

Research Report

S E R I E S

The abuse of methamphetamine—a potent and highly addictive psycho-stimulant—is a very serious problem in the United States. Initially limited to Hawaii and western parts of the country, methamphetamine abuse continues to spread eastward, with rural and urban areas everywhere increasingly affected. According to one national survey, approximately 10 million people in the United States have tried methamphetamine at least once.

Methamphetamine abuse leads to devastating medical, psychological, and social consequences. Adverse health effects include memory loss, aggression, psychotic behavior, heart damage, malnutrition, and severe dental problems. Methamphetamine abuse also contributes to increased transmission of infectious diseases, such as hepatitis and HIV/AIDS, and can infuse whole communities with new waves of crime, unemployment, child neglect or abuse, and other social ills.

The good news is that methamphetamine abuse can be prevented and methamphetamine addiction can be treated. People do recover, but only when effective treatments that address the multitude of problems resulting from methamphetamine abuse are readily available. Primary goals of the National Institute on Drug Abuse (NIDA) are to apply what our scientists learn from drug abuse research to develop new and enhance existing treatment approaches and to bring these effective treatments to the communities that need them.

In this report, we provide an overview of the latest scientific findings on methamphetamine. Our intent is to enlighten readers about the damaging effects of methamphetamine abuse and to inform prevention and treatment efforts.

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from the director

METHAMPHETAMINE

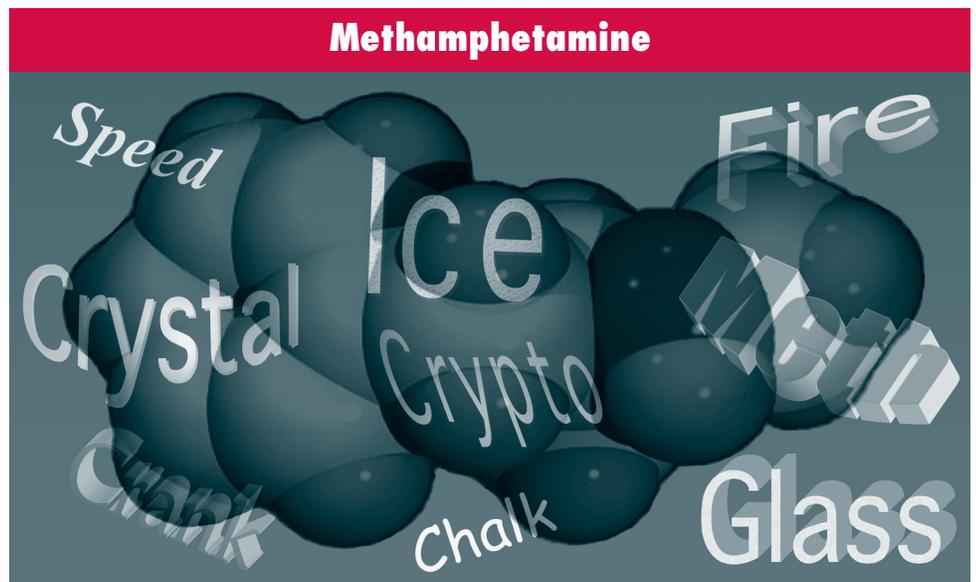
Abuse and Addiction

What is methamphetamine?

Methamphetamine is a highly addictive stimulant that affects the central nervous system. Although most of the methamphetamine used in this country comes from foreign or domestic superlabs, the drug is also easily made in small clandestine laboratories, with relatively inexpensive over-the-counter ingredients. These factors combine to make meth-

amphetamine a drug with high potential for widespread abuse.

