

Book Chapter From: “Cocaine and Methamphetamine Addiction” by Arnold Washton & Joan Zweben, WW Norton, 2009.

Chapter 2

Understanding Stimulant Drugs

This chapter provides a basic understanding of cocaine and methamphetamine, including a discussion of the unique pharmacological properties of these drugs that lead to abuse and dependence. We begin by presenting a brief history of cocaine and methamphetamine use followed by a more detailed discussion of stimulant drugs and their effects, including important similarities and differences between cocaine and methamphetamine. Toward the end of the chapter, we discuss the diagnostic categories of stimulant *abuse* and stimulant *dependence*, as defined by DSM-IV criteria for substance use disorders.

This chapter is not intended to provide in-depth coverage of the pharmacology of stimulant drugs. It does not, for example, address the intricate molecular structure of cocaine and methamphetamine, how they affect various organ systems in the human body, or the complex physiological mechanisms underlying the effects of these drugs on neurotransmitter systems in the brain. This type of information can be obtained elsewhere, including publications that served as primary resources for material in this chapter (Giannini AJ, 1989; Graham & Schultz, 1998; Graham, Schultz, Mayo-Smith, & Ries, 2003; Lowinson, Ruiz, Millman, & Langrod, 1992, 2005; Meredith et al. (2005), Miller, 1991; Rawson, 1999; Schuckit, 2000). Relevant information is also available from a wide variety of government publications that can be obtained at no cost from the National Clearinghouse for Alcohol and Drug Information (1-800-729-6686 or www.health.org).

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Brief History of Cocaine and Methamphetamine Use

Cocaine

Cocaine is derived from the leaves of the coca plant (*Erythroxylon coca*) grown primarily in Peru and Bolivia. The U.S. Food and Drug Administration classifies cocaine hydrochloride as a Schedule II substance-- a drug with high abuse potential and limited medical usefulness. Pure pharmaceutical cocaine is still sometimes used as a local anesthetic in surgery of the eye, ear, nose, and throat.

For literally thousands of years, tribes in the Andean regions of South American have chewed coca leaves to relieve fatigue and for other medicinal purposes-- just as people here and in other parts of the world have routinely used coffee, tea, and other caffeinated beverages as refreshments or “pick-me-ups”. Chewing coca leaves, however, has never been associated with the dramatic problems seen in the past three decades resulting from the use of purified forms of cocaine such as cocaine hydrochloride powder and smokeable cocaine alkaloid or freebase (“crack”).

In the 1860s, the German chemist, Albert Niemann, was the first to chemically extract cocaine hydrochloride from the coca plant and identify its local anesthetic and stimulant properties. As cocaine’s psychoactive effects became known among physicians it was sold in a variety of forms to treat chronic depression, fatigue, and even morphine addiction. Sigmund Freud extolled what he believed to be the remarkable therapeutic powers of cocaine especially for treating depression. Exaggerated claims of cocaine’s curative powers for a wide variety of ailments including dyspepsia (stomach upset), headache, melancholy (depression), and menstrual

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cramps contributed to its widespread popularity in the U.S. in the late 1800s and early 1900s.

Cocaine appeared as the primary ingredient in a variety of patent medicines, tonics, elixirs, wines and other beverages sold across the U.S. at soda fountains, pharmacies, and general stores. The most famous and widely consumed cocaine-containing beverage was the original formula of *Coca-Cola*, created in 1886 by a Georgia pharmacist, John Pemberton, which contained 2.5 mg of cocaine per 100ml of liquid. This unique beverage was marketed primarily as a cure for headache, melancholy, and fatigue. In 1914, when cocaine became illegal with passage of the Harrison Pure Food and Drug Act, it was removed from *Coca Cola* and replaced by another stimulant drug which continues to appear in the beverage today-- caffeine.

From 1914 to the 1970s, legal prohibitions and limited supplies of cocaine contributed to its low profile and the absence of widespread use. Subsequently, due in part to progressive weakening of societal prohibitions against “recreational” drug use starting in the 1960s, there was a dramatic upsurge in cocaine’s popularity on the American drug scene. In the early years of the cocaine epidemic starting in the 1980s, snorting cocaine hydrochloride powder (intranasal administration) was the primary method of using cocaine and most people who used it this way did so occasionally, seeking to experience the pleasures of cocaine-induced energy, euphoria, and sexuality without suffering disruption to their daily functioning. This fueled the growing misconception that cocaine use was relatively harmless—as long as one did not use it “too much”. In those days, the term “addiction” was deemed not applicable to cocaine use. People whose cocaine use had become excessive were referred to as cocaine “abusers” not “addicts” and the absence of a definitive cocaine withdrawal syndrome further reinforced the perception of cocaine as benign and non-addictive. Severe problems resulting from cocaine use were rarely seen, and the high price of cocaine helped to foster its image as the “champagne of drugs” and

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harmless “plaything” of the rich and famous.

By the mid-1980s, cocaine production in South America exploded from small businesses run by rural farmers in South America to a major industry run by large organized crime families known as “cocaine cartels”. Cocaine processing and trafficking became a multibillion dollar international business powerful enough to corrupt the governments and legal systems of several South American countries. Supplies of cocaine shipped into the U.S. increased rapidly, doubling and tripling year after year. The result of huge profit margins and increased drug supplies resulted in lower prices and more potent forms of the drug being increasingly available to an ever-expanding consumer market. Not surprisingly, substance abuse treatment programs began to see a large influx of cocaine users who were unable stop using on their own. These observations coupled with publicity about celebrities entering private rehabs for cocaine addiction began to change the image of the drug from relatively harmless to dangerously addicting.

