serotonin is the battery that starts the engine (reward cascade) that brings about enhanced dopaminergic neurotransmission.

Although serotonin starts the reward cascade engine, the real power behind the pleasure pathway is enkephalin, that internal opiate produced by our brains in response to both internal and external stimuli. It is this euphoric effect that has resulted in enkephalins and their cousins, the endorphins, being referred to as "the keys to paradise." Enkephalins and endorphins, although structurally different, are often grouped together under the generic name endogenous or internal opiates.

Much to our credit—and eternal regret—humankind has been able to find drugs (morphine) and even manufacture drugs (heroin) that have chemical structures similar to our own enkephalins (endorphins) and can produce the feelings of euphoria even more intense than our internal opiates.

The fundamental concept is that a drug or behavior that elicits pleasure and/or reward is accompanied by an increase of dopamine in the nucleus accumbens. Activities as varied as crime, gambling, snorting coke, smoking cigarettes, having sex, and eating chocolate have been shown to increase the level of dopamine in the nucleus accumbens (Milkman & Sunderwirth, 2010).

THE ADOLESCENT BRAIN

Brain Development During Adolescence

The human brain will have more neurons at birth than any other time in life. The baby overproduces neuronal connections (synapses) as the brain responds to new environmental stimuli. Then, at about the age of 3, the brain begins to eliminate the unused connections. It's a typical case of "use it or lose it." A second spurt of synaptic formation occurs just before puberty.

Previously it was thought that no major changes in either organization or function occurred after childhood. Although the overall size of the brain changes very little after childhood, important changes in neuronal connections do occur during adolescence. These changes are especially noticeable in the frontal lobes of the neocortex. Other dramatic changes occur in the brains of adolescents as well. For example, Giedd and colleagues (1999) found that the corpus callosum, which relays information between the two hemispheres of the brain, undergoes growth during adolescence. The cerebellum (Figure 4.2), which is involved in motor coordination, also undergoes changes during adolescence. Studies of rats (Teicher et al., 1991) have shown that dopamine receptors increase in the striatum and the nucleus accumbens in an age that corresponds to adolescence in humans. Also, GABA receptors increase in the cerebellum, the medial septal nucleus, and other subcortical structures.

The prepubscent period of synaptic formation is followed by loss of up to 1% of gray matter (neurons) per year during adolescence. This process enables the brain to consolidate learning by pruning unused synapses and to strengthen and protect used synapses by wrapping the neurons in myelin (white matter). The myelin sheaths protect the neurons of the gray matter and enhance neurotransmission (Hazen et al., 2008).

Adolescent behavior is also strongly influenced by changes in the architecture of the brain. It has been shown by functional magnetic resonance imaging (fMRI) that the prefrontal cortex begins growing just before puberty (Hazen et al., 2008). The prefrontal cortex controls higher functions such as rational thinking, planning, organization, working memory, and behavioral inhibition, and assists in modulating emotions. The continuing maturation of the prefrontal cortex enables older adolescents to exert more control over emotional impulses and make more rational decisions as they mature. This is good news for parents. Since the development of the frontal lobes, which are involved in rational decision making, continues into the 20s, the troubled teenager will very likely mature into a responsible adult. As the cortex begins to control the amygdala, impulsive and emotionally dictated behaviors give way to cortically dominated rationality.

Childress (2006) discusses the likelihood that genetic vulnerabilities (e.g., a low number of dopamine [D2] receptors in the striatum) may interact with adolescent brain development. A "GO!" and

"STOP!" framework is used to explain emerging data showing that individual differences in impulse control may lie in the function and dysfunction of two vital brain systems: (1) the ancient " GO!" system, which is related to seeking out rewards for behaviors that enhance survival such as sex and eating, and (2) the brain's "STOP" system, which is responsible for "putting on the brakes" when an activity is perceived as dangerous or harmful in the long run.

In normal adolescence, changes in the GO! system are self-evident in that hormonal signals prepare the organism for being "ready, willing, and able" when the potential for reproduction arises. In contrast, the brain's STOP! system is not yet fully developed, as evidenced by brain-imaging studies (described above), which show a more gradual development of the frontal lobes. The developmental imbalance of the STOP! and GO! mechanisms (i.e., frontal cortex and amygdala, respectively) during adolescence may account for why teenagers are especially vulnerable to psychoactive drugs. Depite this imbalance, most adolescents who smoke, drink, or use illicit drugs can put them aside and continue their normal developmental trajectory. However, given the GO/STOP imbalance, the "right" environmental configuration (e.g., drug-using peers, poor parental controls) and a genetically loaded neurological template (e.g., low number of D2 receptors) may tip the scales toward addiction (Childress, 2006).

Implications for Drug Abuse and Other Risky Behavior

As discussed above, the younger teenager's ability to make sound judgments may be compromised by the immaturity of the frontal cortex. This concept is supported by studies using fMRI (Hazen et al., 2008), which records activity in the working brain. When processing emotional decisions, adults have a greater activity in their frontal lobes than adolescents processing the same decisions. Adults also have lower activity in their amygdala (the part of the brain involved in emotions) than teenagers when confronted with the same emotional decision. The data imply that the immaturity of the frontal lobes of adolescents prevent them from reliably making rational decisions. Instead, the decisions are processed in the amygdala, the emotional part of the brain (Hazen et al.).

As an example, when pressured by peers to engage in a harmful activity, such as drug use, an adult has the ability to weigh a desire to conform against perceived harmful effects and hopefully arrive at a rational decision. On the other hand, because of immature frontal lobes, the adolescent may not have the capacity to respond in as rational a manner. In this case, the more developed amygdala is likely to be the region of the brain that processes the decision, and the emotional desire to conform overcomes the weak response from the frontal cortex. In other words, "the amygdala hijacks the cortex," and the adolescent takes poorly calculated risks as in delinquent actions, drug abuse, or lapses in self-care and concern for the welfare of others.

ALCOHOL

Possibly the most distressing aspect of alcohol abuse is its effect on the brain. The bad news is that brain damage leading to cognitive impairment can result from even mild to moderate drinking (Evert & Oscar-Berman, 1995). Such impairment interferes with those mental activities that involve acquiring, storing, retrieving, and being able to use information. The good news is that some cognitive impairment due to alcohol is reversible (Volkow, Wang, & Doria, 1995). The really bad news is that *not all* alcohol-related brain damage is reversible. The most devastating and irreversible effect of heavy alcohol consumption on the brain is a disorder known as Wernicke-Korsakoff syndrome, which is a disorder that prevents the affected person from remembering new information for more than a few seconds (Oscar-Berman, 1990). It has also been demonstrated by Pfefferbaum and colleagues (1992) that most alcoholics' brains are smaller; this shrinkage is most notable in the outer layer of the frontal lobe, which may explain the cognitive decline in long-term alcoholics.

Another piece of bad news is that binge drinking on college campuses has increased since 1998 and continues to kill in the range of 2,000 college students ages 18–24 every year in the United States (Hingson, Zha, & Weitzman, 2009). In addition, 599,000 students in this age group are injured, 696,000 are assaulted, 97,000 are sexually assaulted, 400,000 practice unsafe sex, and more than 100,000 report that they are not sure if they consented to sex, all while under the influence of alcohol. Following are common alcohol-related problems and the numbers of college students affected:

- Negative health: 150,000 students.
- Drunk driving: 3.36 million.
- Police involvement/public drunkenness and/or DUI: 110,000.

- Suicide attempts while under the influence of alcohol or drugs: 1.2%–1.5%.
- Property damage sustained by institutions: 25%–50% of schools.
- Vandalism while under the influence: 11% of students.
- Alcohol abuse/dependence: 31% of students/ 6% of students (Hingson et al.).

While students in this age category are approaching the end of what we generally consider adolescence, several parts of their brains are still undergoing transition to adulthood, and alcohol exerts a greater negative influence on their brains than that of older adults.

Neurochemistry 301: Alcohol and Neurotransmission

Now that we have discussed the negative effects of alcohol, let's see if we can handle an advanced course (Neurochemistry 301) on how alcohol affects neurotransmission. However, as usual, before we can do this, we need to look at some more elements of brain chemistry. The brain controls our moods and emotions through synaptic homeostasis (Milkman & Sunderwirth, 2010). To survive, the brain needs a mechanism to calm us down when we become overly excited after escaping from the sabertooth tiger. On the other hand, we cannot sit around in a state of relaxed bliss if we intend to feed our Neolithic family.

Two of the neurotransmitters involved in restoring and maintaining synaptic homeostasis are GABA and glutamate. We have seen how GABA inhibits dopamine-producing neurons. It turns out that GABA is the major inhibitor of neurotransmission in the brain. On the other hand, glutamate and its chemical cousin, N-methyl-D-aspartic acid (NMDA), are the major excitatory neurotransmitters.

Our hope is to maintain a balance of these two neurotransmitters in order not to doze off in times of danger or fly off the handle while watching TV. To understand how our two opposing neurotransmitters work, let's go back to Figure 4.3. When glutamate attaches itself to a postsynaptic receptor site, it allows positive ions to enter the receiving neuron. If enough positive ions (Na+) flow into the receiving neuron, the membrane of this postsynaptic neuron becomes depolarized, and the neuron will fire. That is, it will send the impulse on to the next neuron. Therefore, glutamate is called an excitatory neurotransmitter. On the other hand, when GABA attaches to a postsynaptic receptor, it opens channels that allow negative ions (Cl–) to flow in. If enough of these receptor sites are occupied and enough negative ions enter the postsynaptic neuron, it will not fire. For this reason, GABA is called an inhibitory neurotransmitter.

Braun (1996), in his very readable book *Buzz,* does an excellent job of describing the effect of alcohol on glutamate and GABA receptors as well as the "rush" associated with alcohol. When alcohol enters the brain, it attaches itself to glutamate receptors in many parts of the brain and distorts the structure of the receptor. This alteration of the receptor is just enough to prevent glutamate from activating the neuron. Remember the Cadillac key in the Buick ignition? It will fit but won't start the engine. This inhibition occurs in many parts of the brain involving speech, coordination, heart rate, and, most seriously, the ability to learn. The ability to learn and retain information is the function of the brain's hippocampus (Figure 4.2). Any damage to this structure affects the ability of the brain to convert new information into long-term memories. Damage to the hippocampus thus has a negative effect on memory formation and may explain the phenomenon of alcoholic blackouts experienced by acute alcohol poisoning. E. White (2002) has summarized research conducted over the past few decades that leads to the conclusion that disruption of normal neuronal activity in the hippocampus is partially responsible for alcohol-induced impairment of memory. Interestingly, alcohol interferes with the establishment of new memories more than with remembering previously learned information.

Other brain structures involved in memory are the frontal lobes, which are also involved in cognitive processes besides memory. Damage to the frontal lobes may be responsible for the cognitive impairment in chronic alcoholics. Neuronal connections between the frontal lobes and the hippocampus (Shastri, 2002) indicate that memory and cognition involve both of these brain structures. Therefore, it is not surprising that chronic alcohol use has been associated with frontal lobe damage due to shrinkage (Kubota et al., 2001).