Methamphetamine is commonly known as “speed,” “meth,” and “chalk.” In its smoked form, it is often referred to as “ice,” “crystal,” “crank,” and “glass.” It is a white, odorless, bitter-tasting crystalline powder that easily dissolves in water or alcohol. The drug was developed early last century from its parent drug,

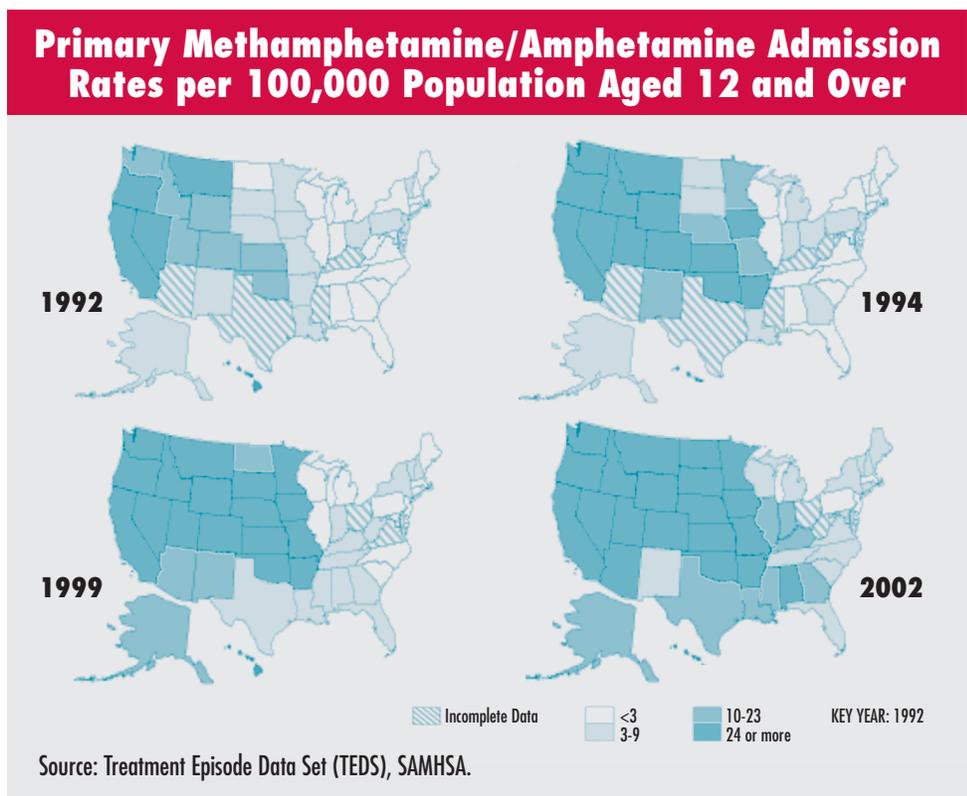


amphetamine, and was used originally in nasal decongestants and bronchial inhalers. Like amphetamine, methamphetamine causes increased activity and talkativeness, decreased appetite, and a general sense of well-being. However, methamphetamine differs from amphetamine in that at comparable doses, much higher levels of methamphetamine get into the brain, making it a more potent stimulant drug. It also has longer lasting and more harmful effects on the central nervous system.

Methamphetamine is a Schedule II stimulant, which means it has a high potential for abuse and is available only through a prescription. It is indicated for the treatment of narcolepsy (a sleep disorder) and attention deficit hyperactivity disorder; but these medical uses are limited, and the doses are much lower than those typically abused.

What is the scope of methamphetamine abuse in the United States?

NIDA's Community Epidemiology Work Group (CEWG), an early warning network of researchers that provides information about the nature and patterns of drug abuse in 21 major areas of the



U.S., reported in January 2006 that methamphetamine continues to be a problem in the West, with indicators persisting at high levels in Honolulu, San Diego, Seattle, San Francisco, and Los Angeles; and that it continues to spread to other areas of the country, including both rural and urban sections of the South and Midwest. In fact, methamphetamine was reported to be the fastest growing problem in metropolitan Atlanta.