In 1985, the appearance of “crack” cocaine on the illicit drug market-- the ready-made freebase or alkaloid form of the drug that can be smoked rather than snorted- further reinforced the changing view of cocaine as a highly addictive street drug and expanded the cocaine epidemic with devastating consequences, especially in large urban areas (Washton & Gold, 1986a,b). Crack cocaine became known for producing faster rates of addiction, more severe medical and psychiatric consequences, and more violent drug-related crimes as members of inner-city street gangs became crack users, dealers, and distributors. By the late 1980s, crack cocaine had replaced heroin as the most prevalent illicit drug problem in the U.S. Crack use also spread to the middle class as more and more users switched from snorting cocaine powder to smoking crack cocaine to achieve a more intense high and/or to override the tolerance they had

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developed to snorting cocaine powder.

Although today revelations about cocaine use no longer capture media headlines, the problem has not disappeared. In fact, there is little evidence to suggest that use of either cocaine powder or cocaine alkaloid (“crack”) has decreased significantly over the past ten years, except perhaps on the west coast where methamphetamine has essentially replaced cocaine as the drug of choice among stimulant users.

Methamphetamine

Commonly known on the street as “speed”, “crank”, “crystal”, “ice”, “glass”, or “meth”, illicit methamphetamine is synthesized in clandestine laboratories from relatively inexpensive over-the-counter ingredients. A potent CNS stimulant drug, methamphetamine comes in a variety of forms and can be smoked, snorted, injected, or taken orally. Like cocaine, pharmaceutically manufactured methamphetamine is classified as a Schedule II drug reflecting its high abuse potential and limited medical usefulness.

Methamphetamine was first synthesized by a Japanese pharmacologist in 1893 from its parent drug, amphetamine, another potent central nervous system stimulant. By 1932 pharmaceutically manufactured amphetamine was being used medically in nasal spray for the treatment of asthma and by 1937 it was available by prescription for the treatment of narcolepsy. Subsequently, more potent forms of the drug were developed including dextroamphetamine (Dexedrine) and methamphetamine (Methadrine). These performance-enhancing drugs were used extensively in the military. During WWII, various amphetamines were widely distributed to

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combat soldiers to counteract fatigue and increase mental acuity. Similarly, both American and Japanese military pilots used amphetamines to stay awake on long reconnaissance and bombing missions. After WWII, amphetamine use reached epidemic proportions in Japan as military supplies were diverted into the civilian population.

In the U.S., intravenous use of methamphetamine and oral use of amphetamine pills became increasingly prevalent in the emerging drug subculture of the late 1950s and throughout the 1960s. Oral amphetamines became especially popular as “diet pills” to suppress appetite and enhance weight loss. As it became increasingly apparent that the dangers of amphetamine use outweighed the therapeutic benefits, many pharmaceutical amphetamines were taken off the market. The 1970 Controlled Substance Act in the U.S. severely restricted the legal production of stimulant drugs which resulted in increased illicit production, particularly of methamphetamine, during the 1980s.

In the 1990’s, use of methamphetamine, previously concentrated primarily on the west coast of the U.S. and in Hawaii, spread to the Midwest, South, and to other regions of the country. In the West, especially in California, methamphetamine quickly replaced cocaine as the most prevalent illicit drug problem. Clandestine laboratories set up to manufacture methamphetamine proliferated as a result of the enormous profits of black market drug sales. A number of other factors contributed to rapid proliferation of methamphetamine including easy access to inexpensive precursor chemicals and the relative ease with which the drug can be manufactured. Recent attempts to reduce illicit methamphetamine production by controlling and/or monitoring bulk distribution of some of these precursor chemicals (e.g., ephedrine, pseudoephedrine, benzyl chloride) have been counteracted by importation of increasing amounts of MA from foreign countries such as Mexico.

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Effects of Cocaine and Methamphetamine

Cocaine and methamphetamine are both potent central nervous system (CNS) stimulants. Other stimulant drugs include the prescription medications dextroamphetamine (Adderall), methylphenidate (Ritalin), and pemoline (Cylert). Cocaine and methamphetamine are often compared to each other because they are both potent stimulants with similar mood-altering (psychoactive) effects and high potential for abuse. Table 1 lists some of the noteworthy similarities and differences between cocaine and methamphetamine.

Insert Table 1 about here

Physiological Effects and Medical Consequences

Cocaine has two main pharmacologic actions. It is both a local anesthetic and a central nervous system (CNS) stimulant, the only drug known to possess both of these properties. Cocaine exerts its local anesthetic (numbing or “freezing”) actions, similar to novocaine, xylocaine, and carbocaine, by blocking the conduction of sensory impulses within nerve cells. In addition to inducing local anesthesia, cocaine causes vasoconstriction (narrowing of the blood vessels), an action that helps to prolong local anesthesia by slowing its absorption into the surrounding

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circulation- an effect that historically has made cocaine the preferred local anesthetic agent for eye surgery and other delicate procedures.