Another neurotransmitter involved in hippocampal function is the previously mentioned cousin of glutamate, NMDA. NMDA is involved in a hippocampal learning process called long-term potentiation (LTP; S. J. Martin & Morris, 2002). If a memory such as an order or a verse from a favorite poem is repeated, the neuronal connections responsible for the memory become strengthened, and the ability to

recognize the order or repeat the verse becomes easier. This process illustrates why repetition can be a valuable learning tool. It is known that alcohol retards LTP by interfering with the activation of the NMDA receptors in the hippocampus (Swartzwelder, Wilson, & Toyyeb, 1995).

Neurotransmitter Regulation and Dysfunction

Heinz (2006) considers the effects of glutamate and GABA in cases of long-term alcohol ingestion. These molecules influence our moods as well as the uncomfortable and sometimes dangerous symptoms of withdrawal. As stated above, glutamate is an excitatory neurotransmitter that enhances or speeds up neurotransmission along the neuronal pathways. Any substance that enhances glutamate release from the presynaptic neuron will increase the rate of neurotransmission; this may result in arousal, depending on the neuronal pathways involved. GABA is an inhibitory neurotransmitter that slows down neurotransmission. The effect of alcohol on these two neurotransmitters is shown in Figure 4.6.

Alcohol blocks glutamate from binding to its NMDA receptors. This decreases glutamate-induced neurotransmission, resulting in relaxation, sleep, or even passing out. This is one of the reasons alcohol is often used for its calming effect in stressful situations. Alcohol also enhances the effect of GABA, resulting in a further decrease in neurotransmission (remember, GABA is an inhibitory neurotransmitter). So the effect of decreased glutamate and increased GABA may be the drunken stupor, slurred speech, instability, impairment, and sleepiness characteristic of excessive alcohol consumption.

We see how alcohol produces powerful states of sedation, but the human brain is not to be trifled with. The term *synaptic homeostasis* describes the brain's reaction to sustained attempts to achieve ecstasy by altering our normal neurotransmission patterns. Consider the attempt, using alcohol, to achieve relaxation by blocking the binding of glutamate to NMDA receptors. For most moderate alcohol consumers, this works well. However, sustained heavy drinking alters the brain in a way that decreases the effect of the amount of alcohol that initially increased positive feelings. In order to counter this blocking of glutamate to NMDA receptors, the postsynaptic membrane creates more NMDA receptors. Then more alcohol must be consumed to achieve the desired pleasure. After a while, alcohol is consumed mostly to not feel "crappy," and the hope of experiencing ecstasy is long gone.

Although high tolerance of alcohol seems like a beneficial adaptation, it functions more like a curse. As shown in Figure 4.6, alcohol affects neural mechanisms that regulate GABA and glutamate. Figure 4.7 provides an illustration for our discussion of why withdrawal occurs.

Figure 4.6 Effect of Alcohol on Neurotransmission. Alcohol excites inhibitory GABA neurons but inhibits excitatory glutamate neurons (left panel). Increased inhibition coupled with decreased excitation reduces neurotransmitter release (right panel).

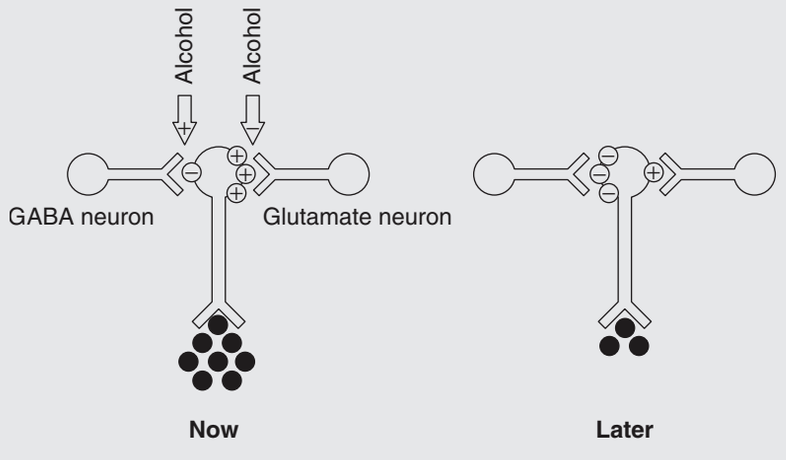
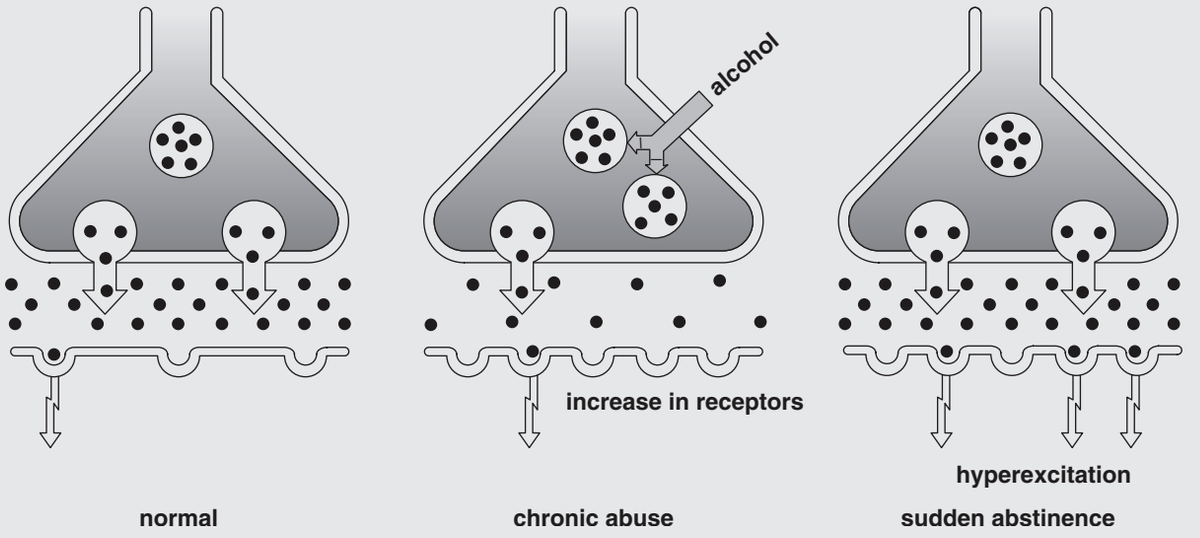


Figure 4.7 Mechanism of Alcohol Withdrawal. The low levels of neurotransmitter in cases of chronic alcohol abuse (Figure 4.6) leads to a compensatory increase in the number of postsynaptic receptors (middle panel). Under these conditions, a normal amount of neurotransmitter (left panel), as would occur when alcohol is not present, stimulates more receptors and thereby causes hyperexcitation (right panel).



Alcohol and the Adolescent Brain

As discussed earlier, the adolescent brain is not fully developed but is undergoing developmental changes that extend into young adulthood (Hazen et al., 2008). Therefore, it would not be unreasonable to expect that drugs such as alcohol, which have a direct effect on the brain, would have a greater effect on the developing adolescent brain than on the mature adult brain. An analogy might be to consider the varying effects of damaging chemicals on a piece of clay during the process of forming a finished vase. When the clay is removed from the potter's wheel, it is still moist and may be molded into any number of shapes. Care must be taken not to add too much water, since some of the smaller molecules of clay will dissolve. Firing of the vessel not only removes water but causes chemical reactions, and the new chemical bonds solidify and strengthen the entire vessel. Because of the formation of these bonds during firing, water and even strong chemicals have very little effect on the finished vase.

Now suppose that a harsh chemical, such as a strong acid, is placed in the vessel right after it has been formed on the potter's wheel (birth to adolescence) and before it has been fired in the furnace (matured into adulthood). Very likely the acid would dissolve many of the molecular components, which have not been stabilized by bond formation through firing. But once the vessel has been fired (matured), many of the chemicals that had such a devastating effect on the raw clay would have little if any effect on the finished vase.

In a similar manner, evidence indicates that alcohol and other drugs have a greater effect on the undeveloped adolescent brain than on the mature adult brain (Markwiese, Acheson, Levin, Wilson, & Swartzwelder, 1998). Ongoing changes in the immature brain make the adolescent brain more vulnerable than that of an adult to alcohol (and other drugs) damage (Spear, 2000).

Learning and Memory: Alcohol and Adolescence

The hippocampus is the primary region of the brain involved in learning and memory. Alcohol has been shown to affect memory by disrupting the functioning of the hippocampus (A. M. White & Best, 2000). Therefore, alcohol-induced memory impairment may be the result of neurotoxic effects on the hippocampus. There is evidence that adolescents who abuse alcohol have a decrease in the size of their hippocampus (De Bellis et al., 2000).

As mentioned earlier, a model for changes in hippocampal structure during learning is called long-term potentiation (LTP). Alcohol is known to have a greater effect on the LTP of adolescents than on that of adults (Pyapali, Turner, Wilson, & Swartzwelder, 1999; Swartzwelder et al., 1995). In fact, alcohol has been implicated in loss of brain cells in many of the areas of the brain besides the hippocampus: the cerebral cortex, hypothalamus, cerebellum, amygdala, and locus cerulus (Harper, 1998). A key neurotransmitter involved in LTP is believed to be the glutamate cousin, NMDA. Alcohol exerts a disrupting influence on the NMDA receptor, thereby interfering with the activation of the cell and correspondingly reducing LTP. It has been shown (Swartzwelder et al.) that alcohol has a greater effect on the NMDA receptor in the hippocampus of adolescents than on adults. Thus, it is not a quantum leap to believe that alcohol has a greater effect on learning and memory in the adolescent brain than in the adult brain. In experiments using rats, Markwiese et al. (1998) showed that alcohol impaired the ability of adolescent rats to navigate a water maze more than that of adult rats. It is not unreasonable to assume that effects found in animal studies would be similar to those expected in humans. After all, at a basic level, the neurobiology of memory formation between humans and animals is not very different.

While it seems clear that adolescents are more vulnerable than adults to alcohol-induced learning and memory impairments, it seems that adolescent rats are less sensitive to the sedative effects of alcohol than adult rats (P. J. Little, Kuhn, Wilson, & Swartzwelder, 1996; Silveri & Spear, 1998; Swartzwelder et al., 1995). As we have seen, the neurotransmitter responsible for calming us down after the sabertooth tiger episode is GABA, our internal tranquilizer. Alcohol enhances the sedative effects of GABA in adults more than in adolescents. This lesser effect of alcohol on GABA receptors of adolescents allows adolescents to drink more than adults before passing out. Alcohol also appears to have less effect on the motor coordination of adolescents than on adults (A. M. White et al., 2002). This allows adolescents to drink more than adults before they exhibit typical signs of intoxication. However, the ability to drink larger amounts without becoming intoxicated enables the teenager to continue drinking alcohol. This increased ability to consume alcohol has a greater neurotoxic effect on the brains of teenagers than on those of adults. Therefore, alcohol is doubly damaging to teenagers: More alcohol is absorbed by a brain that is already more sensitive to alcohol.