According to the 2005 National Survey on Drug Use and Health (NSDUH), an estimated 10.4 million people age 12 or older (4.3 percent of the population) have tried methamphetamine at some time in their lives. Approximately 1.3 million reported past-year

methamphetamine use, and 512,000 reported current (past-month) use. Moreover, the 2005 Monitoring the Future (MTF) survey of student drug use and attitudes reported 4.5 percent of high school seniors had used methamphetamine within their lifetimes, while 8th-graders and 10th-graders reported lifetime use at 3.1 and 4.1 percent, respectively. However, neither of these surveys has documented an overall increase in the abuse of methamphetamine over the past few years. In fact, both surveys showed recent declines in methamphetamine abuse among the Nation's youth.

In contrast, evidence from emergency departments and treatment programs attest to

the growing impact of methamphetamine abuse in the country. The Drug Abuse Warning Network (DAWN), which collects information on drug-related episodes from hospital emergency departments (EDs) throughout the Nation, has reported a greater than 50 percent increase in the number of ED visits related to methamphetamine abuse between 1995 and 2002, reaching approximately 73,000 ED visits, or 4 percent of all drug-related visits in 2004.

Treatment admissions for methamphetamine abuse have also increased substantially. In 1992, there were approximately 21,000 treatment admissions in which methamphetamine/amphetamine was identified as the primary drug of abuse, representing more than 1 percent of all treatment admissions during the year. By 2004, the number of methamphetamine treatment admissions increased to greater than 150,000, representing 8 percent of all admissions.

Moreover, this increased involvement of methamphetamine in drug treatment admissions has also been spreading across the country. In 1992, only 5 states reported high rates of treatment admissions (i.e., >24 per 100,000 population) for primary methamphetamine/amphetamine problems; by 2002, this number increased to 21, more than a third of the states.

How is methamphetamine abused?

Methamphetamine comes in many forms and can be smoked, snorted, injected, or orally ingested. The preferred method of methamphetamine abuse varies by geographical region and has changed over time. Smoking methamphetamine, which leads to very fast uptake of the drug in the brain, has become more common in recent years, amplifying methamphetamine's addiction potential and adverse health consequences.

The drug also alters mood in different ways, depending on how it is taken. Immediately after smoking the drug or injecting it intravenously, the user experiences an intense rush or "flash" that lasts only a few minutes and is described as extremely pleasurable. Snorting or oral ingestion produces euphoria—a high but not an

intense rush. Snorting produces effects within 3 to 5 minutes, and oral ingestion produces effects within 15 to 20 minutes.

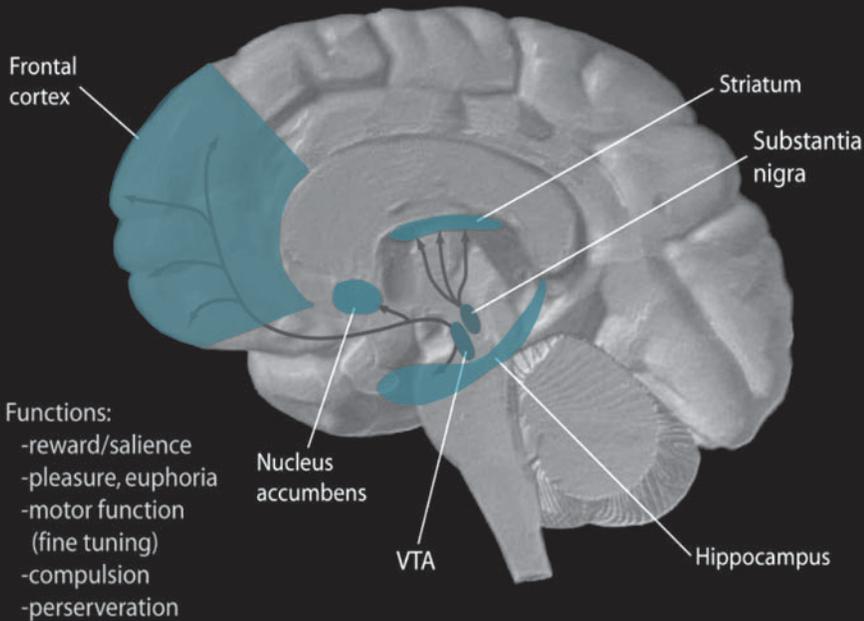
As with similar stimulants, methamphetamine most often is used in a "binge and crash" pattern. Because the pleasurable effects of methamphetamine disappear even before the drug concentration in the blood falls significantly—users try to maintain the high by taking more of the drug. In some cases, abusers indulge in a form of binging known as a "run," foregoing food and sleep while continuing abuse for up to several days.