The local anesthetic effects of cocaine are most pronounced when it is applied to the skin or mucous membranes. Thus, when cocaine is “snorted” it temporarily numbs the user’s nasal and throat passages—an effect familiar to all experienced users. Dealers looking to increase their profits often capitalize on this by adding cheaper local anesthetics such as procaine, lidocaine, or tetracaine to cocaine supplies to reduce its purity and raise profits while still producing the drug’s expected numbing effects.

The CNS stimulant effects of cocaine are mediated primarily by its effects on neurotransmitters in the brain, such as norepinephrine and dopamine. The exact mechanism by which cocaine exerts these effects is uncertain, but it is thought that it both increases the release of these neurotransmitters and prolongs their actions by blocking re-uptake in the synapse. It also stimulates sympathetic activity in the peripheral nervous system, which causes increased heart rate, blood pressure, breathing rate, body temperature, blood sugar, and dilation of the pupils. In combination with its direct stimulant effects on the brain, these changes often induce a strong feeling of being more alert and energetic. These responses are very similar to the body’s normal physiological response to threat, the primitive survival mechanism known as the “fight or flight” response. Its similarity to this natural emergency reaction or warning system may explain cocaine’s tendency to cause exaggerated feelings of anxiety and paranoia at higher doses.

Animal experiments demonstrate dramatically the “raw” addiction potential of cocaine and methamphetamine. Rats and monkeys will work incessantly to the point of exhaustion, debilitation, or death, pressing a bar literally thousands of times for a single dose of cocaine. They will choose cocaine over food, water, sex, and in some cases life itself. They will endure

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painful electric shocks, starvation, and ultimately die from self-administered fatal doses. Cocaine and methamphetamine seem to have “radar” for the brain’s reward center and stimulate these pleasure centers in ways that override even the most basic survival-oriented behaviors. Animal experiments demonstrate that the compulsion to take stimulant drugs can develop in the absence of depression, anxiety, situational stressors, or family dysfunction. When animals become addicted to and/or overdose on self-administered drugs, explanations invoking the role of predisposing factors such as psychiatric illness, developmental trauma, or “addictive personalities.” obviously do not apply.

Crystal methamphetamine is significantly less expensive than cocaine, but its effects are much longer lasting. It can be snorted, swallowed, or dissolved in water and injected intravenously. It can also be converted to a hard crystalline form known as "ice" which can be smoked. Like cocaine, methamphetamine causes the accumulation of the neurotransmitter dopamine in selected brain areas giving rise to the intense stimulation and feelings of euphoria experienced by the user. However, in contrast to cocaine, which is quickly removed and almost completely metabolized in the body, methamphetamine is metabolized more slowly and a larger percentage of the drug remains unchanged in the body thus prolonging its pharmacologic effects. Whereas 50 percent of cocaine is metabolically removed from the body within one hour, 50 percent of methamphetamine is removed within 12 hours.

Other similarities in the acute effects of methamphetamine and cocaine include increased blood pressure, heart rate, and respiration rate; papillary dilation; reduced appetite; insomnia; and, heightens alertness. A very common pattern of use for both drugs is a "binge and crash" pattern, but the crash and rebound depression from methamphetamine tends to be considerably

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more severe. Sleep following a binge of methamphetamine use can last for several days and the drug-induced depression for several weeks.

Medical consequences. Serious medical consequences are relatively uncommon with stimulant drug use as compared to those caused by chronic use of other more toxic substances such as alcohol. As with all drugs, high doses can cause serious or life-threatening health problems. These include cardiac arrhythmias (irregular heart beat), cerebral hemorrhage (stroke), brain seizures, respiratory failure, extreme elevations in body temperature (hyperthermia), and sudden death. Fatal reactions to cocaine and methamphetamine, although rare, can and do occur typically as a result of drug-induced cardiac arrhythmias, brain seizures, and markedly elevated body temperature.

Chronic intranasal use (snorting) of cocaine can lead to serious sinus infections, perforation of the nasal septum, and repeated nose bleeds resulting from cocaine’s vasoconstrictive effects that reduce blood supply to surrounding tissues. Smoking cocaine or methamphetamine can cause chronic chest congestion, lung infections, and impaired breathing capacity as a result of repeatedly inhaling hot vapors into the lungs. Intravenous injection may be associated with abscesses at injection sites and exposure to serious infectious diseases such as HIV and various forms of hepatitis due to sharing of contaminated needles and syringes. The risk of exposure to these and other sexually-transmitted diseases is also increased by high-risk sexual behaviors (e.g., unprotected intercourse with multiple partners) often associated with cocaine and methamphetamine use.

Cocaine use during pregnancy is associated with both prenatal and postnatal complications, especially premature delivery or miscarriage due to drug-induced separation of the placenta- a byproduct of vasoconstriction causing reduced blood flow to the uterine wall. Recent studies

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indicate that fetal exposure to methamphetamine is increasing and has been associated with multiple prenatal complications, such as intraventricular hemorrhage, fetal growth restriction, increased risk of preterm labor, placental abruption, decreased birth weight, cardiac defects, cleft palate, and behavioral effects in neonates (Meredith et al, 2005).