The Dangers of Binge Drinking

As documented earlier, too many young people are caught up in binge drinking. Because the adolescent brain is undergoing rapid changes, it is especially vulnerable to alcohol neurotoxicity with accompanying long-term consequences. Binge drinking has become a serious health problem among late teens on college campuses as well as at high school parties. Repeated binge drinking, sometimes called chronic intermittent exposure (CIE), results in withdrawal seizures that are believed to be responsible for many of the negative effects of alcohol ingestion on the central nervous system (CNS). Using laboratory animals, Becker and Hale (1993) showed that repeated withdrawals from alcohol caused a higher rate of seizures than continuous exposure to alcohol. In humans, those with a history of detoxifications showed a greater tendency to have seizures while undergoing withdrawal (Brown, Anton, Malcolm, & Ballenger, 1998). Binge drinking, which is characterized by repeated withdrawals, has been shown in rats to be associated with impaired learning (Bond, 1979). This CIE-induced cognitive impairment in adolescent rats has been shown to extend into adulthood (A. M. White & Best, 2000). Once again, it is reasonable to expect that similar impairments would be present in adults who had previous CIE episodes. In humans, those with a history of binge drinking showed greater impaired memory function while intoxicated compared to others.

Summary of Alcohol's Effects

Alcohol exerts its damaging effects on both the brain and the body. It exerts its effect on the brain by damaging and destroying neurons in the hippocampus and frontal cortex. These areas of the brain are responsible for learning, memory, and cognition. Alcohol also has serious health effects on the rest of the body, including heart disease, liver disease, and increased incidence of strokes.

METHAMPHETAMINE: NEED A SUDAFED?

One of the most serious drug problems, besides alcohol, in the United States today is methamphetamine (ice, meth, speed, crystal), which is easily manufactured in homes, barns, pickups, and SUVs using a common cold remedy (Sudafed), easily available chemicals such as anhydrous ammonia, and lithium batteries. Unlike cocaine, which is imported from Colombia, Bolivia, and

Peru by way of countries such as Haiti, meth is not only imported but also produced in the United States.

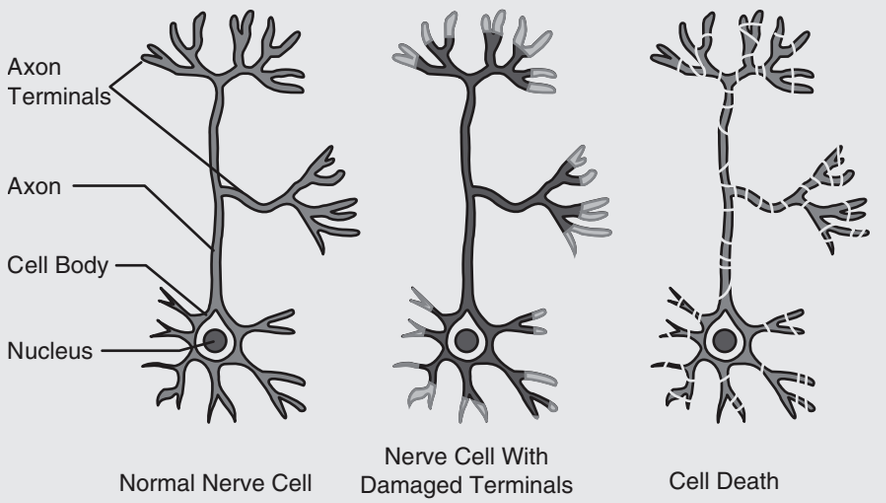
We would expect meth, as a close relative of amphetamine, to have many negative effects on the body, especially the brain and the cardiovascular system. Besides addiction, serious effects from meth usage include rapid and irregular heartbeat and increased blood pressure. The latter results in irreversible damage to small blood vessels in the brain, which in turn may cause strokes. Other damaging effects include increased wakefulness, insomnia, convulsions, tremors, confusion, anxiety, aggressiveness, and paranoia. Possibly the most serious health problem from chronic methamphetamine abuse is damage to the neurons of the brain. Previous studies have shown that meth causes damage to neurons in several parts of the brain, including the frontal cortex, which is responsible for cognitive functioning and decision-making capacity. It is also known to damage cells in the striatum. Damage to these cells could lead to movement disorders resembling Huntington's chorea and tardive dyskinesia. Cadet, Ordonez, and Ordonez (1997) have shown that methamphetamine not only damages neurons but actually destroys them through a process called apoptosis (Figure 4.8).

In experiments using mice, Cadet et al. (1997) showed that neuronal death was also prominent in the frontal cortex and hippocampus; the latter is utilized in the formation of long-term memory. Cell death in the frontal cortex, which is involved in cognition and reasoning, is especially troublesome during adolescence since this area is undergoing rapid changes at this time of life. Immature development makes this part of the brain especially vulnerable to apoptosis. In addition, extensive damage in the striatum was found, which may result in movement disorders (Figure 4.9).

Another serious consequence of meth usage is damage to the nerve endings of dopamine-producing cells. This damage persists for at least 3 years after drug intake has ceased. This damage to dopamine-producing cells is similar to that caused by Parkinson's disease and may be responsible for the addicting aspects of methamphetamine. These earlier studies of the effects of methamphetamine on the brain have been confirmed by Chang et al. (2002) using a technique called perfusion nuclear magnetic imaging (pNMI), which measures blood flow into important brain regions.

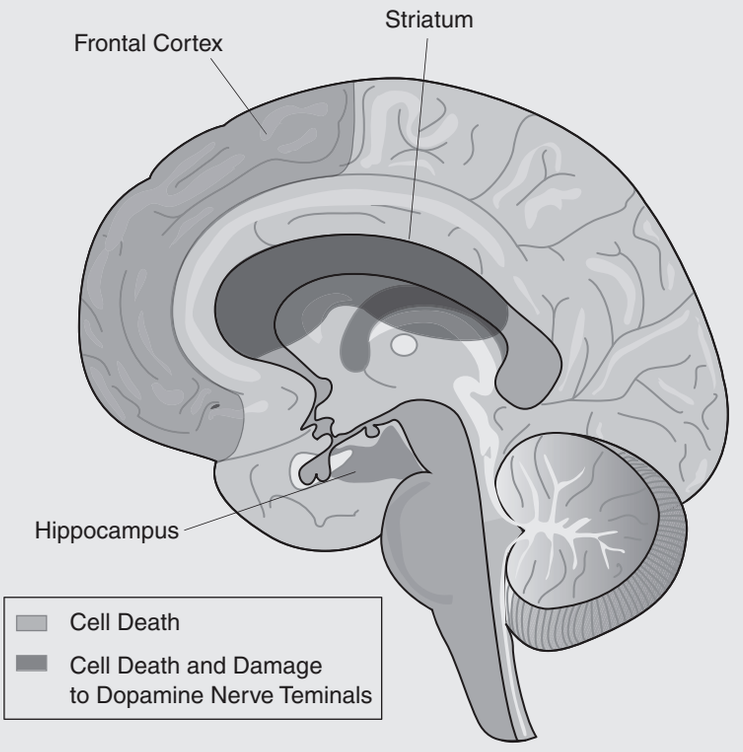
If meth is so harmful, then why is it so popular among not only teens but adults as well? The answer is the same as with most drugs of abuse. It rapidly increases the flow of dopamine into the nucleus accumbens, resulting in euphoria that lasts 8–24 hours. This is much longer than the high from cocaine, which lasts 20–30 minutes (NIDA, 2006).

Figure 4.8 Neurotoxic Effects of Methamphetamine



Source: Mathias, R. (2000). Methamphetamine brain damage in mice more extensive than previously thought. *NIDA Notes, 15*(4). Retrieved from http://www.ehd.org/health_meth_8.php.

Figure 4.9 Human Brain Areas Corresponding to the Mouse Brain Areas Damaged by Methamphetamine. The figure shows that neuronal death is prominent in the frontal cortex, hippocampus, and striatum.



Source: Mathias, R. (2000). Methamphetamine brain damage in mice more extensive than previously thought. *NIDA Notes, 15*(4). Retrieved from http://www.ehd.org/health_meth_8.php.

COCAINE IN THE BRAIN

In the early 16th century, when Francisco Pizarro encountered the Quechua (usually referred to as the Inca) people of present-day Peru, he found that their royalty used the extract of a local shrub known today as *Erythroxyion coca* or simply the coca plant. This was the first contact of Europeans with this drug, which was soon to become one of the most widely abused drugs in the world. Sir Arthur Conan Doyle's famous fictional detective, Sherlock Holmes, used cocaine, and doctors even prescribed it as an antidote to morphine addiction. Cocaine was readily available in the late 19th century and early 20th century, either over the counter or in beverages such as Coca-Cola, which was introduced in 1886. It was claimed to be a brain tonic and a cure for nervous affliction. A typical serving of Coca-Cola contained about 60 mg of cocaine. Today Coca-Cola contains only the name *coca* and not the drug.

Crack: Faster and Stronger

Cocaine is found in the coca plant, where it constitutes less than 1% of the leaf. Cocaine can be extracted from the leaves in hot water to make coca tea, a popular beverage in Peru. After being extracted, the paste can also be treated with hydrochloric acid to form cocaine hydrochloride, an organic salt. This is the form in which it arrives in the United States as a white powder. Cocaine becomes dangerous when concentrated to form pure cocaine hydrochloride. This form is usually snorted since it is not sufficiently volatile to smoke.

The hydrochloride salt may be converted to "crack" by a general chemical reaction (acid plus base) learned by every beginning chemistry student. Treatment of the acid salt with any household base, such as ammonia or sodium bicarbonate, releases the hydrochloric acid to form the volatile "free base," known as crack. Once extracted with ether and dried, crack can be smoked to give a much faster high than can be obtained snorting. Sounds easy, right? Actually,

production of crack is very easy for anyone in a chemistry laboratory equipped with an exhaust hood. The problem arises when inexperienced "chemists" evaporate the ether extract to get the pure cocaine. Ether is very volatile and flammable, and many serious accidents have resulted from igniting the ether during extraction. Comedian Richard Pryor suffered severe burns while attempting to evaporate the ether extract.