How is methamphetamine different from other stimulants, such as cocaine?

Methamphetamine is structurally similar to amphetamine and the neurotransmitter dopamine, but

Methamphetamine	vs.	Cocaine
Stimulant	—	Stimulant and local anesthetic
Man-made	—	Plant-derived
Smoking produces a long-lasting high	—	Smoking produces a brief high
50% of the drug is removed from the body in 12 hours	—	50% of the drug is removed from the body in 1 hour
Increases dopamine release and blocks dopamine re-uptake	—	Blocks dopamine re-uptake
Limited medical use	—	Limited use as a local anesthetic in some surgical procedures

Dopamine Pathways



In the brain, dopamine plays an important role in the regulation of reward and movement. As part of the reward pathway, dopamine is manufactured in nerve cell bodies located within the ventral tegmental area (VTA) and is released in the nucleus accumbens and the prefrontal cortex. Its motor functions are linked to a separate pathway, with cell bodies in the substantia nigra that manufacture and release dopamine into the striatum.

it is quite different from cocaine. Although these stimulants have similar behavioral and physiological effects, there are some major differences in the basic mechanisms of how they work. In contrast to cocaine, which is quickly removed and almost completely metabolized in the body, methamphetamine has a much longer duration of action and a larger percentage of the drug remains unchanged in the body. This results in methamphetamine being present in the brain longer, which ultimately leads to prolonged stimulant effects. And

although both methamphetamine and cocaine increase levels of the brain chemical dopamine, animal studies reveal much higher levels of dopamine following administration of methamphetamine due to the different mechanisms of action within nerve cells in response to these drugs. Cocaine prolongs dopamine actions in the brain by blocking dopamine re-uptake. While at low doses, methamphetamine blocks dopamine re-uptake, methamphetamine also increases the release of dopamine, leading to much

higher concentrations in the synapse, which can be toxic to nerve terminals.

What are the immediate (short-term) effects of methamphetamine abuse?

As a powerful stimulant, methamphetamine, even in small doses, can increase wakefulness and physical activity and decrease appetite. Methamphetamine can also cause a variety of cardiovascular problems, including rapid heart rate, irregular heartbeat, and increased blood pressure. Hyperthermia (elevated body temperature) and convulsions may occur with methamphetamine overdose, and if not treated immediately, can result in death.

Most of the pleasurable effects of methamphetamine are believed to result from the release of very high levels of the neurotransmitter dopamine. Dopamine is involved in motivation, the experience of pleasure, and motor function, and is a common mechanism of action for most drugs of abuse. The elevated release of dopamine produced by methamphetamine is also thought to contribute to the drug's deleterious effects on nerve terminals in the brain.

What are the long-term effects of methamphetamine abuse?

Long-term methamphetamine abuse has many negative consequences, including addiction. Addiction is a chronic, relapsing disease, characterized by compulsive drug seeking and use, accompanied by functional and molecular changes in the brain. In addition to being addicted to methamphetamine, chronic abusers exhibit symptoms that can include anxiety, confusion, insomnia, mood disturbances, and violent behavior. They also can display a number of psychotic features, including paranoia, visual and auditory hallucinations, and delusions (for example, the sensation of

insects creeping under the skin). Psychotic symptoms can sometimes last for months or years after methamphetamine abuse has ceased, and stress has been shown to precipitate spontaneous recurrence of methamphetamine psychosis in formerly psychotic methamphetamine abusers.