Chronic methamphetamine use has been linked to significant impairments in several arenas of neuropsychological functioning (Meredith et al., 2005). . Research in animals and humans has revealed complicated mechanisms of neurotoxicity by which chronic methamphetamine use affects catecholamine neurotransmission. This pathology may underlie the cognitive deficits that affect many chronic methamphetamine users, including impairments in memory and learning, performance on psychomotor tasks, and information processing. Methamphetamine abusers appear to develop different cognitive impairments than do abusers of cocaine or other types of drugs. Active users of methamphetamine and cocaine both demonstrate impaired verbal memory, but methamphetamine abusers also demonstrate deficits on tasks of perceptual speed and information processing, and on tasks that combine these skills with visuo-motor scanning. Additionally, as compared to users of cocaine or heroin, users of methamphetamine or amphetamine also demonstrate deficits on tests of executive function. Clinicians have noted that the cognitive deficits suffered by chronic methamphetamine users can hamper their ability to initially engage in and benefit from psychologically oriented treatment interventions (Rawson, Washton et al. 2002).

Brain neuroimaging studies using PET scans in humans indicate that certain changes in brain neurotransmitter systems that underlie methamphetamine-induced cognitive deficits appear to normalize during the first year or two following cessation of drug use, but other changes

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persist for longer periods of time and it remains unclear whether complete reversal of these effects is attainable (Meredith et al., 2005).

Tolerance. Tolerance often develops after only a few weeks to the euphoria-inducing and other psychoactive effects of both cocaine and methamphetamine as evidenced by the need for higher and higher doses to achieve the same psychoactive effects. Long-term users often self-administer doses that would have been potentially lethal at an earlier stage of use. Especially during prolonged binges, successive doses produce decreasing euphoria and decreasing autonomic changes (heart rate, blood pressure, etc), indicating the development of tolerance. As use escalates and continues, a point is often reached where the user becomes refractory (immune) to the euphorogenic and other reinforcing effects of these drugs regardless of how large a dose of the drug is taken. This phenomenon, well known among cocaine and methamphetamine users as "chasing the high", is a major contributor to rapid escalation in both the frequency and amount of stimulant drug use.

Reverse Tolerance (Sensitization). With repeated use, tolerance develops to nearly all of cocaine's effects, with one major exception. The ability of cocaine to induce a convulsion or brain seizure may actually increase with continued use. That is, the user may become more, rather than less, sensitive to cocaine's seizure-inducing properties as usage continues. A dose of cocaine that had previously not caused any serious medical problems can become a toxic or even a fatal dose, with no warning whatsoever. Most users don't know about this effect. Because a larger and larger dose of cocaine is required to achieve the same high (due to tolerance), users often assume that they are becoming less sensitive to all of cocaine's effects. This can be a fatal

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error.

This phenomenon of reverse tolerance is known as the kindling effect. Animal studies suggest that certain neurons in the central nervous system that are repeatedly exposed to cocaine become sensitized to the drug and thus fire more readily with each successive drug exposure. With long-term use these neurons fire even in the presence of relatively low doses of cocaine. The kindling phenomenon may also explain why some chronic users report a selectively increased sensitivity to the unpleasant stimulant effects of cocaine (feelings of nervousness, restlessness, agitation, etc.).

Physical Dependence. Although stimulant drugs typically produce no dramatic withdrawal syndrome, they are still considered physically addictive. Cocaine and methamphetamine produce profound alterations in brain neurotransmitters which give rise to drug urges and cravings. Moreover, there is reason to believe that repeated exposure of certain brain cells to high concentrations of cocaine or methamphetamine alters cellular metabolism in ways that produce distortions in thinking, reasoning, perceptions, and emotions- all of which serve to further perpetuate the uncontrollable cycle of compulsive drug use. This is consistent with the view that stimulant addiction is a drug-induced brain disorder (Leshner, 1998) resulting from persisting alterations in brain functions caused by the chronic drug use itself. These alterations are believed to generate the compulsion to use the drug, leaving the stimulant-dependent user trapped in a self-perpetuating vicious cycle in which drug use begets more drug use.

Abrupt discontinuation of cocaine or methamphetamine use is generally not known to be medically unsafe or life-threatening, unlike withdrawal from alcohol and other CNS depressants such as barbiturates and benzodiazepines. Also, discontinuing cocaine or methamphetamine does

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not require gradual tapering or pharmacological intervention. Perhaps the greatest risk in the immediate post-drug period is of doing harm to self or others in the midst of profound dysphoria, agitation, and in some cases lingering paranoid delusions. Cocaine-induced dysphoria usually dissipates rapidly, within 24 hours or less, but the more profound and protracted dysphoria following cessation of methamphetamine use can last for several days or more. This can lead to dangerous and volatile behaviors in which suicidal and/or other violent impulses may be easily provoked. To date, no medications have been found to reliably alleviate the post-drug dysphoria (“crash”) or intense drug cravings following either methamphetamine or cocaine use.

Psychoactive (Mood-Altering) Effects

Acute and Chronic Effects. Under the influence of cocaine or methamphetamine individuals who have not yet developed pharmacological tolerance generally report feeling euphoric, energetic, talkative, and more mentally alert. Some users experience increased attention and motivation as well as increased vigilance and enhanced performance on certain attention-demanding tasks. The acute effects of cocaine and methamphetamine may also include increased activity, decreased appetite, and an agitated excitement resembling a manic or hypomanic episode. Other users experience the opposite or no such effects. Still others report seemingly paradoxical effects, particularly from cocaine, characterized by feeling more relaxed and "mellow" rather than more alert and energetic.