Cocaine High

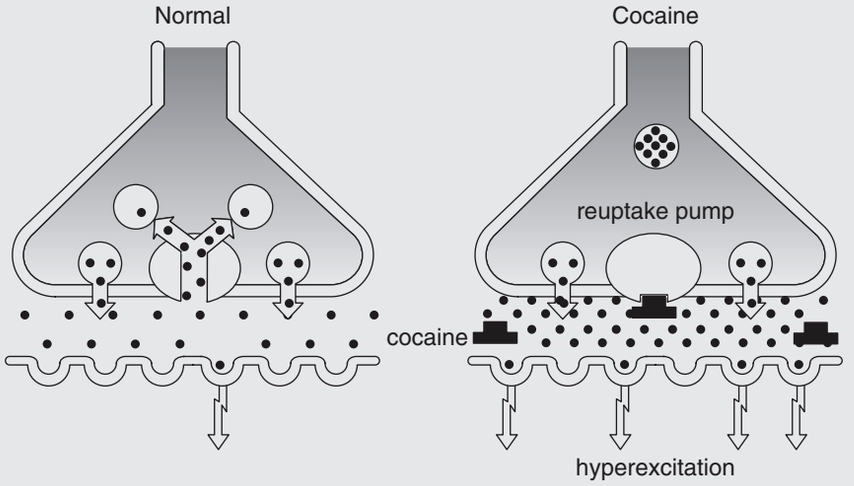
How does cocaine react in the brain to give such an immediate and intense high? Let's return to Neurochemistry 101 for an answer. Briefly stated, cocaine causes a high by increasing the availability of, guess what, our good friend dopamine. No surprise there. When dopamine is released from the presynaptic neurons of the dopamine-producing nerve cells in an area of the brain known as the ventral tegmental area (VTA), it flows into the reward center, the nucleus accumbens, where it produces the expected high (Ikegami, Olsen, D'Souza, & Duvauchelle, 2007). After activating the cells of the nucleus accumbens, dopamine is transported back into the presynaptic VTA cells by transporter receptors. Cocaine blocks these transporter receptors (Figure 4.10), preventing the dopamine from being reabsorbed. Since it stays in the synapse, it is able to be used over and over again and to continually activate the neurons of the nucleus accumbens, giving the user the intense high characteristic of cocaine use.

Health Effects of Cocaine

Cocaine, like most drugs of abuse, exerts its major effect on the brain. Because of the intense high associated with the drug, addiction can occur during a single binge episode. Ciccocioppo and colleagues (2004) showed that a single cocaine binge can establish cue-induced long-term drug-seeking behavior in rats. Once addicted, the user finds him or herself in a continuing spiral of increased usage to obtain the previous high and, especially, to avoid the effects of withdrawal. These effects include severe depression and a resulting intense craving to resume using. Prolonged usage can produce paranoia, especially among crack users, who may become aggressively paranoid. Dopamine activity in the brain of a person expecting a cocaine high is stimulated when he or she sees a conditioned stimulus, meaning if the user sees a place where he or she used the drug, dopamine levels will surge in the reward center and the individual will expect the cocaine or crack rush (Ikegami et al., 2007).

Siegel and colleagues (1999) have shown that cocaine use increases the risk of sudden heart attack and stroke. Also, according to Satran and colleagues

Figure 4.10 Cocaine in the Brain. The amount of neurotransmitter in a synapse depends on the balance between the rate at which neurotransmitter is released into the synapse (from vesicles) and the rate at which neurotransmitter is removed from the synapse by the reuptake pump (left panel). By blocking the reuptake pump, cocaine increases the concentration of neurotransmitters which, in turn, occupy more receptors and cause hyperexcitation (right panel).



(2005) at the Minneapolis Heart Institute, another negative health effect of cocaine is an increased risk of fatal coronary aneurysms. The prefrontal cortex, in control of long-term memory and higher-level thinking, has been shown to be affected by the continued use of cocaine (Ikegami et al., 2007), especially when the use starts in adolescence (Santucci, 2008). Disruption in the prefrontal cortex could explain the errors in judgment frequently displayed by addicts (Ikegami et al.). The use of cocaine in adolescence, a developmentally critical period for the cortical areas of the brain, is especially detrimental, as research has shown that the drug can be more addicting than if started in adulthood (Brenhouse & Anderson, 2008; Santucci). The effects of dependence on a still maturing brain can cause many psychosocial dysfunctions. Even if an individual gets into recovery and addresses the behavioral problems attributed to cocaine addiction, he or she may still have subtle neuronal impairments, specifically involving neurotransmitters. A study by Santucci provides data to "imply that drug use in adolescent humans may have long-lasting consequences on cognitive and emotional functioning" (p. 83). Changes in the brain put teenagers at a higher risk for cue-associated drug-seeking behaviors (Brenhouse & Anderson).

"Crack Babies" Revisited

In the 1980s, scary reports about the effects of cocaine on the brains of the developing fetus were widespread. Women whose fetuses were allegedly damaged by cocaine usage during pregnancy were subject to criminal prosecution. Then in the 1990s, the pendulum swung in the opposite direction. It is now clear that cocaine may not be a "sledgehammer" for the developing brain, but clearly it does have serious negative effects on the brain that appear later in the life of the exposed child. These include behavioral problems such as aggression, inability to stay focused, and impulsivity. In addition, crack-exposed children are more anxious and depressed (Chasnoff, 1997). Mayes (1995) reported that exposed babies at 3 to 6 months of age showed more signs of irritability than those in the control group, whose mothers had been exposed to alcohol, nicotine, and other drugs besides cocaine. At 12 to 18 months, the crack-exposed babies were having more trouble focusing their attention than the control group.

Cocaine and Neuronal Growth

As we have seen, cocaine acts by increasing the supply of dopamine in the synaptic junction of neurons. This enables more dopamine receptors to be activated, which in turn brings about the high characteristic of cocaine. In research on animals, the number of dopamine receptors, designated as D1, is normal in rabbits exposed to cocaine, but the exposed receptors do not transmit their signal as efficiently as those in normal brains. According to P. Levitt, Harvey, Friedman, Simansky, & Murphy (1997), this may result in the abnormal growth of dendrites, which then weave around each other to accommodate their growth. This pattern of development is believed to have a significant effect on their circuitry. The abnormal dendrite growth was found in the anterior cingulated cortex, which is the area of the brain involved in learning and attention. Abnormal growth and interweaving of neurons would be especially significant for adolescents. As we have seen, the cortex of adolescents is undergoing rapid changes, so any alteration in normal growth patterns could have significant effects on cognition.

Summary of Cocaine's Effects

Cocaine exerts its effects on the brain by increasing the amount of dopamine flowing into the nucleus accumbens, a major reward center. There is general agreement that maturing cocaine-exposed babies exhibit attention deficits, irritability, and aggression. Cocaine interferes with the normal growth of dendrites, especially in the area of the brain involved in learning and attention. This is especially troubling for adolescents, whose brains are in the process of rapid development.

MARIJUANA: "REEFER MADNESS" REVISITED

Marijuana is the most widely used illicit drug in the United States. It can be taken orally, mixed with food, smoked in concentrated form as hashish (more common in Europe), smoked in rolled cigarettes called "joints" (the form of nearly all consumption in the United States), or smoked in pipes and occasionally hollowed out cigars called "blunts." In 2009, 16.7 million Americans age 12 and older had used marijuana at least once in the month prior to being surveyed (SAMHSA, 2010). The NIDA-funded 2010 Monitoring the Future Study showed that 13.7% of 8th graders, 27.5% of 10th graders, and 34.8% of 12th graders had used marijuana at least once in the year prior to being surveyed (Johnston et al., 2011). Table 4.1 summarizes some of the potential adverse

Table 4.1 Adverse Health Effects of Marijuana

Acute (present during intoxication)

- Impairs short-term memory.
- Impairs attention, judgment, and other cognitive functions.
- Impairs coordination and balance.
- Increases heart rate.

Persistent (lasting longer than intoxication but may not be permanent)

- Impairs memory and learning skills.

Long-term (cumulative, potentially permanent effects of chronic abuse)

- Can lead to addiction.
- Increases risk of chronic cough, bronchitis, and emphysema.
- Increases risk of cancer of the head, neck, and lungs.

Source: NIDA (National Institute on Drug Abuse), 2010d.

health effects of this widely used drug. Given its well-known threat potential, why do so many people—some brilliant and well established and even some health professionals—use it anyway?

Medical Marijuana and the "Benefits" of Pot: Why Do So Many People Smoke?

Those who are pro-legalization assert that the beneficial uses of marijuana have been documented for thousands of years (Nadelmann, 2004). The cases for and against medical marijuana involve a potpourri of political, medical, psychiatric, and criminal justice issues.

The recent trend of state-level legislation permitting the use of medical marijuana may simply make the drug more accessible. These laws facilitate access to marijuana, but they "do little to advance the development of standards that address the potency, quality, purity, dosing, packaging, and labeling of marijuana" (Hoffmann & Weber, 2010). Furthermore, a lack of standards has resulted in a vast disparity among states in terms of how much marijuana can be possessed and/or cultivated. A "60-day supply," for example, ranges from 1 ounce and 6 plants in Alaska to 24 ounces and 15 plants in Washington (Hoffmann & Weber). A lack of scientific research is largely to blame for this inconsistency. Physicians are unaware of which conditions may require the medicinal benefits of marijuana, what the appropriate doses are, or if equally effective alternatives exist. Medical experts are pushing to reclassify marijuana as a Schedule II drug in order to facilitate more scientific evaluation and clinical trials.

A survey of child psychiatrists in California (S. L. Jaffe & Klein, 2010) found that, with the advent of medical marijuana, adolescent patients have been influenced to view marijuana as being more beneficial and available. This new positive outlook was accompanied by reduced recognition of the major side effects of marijuana, which include decreased short-term memory and loss of motivation. The survey also found that adolescents are obtaining medical marijuana cards with and without parental permission and that some adolescents are even writing negative reviews on practice websites if a psychiatrist refuses to prescribe medical marijuana.

Why does pot retain its status as the most popular illicit drug? Essentially, marijuana aficionados expect positive effects and have a less negative view of possible problems. Gaher and Simons (2007) investigated users' and nonusers' appraisals of the "benefits" of relaxation and tension reduction, facilitation of social and sexual contexts, and enhancements of mind and perception. They found that cannabis users anticipated positive outcomes in each of these domains while forecasting fewer and less frequent problems. Johnston et al. (2011) have shown that since 1975,

there has been an inverse relationship between the percentage of high school students who smoke pot and their perception of risk; for example, the period 1990–1991, in which the lowest percentage of high school students reported marijuana use in the preceding 12 months (about 20%), corresponds to the period where the highest percentage (about 80%) reported seeing "great risk" in regular use. Further, users find pot to be more morally acceptable (Amonimi & Donovan, 2006), and a primary reason that adolescents initiate use is peer approval (D. B. Henry & Kobus, 2007). When peers discourage use, chances of abstinence increase significantly. Of course, the opposite is true as well (D. B. Henry & Kobus).

Tidal social forces appear to be far more powerful determinants of contemporary pot culture than an individual's attitudes about the benefits or risks of using marijuana. In *Drug, Set, and Setting: The Basis for Controlled Intoxicant Use,* Zinberg (1984) presents compelling evidence that social setting is a primary (perhaps the major) determinant of an individual's choice to use an intoxicant. Drug use is intimately related to large social influences such as media, war, and massive environmental change (Carpenter & Pechmann, 2011; S. Halperin & Bloom, 2007; Stryker, 2003; Zinberg).

Marijuana's Effects on the Brain

According to the Drug Abuse Warning Network (SAMHSA, 2011), the most frequent drug-related visits to hospital emergency rooms for youths ages 12 to 19 are for marijuana abuse. In 2001, there were over 26,000 visits by youths in this age group to emergency rooms for marijuana or marijuana in combination with other drugs.