The acute psychoactive effects of cocaine and methamphetamine, as with other drugs, depend on a variety of pharmacologic and nonpharmacologic factors. These include: dosage, route of administration, the particular setting in which the drug is taken, the user’s prevailing

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mood and emotional state, and the degree of physiological tolerance to stimulant effects. The onset and duration of immediate effects of each drug depend to a large extent on the route of administration and, of course, dosage. The more quickly a drug gets into the bloodstream and brain, the faster the onset of effects, the more intense the high, and the shorter its duration of action. For example, the high from snorting cocaine is relatively slow in onset (approximately 5 to 10 minutes after inhalation), mildly or moderately intense (depending on dose), and may last for 15 to 30 minutes before wearing off gradually. By contrast, smoking or injecting cocaine produces an almost instantaneous and extraordinarily intense high (“rush”) that peaks within 2-3 minutes and then wears off almost as quickly. Similarly, smoking methamphetamine produces an almost instantaneous intense high, but instead of wearing off within a few minutes, the methamphetamine high can last for a few hours. After reaching peak levels of drug-induced euphoria, and as the concentration of cocaine or methamphetamine in the brain falls off, the user’s mood falls off as well, and continues to fall below levels pre-drug levels producing a dysphoric rebound reaction known as the “crash”. As described previously, this unpleasant post-euphoria “crash” is characterized by agitation, irritability, depressed mood, and intense cravings for the drug. This high-crash cycle with stimulant drugs is thought to be an important factor that drives the development of compulsive use and eventual dependence.

When cocaine or methamphetamine is smoked or taken intravenously, all of the pharmacologic factors that drive compulsive use are intensified; i.e., the addiction potential increases. The neurochemical impact of cocaine and methamphetamine on brain function is more profound when drug delivery to the brain is accomplished by the more rapid and intensive routes of administration (i.e., smoking or intravenous injection) as compared to snorting (nasal inhalation). The “crash” is also intensified and physiological tolerance develops more quickly. Thus, all of

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the factors that promote the compulsive stimulant use are accelerated and intensified when the rapid delivery systems of smoking or injecting are employed.

Chronic stimulant use can lead to a drug induced psychosis characterized by hallucinations, paranoid delusions, and in some cases extreme agitation leading to aggressive or violent behavior. Psychotic reactions appear more likely to occur and to last longer with methamphetamine as compared to cocaine use. Remission of drug-induced psychotic symptoms often occurs within 1 to 3 days after stopping cocaine use, but may require as long as several weeks or even months following cessation of methamphetamine use.

Sexual Effects. Many but not all users find that cocaine or methamphetamine initially enhances their sexuality and performance, perhaps through a combination of increased desire, decreased inhibitions, and greater physical endurance. As discussed more fully in Chapter 3, in some individuals cocaine and methamphetamine produces a striking hypersexual response, especially in male users (Rawson et al, 2002). This aphrodisiac response is characterized by increased sex drive, increased sexual fantasies, and disinhibited sexual behaviors. These effects are significantly more intense and longer lasting with methamphetamine as compared to cocaine and with smoking as compared to snorting either drug. Sometimes cocaine or methamphetamine use initiates or enhances an individual’s desire and/or willingness to engage in sexual experimentation which may involve sex with prostitutes, group sex, mate swapping, and homosexual encounters by men who claim to be fundamentally heterosexual. Marathon binges of stimulant drugs and sex lasting 24-72 hours are quite common among men seeking treatment for stimulant dependence.

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Tolerance to methamphetamine sexual effects appears to develop more slowly and in some cases not at all as compared to cocaine; and, impairment of sexual functioning (e.g., impotence and/or inability to achieve orgasm) occurs less frequently with chronic methamphetamine use. Accordingly, the drug-induced hypersexuality and disinhibited sexual behaviors evoked by methamphetamine use appear to be substantially more intense and dramatic than those evoked by comparable levels of cocaine use (Rawson et al, 2002).

Use of Other Substances. Cocaine and methamphetamine use is often associated with the use of alcohol and other depressants and sometimes with the use of opioids, including heroin and prescription painkillers (e.g., hydrocodone, oxycodone, codeine). Depressants are commonly used to counteract the unpleasant overstimulation induced by cocaine or methamphetamine such as rapid heart beat, agitation, restlessness, and inability to fall sleep. Stimulant users often drink alcohol before, during, and/or after using cocaine or methamphetamine in order to prolong the drug-induced euphoria and decrease the post-drug “crash”. The concurrent use of cocaine and alcohol is consistent with scientific evidence showing that this combination produces a chemical byproduct known as cocaethylene which mimics the psychoactive effects of cocaine, but has a longer duration of action. Intravenous users of cocaine sometimes mix heroin and cocaine in the same syringe (a drug combination known as a “speedball”) to attenuate the undesirable side effects of each drug. More recently, snorting heroin or oral ingestion of prescription opioids (e.g., hydrocodone, oxycodone) have become increasingly popular particularly among middle-class cocaine users as a way to “take the edge off” or “come down” from stimulant drugs.. Alcohol, opioids, or other substances that are reliably paired with cocaine or methamphetamine use acquire the ability through associative conditioning to act as “triggers” for drug cravings and

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drug seeking behavior. As a result, attempts to refrain from using cocaine or methamphetamine are often interrupted by cravings and urges elicited by using alcohol and/or other substances with previously paired with drug use.

Patterns of Use

There are many different patterns of stimulant use. Although some cocaine and methamphetamine users do appear able to use intermittently and/or infrequently without developing dependence, it is not clear how long this nondependent pattern of stimulant drug use can continue and for what proportion of users. As with other psychoactive drugs, progression from nonproblematic use to abuse and dependence is not inevitable, but it is also not predictable. In the early stages, cocaine or methamphetamine use may cause little or no interference with daily functioning and other activities. In fact, most who seek treatment for stimulant dependence report that their pre-addiction level of functioning and productivity was initially enhanced by the heightened energy, focus, and self-confidence they experienced from cocaine or methamphetamine. Based on current knowledge, it is impossible to predict which users will progress toward eventual addiction and which ones will not. It can be noted, however, that route of drug administration is a significant variable. As compared with individuals who use cocaine or methamphetamine intranasally, those who smoke or inject these drugs intravenously are more likely to progress from occasional to compulsive use and to experience more severe psychosocial dysfunction and other drug-related consequences.. Intranasal use can also lead to full-blown stimulant dependence, but this usually takes longer to develop.

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Patterns of episodic binge use in which large quantities of the drug are consumed during marathon sessions sometimes lasting several days alternating with variable periods of abstinence are common among individuals seeking treatment for stimulant dependence. Binge use is especially common among individuals who smoke versus those who snort cocaine or methamphetamine. Binges usually start on weekends, paydays, or at other times when the individual senses a “window of opportunity” for using. For example, many clients report that their binges are most likely to occur when their spouse or significant other goes out of town and/or when they have free time from work or other responsibilities. The “runs” or binges can last anywhere from 24 hours to several days until the drug or money supply is depleted or the user collapses from physical exhaustion. During the course of a binge most users reach a point where they become refractory to the euphoric effects of the drug and experience increasingly severe dysphoria, depression, anxiety, and irritability, compounded by extreme sleep deprivation. As mentioned earlier, binges of cocaine or methamphetamine use often involve heavy alcohol consumption to counteract and alleviate some of the unpleasant aftereffects of high-dose stimulant use. And sometimes heroin or other opioids are used as antidotes for the “crash”. Alcohol is by far the substance most commonly used in conjunction with stimulants, and as a result of repeated pairings of alcohol and cocaine use, drinking alcohol becomes a conditioned stimulus that often evokes strong drug cravings and relapse in individuals trying to abstain from cocaine or methamphetamine.

Because stimulants are commonly used in binges separated by sustained periods of nonuse, it often appears that binge users are not addicted. Immediately following a binge, the user may feel guilty and remorseful, overwhelmed by adverse psychosocial consequences, and strongly motivated to not repeat the pattern again. However, as time passes from the last binge there is a

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tendency for the binge user to progressively minimize or forget about the drug-related consequences, fostering denial that he/she is embroiled in an addictive pattern of use even though use is not daily. It is important to keep in mind that addiction is defined not by the frequency or amount of use, but rather by the role that the drug use plays in the individual’s life and by the user’s pathological, obsessive relationship with the drug (as discussed in more detail below). Some individuals who snort relatively small amounts of cocaine or methamphetamine infrequently seem to demonstrate no signs of addiction or compulsive use. As tolerance develops, however, even the occasional user’s brain requires a larger dose to achieve the same high, and somewhere along the line many individuals increase the amount and frequency of their use—especially if they enjoy the effects. Furthermore, cocaine affects the brain incrementally, so that the addictive process may be set in motion and operate without the user’s awareness.

Some clinicians have observed that in contrast to cocaine users, methamphetamine users are more likely to use on a daily basis and to shift from snorting or smoking methamphetamine to injecting it intravenously. This may be attributable in part to the fact that methamphetamine is severely irritating to both the nasal mucosa and lungs, but also to financial motivations. Smoking methamphetamine requires roughly twice the volume of powder as injecting it to achieve equivalent effects.

Substance Abuse and Dependence

The diagnostic system used most widely in the U.S. for mental health problems, the DSM-IV-TR (American Psychiatric Association 1994), defines two categories of substance use disorders: substance *abuse* and substance *dependence*. These definitions are based not on how much or how often a person may use, but rather on the nature of a person’s involvement with the drug, the

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nature/severity of drug-related consequences, and the role that the substance plays in the individual’s life. Central to these definitions are the concepts of pathological use and its maladaptive nature, progressively impaired control over the amount and frequency of use, continued use despite adverse consequences, and the elevated importance of drug use in the person’s life.

A formal diagnosis of stimulant dependence is indicated by the presence of at least three of the seven criteria listed in Table 2. Moreover, these definitions reflect a consensus that pathological use of a

Insert Table 2 about here-- DSM IV-TR Diagnostic Criteria for Substance Dependence

drug is manifested as a *behavioral* syndrome characterized by *behavioral* indicators such as loss of control over use, preoccupation and obsession with use, and continued use despite adverse consequences- even in the absence of any classical signs of physical dependence (i.e., tolerance and withdrawal).