Cabral (1995) summarizes the effects of chronic marijuana abuse on the brain, endocrine system, and the immune system. Since marijuana in sufficient doses is hallucinogenic, we would expect that the main ingredient responsible for this effect, tetrahydrocannabinol (THC), would have receptors in the brain. Such receptors have been found in the hippocampus, the cortex, and the cerebellum. These are the areas of the brain involved in memory, cognition, and coordination. Our brains are programmed to react to THC by conveniently providing receptors for a naturally occurring cousin of THC, anadamide, named after the Sanskrit word for "bliss."

These naturally occurring neurotransmitters are referred to as endocannabinoids (endogenous cannabinoids). As shown in Figure 4.11, THC receptors have been found in the cerebellum (coordination), hippocampus (memory), neocortex (cognition), nucleus accumbens (reward), basal ganglia (movement), hypothalamus (temperature regulation), amygdala (emotion), spinal cord (pain), central gray (analgesia), brain stem (sleep, arousal), and nucleus of the solitary tract (nausea, vomiting; Nicoll & Alger, 2004).

In addition, marijuana has a negative effect on psychomotor speed and manual dexterity. It is obvious from the effects listed above that driving while under the influence is very hazardous. The 1939 film *Reefer Madness* (Esper & Gasnier, 1939) became a cult classic in the 1960s and 1970s because of its outlandish claims about the harmful effects of marijuana. This type of ridiculous treatment of a serious drug problem does a disservice to law enforcement and the medical profession as well as making a joke out of the actual negative health effects of marijuana.

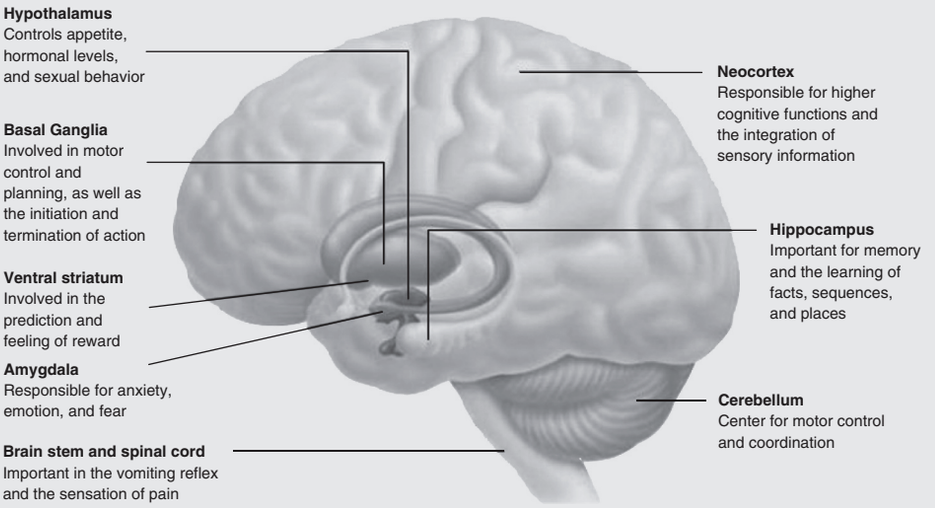
Withdrawal

One of the hallmarks of addiction is the presence of negative physiological and psychological effects upon removal of the drug. The sometimes proclaimed view that marijuana in nonaddicting is contradicted by observed withdrawal effects. Researchers have found that long-term marijuana users became more aggressive during withdrawal than did former users (Arendt, Rosenberg, Foldager, Sher, & Munk-Jorgensen, 2007; Kouri, Pope, & Lukas, 1999). Haney, Ward, Comer, Foltin, and Fischman (1999) found that chronic users experience other withdrawal symptoms such as anxiety, stomach pain, and irritability. Vandrey, Budney, Hughes, and Liguori (2008) showed that during abstinence, marijuana smokers experienced sleep difficulties; decreased appetite; and increased anger, aggression and irritability. These studies on withdrawal effects clearly indicate that, contrary to earlier opinions, marijuana use can be associated with drug dependence.

Marijuana's Effects on Cognition

One area in which there is little difference of opinion is that marijuana causes deficits in cognition. This observed impairment is not surprising since animal studies have shown that marijuana causes structural damage to the hippocampus, a brain region involved in memory and learning. Research has found that, compared to light abusers of marijuana, heavy abusers suffer deficits in verbal and visual memory, executive functioning, visual perception, psychomotor speed,

Figure 4.11 Effects of Marijuana on the Human Brain



When manijuana is smoked, its active ingredient, THC, travels throughout the body, including the brain, to produce its many effects. THC attaches to sites called cannabinoid receptors on nerve cells in the brain, affecting the way those cells work. Cannabinoid receptors are abundant in parts of the brain that regulate movement, coordination, learning and memory, higher cognitive functions such as judgment, and pleasure.

Source: NIDA (National Institute on Drug Abuse). (2010d). *Research report series: Marijuana abuse* (NIH Publication Number 10-3859). Retrieved from http://www.nida.nih.gov/PDF/RRMarijuana.pdf. (Revised; originally published 2005.)

and manual dexterity (Crean, Crane, & Mason, 2011). These impairments existed for at least 28 days and possibly longer. Abstinence from heavy and chronic cannabis use, however, may not be associated with the remittance of some impairments. Heavy use that is initiated in adolescence can be particularly harmful in this regard, as maturation of executive functions has not been fully achieved (Crean et al.). An interesting observation by Bolla, Brown, Eldreth, Tate, and Cadet (2002) is that cognitive impairment from smoking marijuana is greater among those students with lower IQ scores than those with higher scores. Bolla and colleagues believe that those with higher IQs have more cognitive reserves; therefore, the impairment from marijuana is not as obvious as with lower cognitive reserves. Earlier research by Pope, Gruber, Hudson, Huestis, and Yurgelun-Todd (2001) indicates that cognitive impairment from heavy marijuana use seems to disappear after 1 month, but recent reports show subtle, long-term effects on cognition and brain functioning (Bolla, Eldreth, Matochik, & Cadet, 2005).

According to Pope and Yurgelun-Todd (1996), it is very clear that heavy marijuana use decreases the ability to learn and remember while under the influence of the drug. The problem is not so much with getting the abuser to remember a previously learned item; the basic problem is activating the learning process (attention, concentration) in the first place. Therefore, students who smoke marijuana might be expected to get lower grades in school than those who abstain.

Serious Mental Disorder

Perhaps the most devastating insult to cognition, besides Alzheimer's disease, is the development of delusions and hallucinations, the most salient symptoms of psychosis and the chronic brain disease schizophrenia. Studies conducted in Holland, New Zealand, and the United States examined links among

cannabis use, psychosis, and schizophrenia. Although a causal link between excessive marijuana use and severe mental disorder has not been proven, the following conclusions have been drawn:

- There is a strong association between use of cannabis and age at first psychotic episode in male schizophrenic patients (Veen et al., 2004).
- There is either a common vulnerability with cannabis and psychosis or a two-way causal relationship between the two (Ferdinand et al., 2005; Minozzi et al., 2010).
- Cannabis is the trigger for psychosis in genetically predisposed frequent marijuana users (Fergusson, Horwood, & Ridder, 2005).
- Cannabis psychosis cases are arguable misdiagnoses of extreme cases of acute cannabis intoxication and harmful cannabis use and/or mental/behavioral disorders stemming from other or multiple drug use (W. D. Hall, 2006; Newcombe, 2005).
- Cannabis use is not a sufficient cause for psychosis but is rather a component cause (i.e., part of a complex mix of factors that lead to psychosis; Arseneault, Cannon, Witton, & Murray, 2004; Minozzi et al.).

Marijuana and the Endocrine System

Murphy (1995), speaking at the National Conference on Marijuana Use: Prevention, Treatment, and Research, indicated that several studies have shown that the reproductive system of marijuana users may be affected by alteration of the secretion of hormones from the pituitary gland. Pituitary hormones that control reproductive function in humans include follicle stimulating hormone (FSH), luteinizing hormone (LH), and prolactin, all of which play a role in the secretion of both the female hormone estrogen and the male hormone testosterone. More recent studies have explored and corroborated this relationship between cannabis use and endocrine function (Gorzalka, Hill, & Chang, 2010; Ranganathan et al., 2008). Clearly, tinkering with Mother Nature at this basic level is a prescription for disaster.

Marijuana and the Immune System

The human immune system is a complicated system that enables the body to resist the invasion of bacteria, viruses, and other microbes. This system also offers protection against tumors by inhibiting cancer growth. Cabral (1995), speaking at the National Conference on Marijuana Use: Prevention, Treatment and Research, presented evidence that the ingredient in marijuana that is responsible for the negative effects observed in the immune system is our familiar hallucinogenic compound THC. Not exactly a surprise. The scavenger cells of the immune system, which are responsible for ridding the body of pathogens, are subject to damage by exposure to THC (Eisenstein, Meissier, Wilson, Gaughan, & Adler, 2007; see also Tanasescu & Constantinescu, 2010). Marijuana has also been shown to have a negative effect on T- and B-lymphocytes, which are important in fighting bacterial and viral infections (El-Gohary & Eid, 2004). Because marijuana use is often associated with sexual promiscuity, impairment of the immune system creates an additional risk factor that may be associated with the spread of herpes, type B hepatitis, and HIV.

Marijuana's Long-Term Effects on Health

Although there may be some conflicting evidence on long-term brain damage from smoking marijuana, there is no difference of opinion on the damage to the lungs. The effects from long-term abuse of marijuana are similar and in many cases worse than those from cigarette smoking (Aldington et al., 2007). Marijuana smokers experience frequent respiratory illnesses, daily coughing with phlegm production, obstructed breathing pathways, and frequent lung infections. Other effects on the lungs of marijuana smoking include acute pneumonia, inflammation of airways, chronic bronchitis, acute chest illnesses, and possibly emphysema (Moore, Augustson, Moser, & Budney, 2005). The carcinogenic molecules and tars in marijuana smoke make users especially vulnerable to lung cancer, as well as head and neck cancers.

OPIATES: EVERYONE MAKES THEM

Opiates include heroin and morphine as well as our internal opiates, enkephalin and endorphins. In fact, the term *endorphin* is a compilation of the words *endogenous morphine*. Recently, prescription opiates such as Vicodin and Oxycontin have hit the illegal street trade and are replacing the old standby, heroin, as the opiate of choice among adolescents.

Opiates and the Brain

To understand the effect of opiates on the brain, let's return to the reward cascade (Figure 4.5) and the role of GABA. As we have seen, opiates, including our own opiates (endorphin and enkephalin), act on the brain by binding to opiate receptors and inhibiting the release of neurotransmitters from those neurons on which they have receptor sites. If these neurons also happen to impinge on GABA neurons, the release of GABA is inhibited. GABA inhibits the release of our pleasure-inducing neurotransmitter, dopamine (DA). So, if we inhibit the inhibitor, we get an increase in the flow of DA into the reward center, the nucleus accumbens, and feel intense pleasure. Let's begin by looking at a long-standing opiate of abuse, heroin.

Heroin: The Ultimate Pipe Dream

Heroin, a synthetic derivative of morphine, is also known as diacetylmorphine. The Adolph Von Bayer Company made it by the same process they used to make Bayer aspirin. This is not to imply that there is any relationship between the two in terms of physiological action. Heroin was first marketed as a nonaddicting form of morphine and was even found in some cough syrups. It soon became apparent that not only was heroin addicting but it was actually more addicting than morphine itself.

Heroin is administered by smoking, snorting, injecting, or sniffing. In those who use injection as the method of delivery, many inject up to four times a day. Intravenous injection provides euphoria within 7 to 8 seconds, whereas smoking requires 10 to 15 minutes for the euphoria to peak. Injection continues to be the primary method of heroin administration among addicts, although recently there has been a trend toward snorting/sniffing as a preferred method of administration. This move away from injection has prompted drug traffickers to produce high-purity heroin, which is being marketed to middle-class Americans as a "nonaddicting" way to use the drug.

Summary of Heroin Effects

Heroin crosses the blood-brain barrier soon after injection and binds to opiate receptors (Figure 4.5), where it soon produces the expected "rush" as well as suppression of pain. It can also depress respiration, which can be fatal, especially if heroin is used with alcohol. Clouded mental functioning is a short-term consequence of heroin usage, as is occasional nausea and vomiting. The most obvious and detrimental long-term effect is addiction, characterized by compulsive drug seeking and use. Physical dependence requires the abuser to continue taking the drug to avoid withdrawal symptoms, which include restlessness, bone pain, explosive diarrhea, vomiting, cold flashes, and goose bumps. These withdrawal symptoms peak within 24 to 48 hours and subside after about a week. Some serious effects of intravenous heroin injections are infectious diseases such as HIV/AIDS and hepatitis. Collapsed veins, abscesses, and bacterial infections are common among those who inject heroin.

ECSTASY: LET'S PARTY

Ecstasy (B-bombs, disco biscuit, essence, go, wheels, X, Scooby snacks, sweeties, hug drug, love drug) is called a "party drug" since it is often present at all-night dance parties or "raves," which are growing in popularity among teenagers. It is reported and believed by many adolescents that Ecstasy produces euphoria and boosts energy, allowing users to dance and party all night. Users also claim that it is a sex enhancer.

Health Effects of Ecstasy

Ecstasy is the drug of choice for many late teens and other young adults (Wu et al., 2010). Most of these users are not aware of the risk to their health. Chemically, Ecstasy is 3,4-methylenedioxymethamphetamine (MDMA). The significant part of the name is *methamphetamine*, which should be a red flag. As a derivative of meth, Ecstasy would be expected to exhibit many of the deleterious effects of that drug, discussed earlier. This it does well, with a few added zingers of its own.

Since any drug that causes the type of mood swing attributed to Ecstasy obviously has significant effects on the brain, let's examine these effects first. It is believed that the major contributor to the euphoria experienced by MDMA users is our familiar neurotransmitter serotonin. The euphoria brought about by Ecstasy is due, at least in part, to the rapid release of serotonin from nerve endings. This overstimulation of these nerves causes what appears to be irreversible damage to the nerve endings (McCann, Szabo, Scheffel, Dannals, & Ricaurte, 1998). Even if the serotonin neurons do regrow, they don't grow back normally and in the right location in the brain. Some studies in monkeys have shown that after only 4 days of exposure to Ecstasy, brain damage was apparent

6 to 7 years later (NIDA, 2010b), pointing to the strong possibility of permanent brain damage in humans.

It has also been shown that unborn rats exposed to MDMA during what corresponds to the third trimester of human pregnancy suffered memory and learning deficiencies throughout their adult lives (Broening, Morford, Inman-Wood, Fukumura, & Voorhees, 2001). Rodgers and colleagues (2003) have shown that people who take Ecstasy regularly report long-term memory difficulties and are 23% more likely to recount problems with remembering things than nonusers. Even after at least 2 weeks of abstinence, users have significant memory problems.

Ricaurte, Yuan, & McCann (2000), in a widely cited work, reported that monkeys that were exposed to Ecstasy suffered severe damage to the part of the brain that produces serotonin and that Ecstasy kills dopamine-producing cells after only one dose. Damage to these cells would put users at risk for Parkinson's disease, which is characterized by nonfunctioning or poorly functioning dopamine neurons. However, Ricaurte and colleagues' work has been widely criticized, as it was later discovered that the primates used in their study were injected with methamphetamine and not Ecstasy (T. Bartlett, 2004).

An added health risk for Ecstasy users is the fact that the drug is often consumed with other drugs, especially marijuana and/or alcohol, an especially potent combination with respect to permanent brain damage. Liechti, Gamma, and Vollenweider (2001) also reported that women seem to be more susceptible than men to the subjective effects of Ecstasy such as perceptual changes, thought disturbances, and fear of loss of body control.

Many of the emergency admissions to hospitals are not for Ecstasy-induced memory deficits but for dehydration due to disruptions in body temperature and cardiovascular regulation (NIDA, 2010b). The extremely high room temperatures often found at raves, as well as the stimulating effects of the drug, greatly increase the severity of dehydration. These conditions are conducive to hypertension, hyperthermia, and heart and kidney failure. In addition, ravers compensate for expected dehydration by drinking excessive amounts of water, which in some cases results in swelling of the brain.

Summary of Ecstasy's Effects

Escalating use of Ecstasy among college and high school students indicates that the drug is rapidly becoming the drug of choice within this age group. According to one study, MDMA causes what appears to be irreversible and long-term damage to dopaminergic neurons and damage to serotonergic nerve endings. Therefore, it would not be surprising if users suffer long-term memory and other cognitive deficits. However, some of this research has been criticized. So what are we to believe? The conflicting data do show damage to serotonin-releasing neurons. However, the extent of this damage is controversial. Other effects on health that seem to be substantiated are dehydration, hypertension, brain swelling, hyperthermia, and heart and kidney failure. Considering the potential damage to the brain and the rest of the body, use of Ecstasy appears to present considerable risk.

INHALANTS: HOW STUPID CAN YOU GET?

Inhalants, volatile substances that produce breathable vapors, include paint sprays, paint thinners and removers, spray paints, deodorant, vegetable oil, gasoline, glues, and other aerosols. In addition, certain medical anesthetics found in commercial and household products are abused. These include chloroform, ether, nitrous oxide (laughing gas), and aliphatic nitrites. A recent study found that more than one third (38.6%) of juvenile offenders reported lifetime inhalant use. Among users, almost half met criteria for a lifetime *DSM-4* inhalant use disorder (either abuse or dependence; Perron & Howard, 2009). The same study linked inhalant use with high levels of anxiety and depressive symptoms, more impulsive and fearless temperaments, and more antisocial behavior problems.

Nitrites: Nonprescription Viagra

Nitrites, which include cyclohexyl, amyl, and butyl nitrite, are often used to enhance sexual performance. Nitrites act much like Viagra by dilating blood vessels and relaxing muscles. Cyclohexyl nitrite is found in room deodorizers, while amyl nitrite is sometimes prescribed by doctors for heart pain. Both amyl and butyl nitrites are packaged in small bottles (butyl nitrite) and are referred to as "poppers."

Inhalants and the Brain

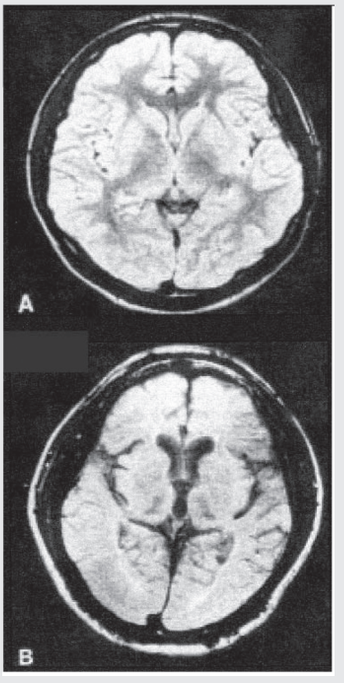
One of the most dangerous as well as widely used inhalants is the organic aromatic compound toluene. It is used commercially to make TNT (trinitrotoluene), an explosive used in military bombs. Although

quite different from TNT, toluene affects the brain in a way not unlike the way TNT affects a building. But first, let's see if we can explain why anyone would use inhalants such as toluene.

Toluene and most other inhalants (except nitrites) activate the brain's dopamine reward system. That should not come as any surprise at this point. The rapid high produced by inhalants resembles that of alcohol intoxication. This high is followed by drowsiness, lightheadedness, apathy, impaired functioning and judgment, disinhibition, and belligerence. The other short-term effects of inhalant abuse are too numerous to mention here but include dizziness, slurred speech, increased lethargy, muscle weakness, and stupor. Heart failure and death can occur within minutes after a prolonged "sniffing." While long-term effects include weight loss, irritability, decreased coordination, depression, and withdrawal, the real "bomb" is damage to the brain.

Toluene's effects on the brain are shown in Figure 4.12. The brain actually shrinks in size with chronic toluene abuse. The neurons are destroyed in a manner similar to that of buildings in a city being destroyed by TNT. Since toluene affects nearly all areas of the brain, it is like a "dumb bomb," indiscriminately destroying everything it hits. This is really bad news, since the two areas we need to preserve are the hippocampus, for memory, and the frontal cortex, for cognition. These are the areas of the adolescent brain that are not mature. In a manner similar to chemicals used on a pottery vessel before firing, inhalants damage the "uncured" brain more than the adult brain.

Figure 4.12 Brain Damage in a Toluene Abuser



Brain images show marked shrinkage of brain tissue in a toluene abuser (B) as compared to a nonabusing individual (A). Note the smaller size and the larger (empty) dark space within the toluene abuser's brain

Source: NIDA (National Institute on Drug Abuse). (2010c). *Research report series: Inhalant abuse* (NIH Publication Number 10-3818). Retrieved from http://www.nida.nih.gov/Researchreports/inhalants/inhalants.html. (Revised; originally published 1999.)

Photos: Courtesy of Neil Rosenberg, MD.