A diagnosis of *abuse* is a less severe than dependence and is applicable only if the individual previously never met criteria for a dependence diagnosis for the same or similar class of drugs. Four criteria define substance abuse, but only one of these four must be met within a 12-month period to qualify for a diagnosis of abuse: (1) recurrent substance use resulting in failure to fulfill major role obligations such as those at home, work, or school; (2) recurrent substance use in situations in which it is physically hazardous (e.g., while driving a vehicle or operating other

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dangerous machinery); (3) recurrent substance-related legal problems (e.g., arrest for DWI/DUI or possession of controlled substances); (4) continued substance use despite persistent or recurrent social or interpersonal problems caused or exacerbated by the use.

Both types of substance use disorders (abuse and dependence) are characterized by substance-related psychosocial dysfunction and continued use despite adverse consequences, but dependence is distinguished by the additional features of impaired control of substance use and preoccupation or compulsion regarding the use. Whereas a diagnosis of abuse presumes that the individual still has some ability to control or moderate the drug use and is neither obsessed with the substance or at a point where it dominates his/her life, dependence is characterized by a stereotyped, compulsive pattern of use that is no longer under volitional control and increasingly dominates various aspects of the person’s life.

In addition to the typology offered by the DSM-IV TR criteria, some of the clinical manifestations of stimulant dependence are include the following:

(1) Intense urges and cravings for the drug. The stimulant dependent user is usually preoccupied with obtaining and using the drug which has higher priority most other activities, even though the he or she no longer experiences a euphoric high from using the drug.

(2) Impaired control. A person who is dependent on cocaine or methamphetamine often can stop using temporarily, for days, weeks, or months at a time, but finds it extraordinarily difficult if not impossible to stay away from the drug on a more permanent basis, even with strenuous efforts to exert willpower and self-control. The stimulant-dependent person has usually broken many promises to self and others to stop using the drug once and for all and is likely to feel ashamed, guilty, and humiliated by this behavior.

(3) Continued use despite serious and potentially life-damaging negative consequences. Stimulant use may continue even in the face of depression, paranoia, suicidal feelings, loss of

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productivity at work or school, loss of job, loss of financial well-being, loss or irreversible damage to important relationships, legal problems, etc.

(4) Denial that the drug use is actually a problem. The stimulant-dependent person typically downplays the seriousness of adverse consequences resulting from the drug use, denies that there is a problem, and gets angry and defensive when if someone suggests otherwise.

In addition to the above, the Stimulant Abuse Severity Questionnaire in Table 2 developed by the first author (AMW) is a clinically useful tool that can help to further elucidate the nature and extent of a client’s cocaine or methamphetamine use. There are no normative data or established cutoff scores for this instrument, although higher scores are clearly indicative of more severe problems.

FINAL COMMENT

In this chapter we have described the history, clinically relevant pharmacology, and common patterns of use of cocaine and methamphetamine including important similarities and differences between these two potent CNS stimulant drugs. We have also described various types of medical, psychiatric, psychosocial, and sexual consequences associated with chronic cocaine and methamphetamine use and the clinical criteria used to arrive at a diagnosis of stimulant abuse or dependence. The next chapter focuses on the problem of compulsive sexuality linked to cocaine and methamphetamine use and the importance of reliably identifying and addressing this problem in clients (especially males) who appear for treatment of stimulant dependence.

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Table 1: Comparison of Cocaine (COC) and Methamphetamine (MA)

Adapted from Rawson (1999)

Source

- MA is man-made, chemically synthesized in clandestine laboratories here in the U.S.
- Cocaine is derived from the coca plant (*Erythoxylon coca*) grown in various regions of Central and South America.
- MA is much less expensive than COC. This is mainly because MA is synthesized domestically in bulk quantities from inexpensive precursor chemicals whereas COC production requires growing and harvesting plants in foreign countries, a labor-intensive extraction process, and smuggling operations to ship the drug across U.S. borders.

Common Methods and Patterns of Use

- Both MA and COC can be smoked, injected intravenously, or snorted.
- MA is also taken orally, but this method of use is uncommon with cocaine because its psychoactive effects are diminished by digestive enzymes in the stomach.
- To be smoked, cocaine hydrochloride powder must first be chemically converted to cocaine alkaloid commonly known as “freebase” or “crack”. MA requires no such conversion for smoking.
- Recent studies indicate that the typical MA user uses more than 20 days a month. Use is evenly spaced throughout the day and MA users use fewer times per day than do cocaine users. Fewer cocaine users are continuous users, and they are more likely to use in the evening rather than the daytime. Binge use is a common use pattern for both drugs.

Geographic Patterns of Use

- MA use is highest in western areas of the United States, particularly large urban areas of California, Washington, Oregon, Colorado, and Arizona. Over the past decade or so, MA has essentially replaced COC as the stimulant drug of choice in these areas. Moreover, evidence indicates that in many western US cities, MA is used extensively by gay males and is frequently associated with high-risk sexual behavior, a major factor in the transmission of HIV.
- MA use has also increased significantly in both urban and rural areas of the South and Midwest. By comparison, MA use has remained relatively low in the Northeast where it is found primarily among gay men. Unlike other areas of the country, COC continues to be the stimulant drug of choice in the Northeast.
- COC use is highest in large metropolitan areas across the country, whereas MA use is found in both small and large metropolitan areas as well as in rural areas.