Summary of Inhalants' Effects

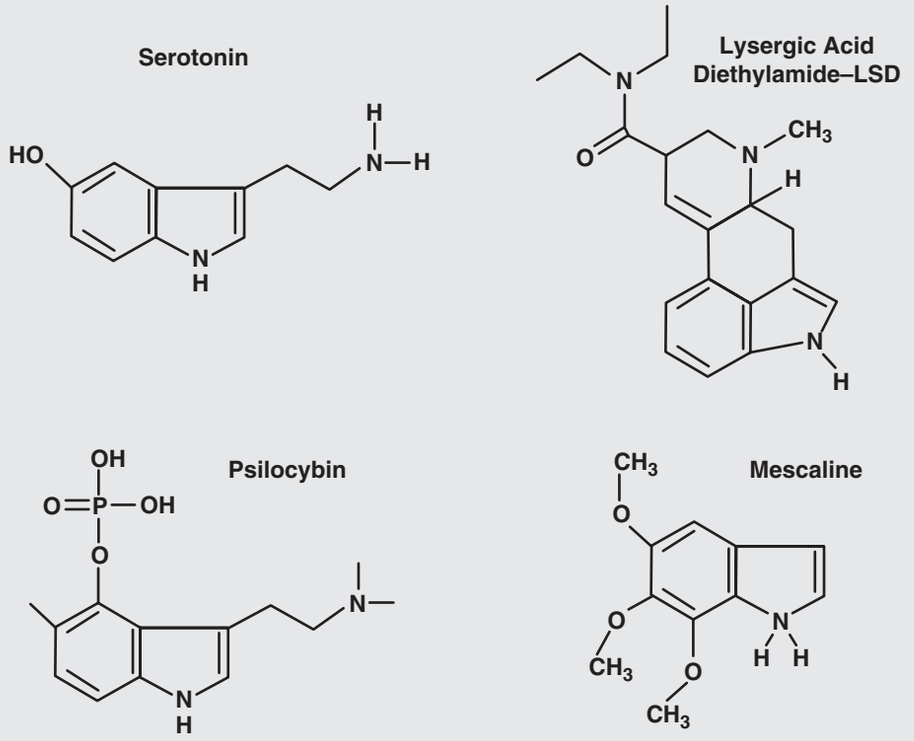
Inhalants exert their effects on the brain by activating the dopamine reward system. In many ways, the high produced by inhalants resembles that produced by alcohol, but it is much more damaging to the neurons in the brain. Damage is done to the protective myelin sheath that surrounds nerve fibers in the brain and other parts of the nervous system. Many health care workers believe that adolescent inhalant users are the most brain damaged of the adolescent drug users, and much of this damage is irreversible.

HALLUCINOGENIC DRUGS: CHEMICAL VISION

When Hernán Cortés entered Mexico in the early 16th century, he found that the inhabitants conducted religious ceremonies that included use of psychedelic plants such as "magic" mushrooms and the buttons of the peyote cactus. The Aztecs were especially known for using magic mushrooms (*Psilocybe mexicana*) in their religious ceremonies. The Nahuatl (language of the Aztecs) name for the mushrooms was *teonanactl*, which means "flesh of the gods." In 1958, Albert Hofmann, the Swiss chemist who had discovered LSD, isolated the active ingredient of the mushroom, psilocybin (Figure 4.13).

The inhabitants of Mexico as well as the southwest United States also used peyote cactus buttons in their religious ceremonies. The active ingredient of the cactus buttons was identified in 1886 by Arthur Heffter, a German scientist. The compound, mescaline, was named after the Mescalero Apaches, who were known to use the buttons in their religious ceremonies. The chemical structure of mescaline was determined in 1918 by Ernst Späth, another German, and is similar to the chemical structure of our brain's own neurotransmitter, serotonin (Figure 4.13). It is interesting to note that the active ingredients of

Figure 4.13 Molecular Structures



Hallucinogenic drugs are much like the neurotransmitter serotonin in their molecular structure as well as where and how they act in the brain.

"magic mushrooms" are also structurally related to serotonin, as is the infamous hallucinogen LSD.

Hoffman's Nightmare

Albert Hofmann, the Swiss chemist who isolated the active ingredient in magic mushrooms, also synthesized LSD (lysergic acid diethylamide) from compounds that he isolated from ergot, a fungus that grows on rye grass. Five years after Hofmann created the drug, he accidentally ingested a small amount of the compound and experienced the first recorded "trip" with LSD (Hofmann, 1979/2005).

> My surroundings . . . transformed themselves in more terrifying ways. Everything in the room spun around, and the familiar objects and pieces of furniture assumed grotesque, threatening forms. They were in continuous motion, animated, as if driven by an inner restlessness. . . . Even worse than these demonic transformations of the outer world were the alterations that I perceived in myself, in my inner being. Every exertion of my will, every attempt to put an end to the disintegration of the outer world and the dissolution of my ego, seemed to be wasted effort. A demon had invaded me, had taken possession of my body, mind, and soul. (pp. 48–49)

Effects of LSD

Because of the structural similarity between LSD and serotonin, it is not surprising that scientists believe that LSD, as well as the other plant-derived hallucinogens, acts on serotonin receptors in two brain regions (Sanders-Bush, 1994). One is the cerebral cortex, which as we have indicated is involved in cognition, perception, and mood. The other is the locus ceruleus, an area of the brain affected by external stimuli. This would partially explain why LSD users experience short-term effects such as rapidly changing moods and are also overstimulated by colors, sounds, and smells. Long-term effects include tolerance, including tolerance to psilocybin and mescaline but

not to marijuana and amphetamine, which do not target serotonin receptors. A quick glance at the chemical structures shown in Figure 4.13 will explain why this is to be expected.

Other long-term effects are persistent psychosis and occasional "flashbacks." The psychosis is characterized by distortion of reality as well as inability to think rationally. Some users experience long-lasting psychotic states, including dramatic mood shifts, visual disturbances, and hallucinations.

Other Mind-Altering Drugs

Two other mind-altering drugs, PCP (phenylcyclidine) and ketamine, were originally developed in the 1950s and 1960s to be used as general anesthetics during surgery. They are often referred to as hallucinogenic drugs because they cause feelings of detachment from reality and distortions of space, sounds, sight, and body image. Because of these effects, which are not true hallucinations, PCP and ketamine are known as "dissociative" rather than hallucinogenic drugs.

PCP: "Zombie" an Accurate Description

Known by such street names as zombie, dummy dust, angel dust, boat, and peace, PCP acts on the brain by altering the receptor sites for the neurotransmitter glutamate. These receptors are associated with the way we perceive pain, as well as with emotion and cognition, and altering them affects our ability to learn and to remember. It is not surprising that the rush from PCP is caused by an increase in the release of the neurotransmitter dopamine into the nucleus accumbens. Generally, the effects are felt within minutes and last several hours or even days. Even after 1 year of abstinence, the user may experience memory loss and depression. PCP has effects on other parts of the body besides the brain. These include elevated body temperature, increased heart rate, and dangerous increases in blood pressure.

Ketamine: Let Me Fix You a Drink

A less violent chemical cousin of PCP is ketamine, known as K, Special K, and even cat valium. It was developed in 1963 to replace PCP in surgery and is used in human anesthesia as well as veterinary medicine (cat valium). Although its effects are similar to those of PCP, they are milder and of shorter duration. It has been used as a "date rape drug." Since it is tasteless and odorless, it can be slipped into drinks to bring about amnesia in its victims. The victim may not remember the resulting sexual assault.

Dextromethorphan: Cough Syrup Anyone?

The amount of dextromethorphan found in most cough syrups is not harmful. However, the extra-strength variety can be abused. If the dosage exceeds 4 ounces of dextromethorphan, dissociative effects similar to those from PCP and ketamine may result. However, the chance of this amount of the drug being ingested with normal use of a cough suppressant is very unlikely.

Summary of Hallucinogenic Drugs' Effects

Plant-derived hallucinogenic drugs have been used by ancient societies for many hundreds of years. Many of these societies, such as the Aztecs as well as Native American tribes in what is now the United States, used mushrooms and peyote cactus buttons in their religious societies to create visions, which they believed enabled them to communicate with their gods. LSD was synthesized by a Swiss chemist who accidentally ingested some of it and experienced the first acid trip. LSD affects the cerebral cortex and the locus ceruleus, resulting in short-term effects such as rapid mood changes and amplification of sights, sounds, and smells. Other mind-altering drugs are PCP (phenylcyclidine) and ketamine. Even the cough syrup ingredient, dextromethorphan, can be abused to produce dissociative effects.

TOBACCO: THE ULTIMATE DRUG

We have saved a discussion of tobacco until the last because it is the *crème de la crème* of addictive drugs. Smoking causes from 450,000 to 500,000 deaths per year in the United States and over 3 million worldwide. By 2025, it is estimated that if the present trend continues, tobacco will account for over 10 million deaths per year. This is more than all other legal and illegal drugs combined. Smoking tops the list of deaths from preventable diseases; it is closely followed by diet and inactivity, which are accompanied by diseases associated with obesity. The Centers for Disease Control and Prevention (CDC, 2002) has estimated that the medical cost ($3.45) and loss of productivity ($3.73) is $7.18 per pack of cigarettes smoked; smoking also causes the average male smoker to lose 13.2 years of life and the average woman to lose 14.5 years.

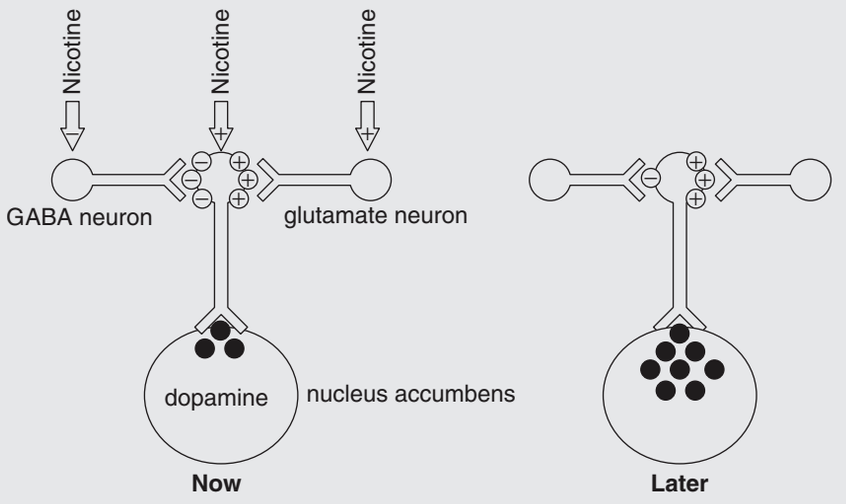
Tobacco's Effects on the Brain

Nicotine is one of the active ingredients of cigarette smoke, which partially accounts for the addicting power of cigarettes. By now, if you don't know that the addicting power of tobacco is due to an increase of dopamine (DA) in the nucleus accumbens (NAc), you should re-enroll in Neurochemistry 101. Nicotine directly stimulates the flow of DA into the NAc (see Figure 4.14). Nicotine also stimulates the release of the excitatory neurotransmitter, glutamate (glu), which triggers additional release of DA. But as we have seen, GABA (produced by the ventral tegmental area [VTA]) moderates DA release. The VTA initially enhances GABA release to moderate the increase of DA produced by nicotine. However, within a few minutes, nicotine kicks in to inhibit the release of GABA (Mansvelder & MeGehee, 2000, 2002). As we have seen, inhibiting the DA-releasing inhibitor results in high DA levels in the NAc. The combination of these effects—direct stimulation of DA release and inhibition of the inhibitory effects of GABA on DA—result in an increase in DA in the NAc and an amplification of the rewarding properties of nicotine (Mansvelder & MeGehee, 2002).

It gets even worse. There appears to be an unknown substance in cigarette smoke that blocks the action of monoamine oxidase (MAO), which is responsible for breaking down (destroying) DA in order to maintain a balance of this neurotransmitter. So now it seems that smoking is a triple-edged sword: one that directly enhances DA, one that inhibits the DA inhibitor, and one that blocks the DA destroyer (MAO). It would not be possible for the best pharmaceutical company in the world to design a better combination of drugs (nicotine and the unknown MAO inhibitor) to produce addiction.

Even this is not the end of the nicotine story. Many smokers, even though they know that smoking is really stupid, claim that smoking makes them temporarily smarter and more alert. Actually, this is probably true. It is known that the chemical structure of nicotine is similar to that of the neurotransmitter acetylcholine, which is involved in many brain functions, including memory and mental alertness. Because of the similarity in chemical structure, nicotine is able to attach itself to and activate acetylcholine (cholinergic) receptor sites. On the other hand, A. Ott and colleagues (2004) have shown that smoking retards mental functioning in the elderly by a factor of 5 compared to elderly nonsmokers. They also observed a close response, in that those who smoked more declined faster than those who smoked less. This is especially significant as we observe an increase in the average age of the population in the United States and around the world. But as is the case with all addicting drugs, continued activation of either the DA-enhancing neurons or the cholinergic receptors changes the sensitivity of these neurons to nicotine, resulting in tolerance, dependence, and addiction.

Figure 4.14 Neurochemical Effects of Nicotine. Nicotine inhibits inhibitory GABA neurons, stimulates dopamine-releasing neurons, and stimulates excitatory glutamate neurons (left panel). Each of these effects increases the amount of dopamine released in the nucleus accumbens (right panel).



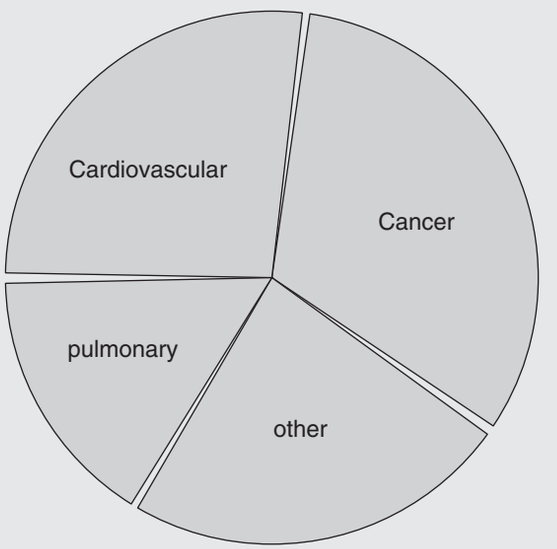
Other Health Effects of Smoking

The truly devastating effects of smoking are not the multifaceted action of nicotine in the brain. Figure 4.15 from the Centers for Disease Control and Prevention shows serious health effects of smoking in the United States in the early 1990s. Obviously, lung cancer is the greatest problem, followed by heart disease. In terms of health effects and deaths, cigarette smoking is the most serious drug problem in the United States today.

Summary of Tobacco's Effects

Tobacco is the most widely used of the drugs of abuse and is responsible for more deaths and costs due to health problems and lost productivity than all other legal and illegal drugs combined. Nicotine activates the dopamine reward system by direct stimulation of dopamine release, release of glutamate, and inhibition of the inhibitory neurotransmitter GABA. In addition, a component of cigarette smoke inhibits monoamine oxidase from destroying dopamine. These combined effects make nicotine one of the most addicting drugs, legal or illegal, in our society. The major health effects of tobacco are due to smoking (and chewing) and not to the nicotine. In fact, some evidence indicates that nicotine may increase cognition, at least in the short term. Smoking is responsible for most of the lung cancer in the world as well as cancers of the larynx, esophagus, bladder, kidney, pancreas, stomach, and uterine cavity. It is also the major cause of chronic bronchitis and emphysema.

Figure 4.15 Smoking-Related Deaths. Of the 430,000 annual deaths in the United States attributable to cigarette smoking, 35% are due to lung (125,000) and other (30,000) cancers, 28% are due to cardiovascular disease such as coronary heart disease (100,000) and stroke (25,000), and 17% are due to pulmonary disease.



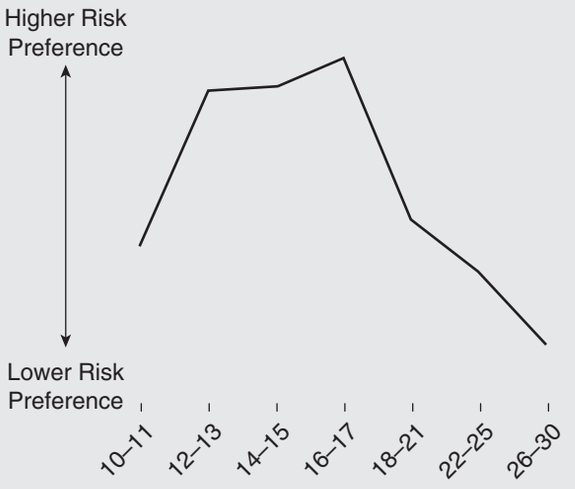
CHAPTER REVIEW

To understand the effects of drugs on the adolescent brain, it is necessary to have a basic knowledge of how the human brain works as well as the cultural concept and biology of adolescence. The human brain has been compared to a computer that uses only on and off signals among the billions of neurons that make trillions of connections. The various molecules known as neurotransmitters can be thought of as the "software" of the brain. Neurotransmitters carry messages from one neuron to the other with lightning speed. The neurotransmitter believed to be responsible for the "rush" of most drugs is dopamine. Dopamine is produced in one area of the brain (the ventral tegmental area) and sent to a major reward center (the nucleus accumbens), where it produces feelings of pleasure and well-being. In addition to drugs, many activities (eating, hugging, sex, even crime) produce a flow of dopamine into the nucleus accumbens.

Adolescence is both a cultural concept and a biological condition. The cultural view of adolescence as a distinct period in child development has received much more attention in the last 70–80 years than was the case before, say, 1930–1940. Then, children were thought to go simply from childhood to adulthood. Of course, we now know that adolescence is a time of rapidly changing hormones in the body and even more rapid changes in several parts of the brain. The ability of the teenager to make rational decisions is compromised by the inability of the immature frontal cortex to control the amygdala, which is the part of the brain involved in emotions. For this reason, many decisions by adolescents are made on an emotional rather than a rational basis.

As shown in Figure 4.16: Risky Business, through the age of about 18, adolescents place increasing value on rewards associated with novelty and pleasure than on the possible harm that might ensue.

Figure 4.16 Risky Business



Teens may understand that risky behaviors such as smoking and unprotected sex carry consequences. Yet adolescents tend to give more weight to the pleasures than to the costs.

Source: Dobbs, D. (2011, October). Beautiful teenage brains. *National Geographic*, p. 49.

The usage and effects of drugs on the human brain and body are summarized below:

- **Alcohol.** Biggest drug killer of college students. Those who survive often suffer irreversible brain damage. In the general population, alcohol is estimated to kill 100,000 people per year in the United States. This is in addition to 16,000 killed and 1 million injured as a result of traffic accidents in which alcohol is a factor. The annual cost of alcohol abuse in the United States alone is estimated to be $185 billion. Alcohol ranks second after tobacco in deaths attributable to drugs. Alcohol effects are especially damaging to adolescents, whose brains are undergoing rapid changes.
- **Cocaine.** Introduced to Europe through the conquest of Peru by Francisco Pizarro, who observed the natives of that country chewing the leaves of the coca plant. The most deadly form is crack, which is "free base" and can be smoked. Cocaine causes its effect by blocking the reuptake of dopamine into the presynaptic neurons, therefore prolonging the high. Once again, cocaine is especially hazardous to adolescents since it interferes with the normal growth of dendrites in their rapidly developing brains.
- **Marijuana.** The active ingredient of marijuana is tetrahydrocannabinol (THC), which attaches to anandamide (Sanskrit for "bliss") receptors in the brain to bring about its effects. Long-term use of marijuana produces deficits in cognition. The other deleterious effects of smoking marijuana are on the endocrine system, the immune system, and especially the lungs.
- **Opiates.** This category includes morphine, heroin, Vicodin, Oxycontin, and our own internal endorphins and enkephalins. Opiates exert their influence on the brain by inhibiting GABA neurotransmission. This in turn causes a cascade of dopamine to flow into the nucleus accumbens, bringing about the euphoria characteristic of opiates. It was estimated in 1998 that 87% of the 130,000 users in the past month were under the age of 26. In that same year it was estimated that 14% of all hospital emergency room admissions were for heroin abuse. In 2010, it was estimated that 1.3% of 8th graders, 1.3% of 10th graders, and 1.6% of 12th graders had used heroin at some time in their lives.
- **Ecstasy.** This "party drug" is believed to deliver its euphoria by enhancing serotonin release from serotonergic nerve endings in the brain. This over stimulation causes irreversible damage to these neurons. There is some controversy regarding the actual amount of nerve damage since some earlier research has come under considerable criticism. One of the major causes of Ecstasy-related emergency room admissions is dehydration due to the combined high temperature found at raves and the stimulation of the drug.
- **Inhalants.** This category includes paint sprays, nitrites, aerosols, glue, etc. These are especially damaging to the protective lining (myelin sheath) of the nerve fibers in the brain, including those in the hippocampus and the frontal cortex.
- **Hallucinogens.** These include the synthetic compound LSD (lysergic acid diethylamide) as well as plant-derived compounds such as psilocybin (magic mushrooms) and mescaline (peyote cactus buttons). The chemist who synthesized LSD accidentally ingested some of the compound and experienced the first

recorded "acid high." LSD acts on the neurons in the cerebral cortex and the locus ceruleus to bring about alterations of the perception of external stimuli. Other mind-altering drugs are phenylcyclidine (PCP) and ketamine (known as a "date rape drug"). Even the common ingredient in cough syrup, dextromethorphan, has been abused. The last three mind-altering drugs are, strictly speaking, not hallucinogens but are classified as dissociative drugs since their major effect is to produce feelings of detachment from reality.

- **Tobacco.** This is the major killer drug today, causing 450,000 to 500,000 deaths per year in the United States alone and over 3 million worldwide. The active ingredient of tobacco is nicotine, which acts in several ways to enhance dopamine levels in the nucleus accumbens. It directly stimulates dopamine release, enhances glutamate release, and inhibits GABA release. Another ingredient in cigarette smoke inhibits the dopamine-destroying enzyme, monoamine oxidase. All of these effects increase the level of dopamine in the nucleus accumbens. Because of its action on cholinergic receptors, nicotine brings about a temporary improvement in cognition. However, more recent research has shown that nicotine retards mental functioning in the elderly. The most serious effect of smoking is not a result of nicotine but of the hazardous chemicals in the smoke. Smoking is the leading cause of lung and other cancers in the United States and is a major contributor to heart disease. In terms of health effects, tobacco is the most serious drug problem in the United States today.