Euphoric Effects

- When smoked or injected intravenously, both MA and COC produce an intense, euphoric “rush” or “high.”
- When snorted, both drugs produce a more moderate high that comes on more gradually. Orally ingested MA produces a similar effect.

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- The effects of MA as compared to COC are much longer lasting because MA has a much longer half-life (i.e., is metabolized much more slowly) than COC. The MA high typically lasts anywhere from 8 to 24 hours with 50 percent of the drug cleared in 12 hours whereas the COC high typically lasts 20 to 30 minutes with 50 percent of the drug cleared in only 1 hour.

Physical and Mental Effects

- The immediate effects of both drugs may include irritability and anxiety; increased body temperature, heart rate, and blood pressure; and in rare cases overdose death due to extreme hyperthermia (fever), cardiac arrest, or respiratory failure.
- Short-term effects of COC and MA also may include increased activity, respiration, wakefulness, and reduced appetite.
- Longer-term use of COC or MA often leads to dependence characterized by drug cravings, inability to limit use once it starts, and continued use despite adverse consequences. Depression is also a common complaint among chronic users.
- There is no clearcut physical withdrawal syndrome associated with abrupt cessation of either drug.
- Tolerance develops to the euphorogenic and other psychoactive effects with chronic use of both drugs as evidenced by the need for higher and higher doses to achieve the same effects.
- Chronic use of either drug can lead to psychosis characterized by paranoia, hallucinations, mood disturbance, and violent behavior. Clinical observations suggest that paranoia and violent behavior are more common among chronic MA users than among chronic COC users.
- Catastrophic medical complications (including death) are more likely to occur with COC than MA, but MA users are much more likely than COC users to experience severe psychotic reactions resulting from chronic use including confusion, delusions, hallucinations, paranoia, agitation, suicidal ideation, and aggressive or violent behavior.

Transmission of HIV/AIDS

- Both MA and COC use contribute to transmission of HIV/AIDS, Hepatitis C, and other life-threatening diseases through intravenous injection with contaminated needles and syringes.
- Both MA and COC use are associated with a wide range of high-risk sexual behaviors that also contribute to transmission of HIV/AIDS.
- MA use is especially popular among gay men and frequently associated with high-risk sexual behaviors, such as unprotected anal intercourse, a significant factor in HIV transmission.

Mechanism of Action and Neurotoxic Effects

- There are major differences in how COC and MA work at the level of the nerve cell, but the net result is essentially the same: they both produce an accumulation of the neurotransmitter dopamine which gives rise to the stimulation and euphoria.
- MA is neurotoxic (i.e., damages or destroys neurons in the brain) in animal species ranging from mice to monkeys; it is particularly neurotoxic in brain areas that produce

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the neurotransmitters dopamine and serotonin. The usual doses taken by human MA users are comparable to the doses that have been shown to produce brain neurotoxicity in animals.

- COC does not appear to be as neurotoxic as MA to dopamine and serotonin neurons

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Table 2: Stimulant Use Severity Questionnaire

Please answer yes or no to each question below with regard to your use of cocaine and/or methamphetamine.

1. Do you have trouble turning down drugs when offered to you?
2. Do you tend to use up whatever drug supplies of you have on hand even though you try to save some for another time?
3. Have you been trying to stop using drugs but find that somehow you always go back ?
4. Do you go on binges for hours or days at a time?
5. Do you need to be high to have a good time?
6. Are you afraid that you will be bored or unhappy without using drugs?
7. Are you afraid that you will be less able to function without using drugs?
8. Does the sight, thought or mention of drugs trigger urges and cravings ?
9. Are you often preoccupied with thoughts about using?
10. Do you sometimes feel an irresistible compulsion to use?
11. Do you feel psychologically addicted to drugs?
12. Do you feel guilty and ashamed about your use and dislike yourself for doing it?
13. Have you been spending less time with “straight” people since you’ve been using more often?
14. Are you frightened by the strength of your drug habit?
15. Do you tend to spend time with certain people or go to certain places because you know that drugs will be available?
16. Do people tell you that your behavior or personality has changed even though they might not know it’s due to drugs?
18. Has drug use led you to drink more heavily or use other substances?
19. Do you ever drive a car while high on drugs?
20. Have you neglected any significant responsibilities at home or at work due to drug use?
21. Have your values and priorities been altered by drug use?
22. Would you be using even more if you had more money to spend on drugs?
24. Do you hide your drug use from straight friends or family members because you’re afraid of their reactions?
25. Have you become less involved in recreational activities and/or exercise due to drug use?
26. Have you become less interested or motivated in your job or career due to drug use?
27. Do you find yourself lying and making excuses because of drug use?
28. Do you tend to deny and downplay the severity of your cocaine problem?
29. Have you been unable to stop using even though you know that it is having negative effects on your life?
30. Has drug use jeopardized your job or career?
31. Do you worry whether you are capable of living a normal and satisfying life without using?
32. Are you having financial problems due to drug use?
33. Are you having problems with your spouse or mate due to drug use?
34. Has drug use negatively affected your physical health?
35. Is drug use having a negative effect on your mood or mental state?
36. Has your sexual functioning been disrupted by drug use?

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37. Have you become less sociable due to drug use?
38. Have you missed days of work due to drug use?