With chronic abuse, tolerance to methamphetamine's pleasurable effects can develop. In an effort to intensify the desired effects, abusers may take higher doses of the drug, take it more frequently, or change their method of drug intake. Withdrawal from methamphetamine occurs when a chronic abuser stops taking the drug; symptoms of withdrawal include depression, anxiety, fatigue, and an intense craving for the drug.

Chronic methamphetamine abuse also significantly changes the brain. Specifically, brain

imaging studies have demonstrated alterations in the activity of the dopamine system that are associated with reduced motor speed and impaired verbal learning. Recent studies in chronic methamphetamine

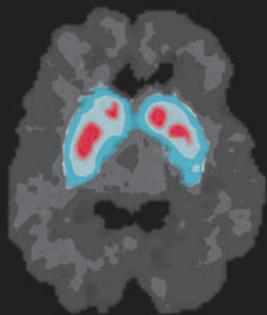
Short-Term Effects May Include:

- Increased attention and decreased fatigue
- Increased activity and wakefulness
- Decreased appetite
- Euphoria and rush
- Increased respiration
- Rapid/irregular heartbeat
- Hyperthermia

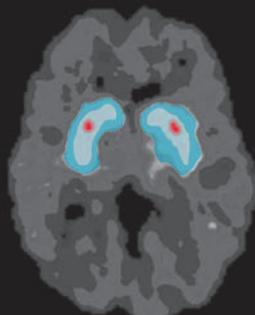
Long-Term Effects May Include:

- Addiction
- Psychosis, including:
 - paranoia
 - hallucinations
 - repetitive motor activity
- Changes in brain structure and function
- Memory loss
- Aggressive or violent behavior
- Mood disturbances
- Severe dental problems
- Weight loss

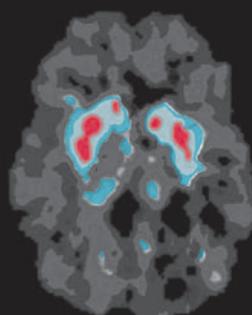
Recovery of Brain Dopamine Transporters in Chronic Methamphetamine (METH) Abusers



Normal Control



METH Abuser
(1 month abstinence)



METH Abuser
(24 month abstinence)

Source: Volkow ND et al., *Journal of Neuroscience* 21:9414–9418, 2001.

abusers have also revealed severe structural and functional changes in areas of the brain associated with emotion and memory, which may account for many of the emotional and cognitive problems observed in chronic methamphetamine abusers.

Fortunately, some of the effects of chronic methamphetamine abuse appear to be, at least partially, reversible. A recent neuroimaging study showed recovery in some brain regions following prolonged abstinence (2 years, but not 6 months). This was associated with improved performance on motor and verbal memory tests. However, function in other brain regions did not display recovery even after 2 years of abstinence, indicating that some methamphetamine-induced changes are very long-lasting. Moreover, the increased risk of stroke from the abuse of methamphetamine can lead to irreversible damage to the brain.

What are the risks of methamphetamine abuse during pregnancy?

Prenatal exposure to methamphetamine may also be a problem in the United States. Although according

to the NSDUH, less than 1 percent of pregnant women aged 15–44 had used methamphetamine in the past year, any use among this population is of concern. Unfortunately, our knowledge of the effects of methamphetamine during pregnancy is limited. The few human studies that exist have shown increased rates of premature delivery, placental abruption, fetal growth retardation, and heart and brain abnormalities. However, these studies are difficult to interpret due to methodological issues, such as small sample size and maternal use of other drugs. Ongoing research is continuing to study developmental outcomes such as cognition, social relationships, motor skills, and medical status of children exposed to methamphetamine before birth.

Are methamphetamine abusers at risk for contracting HIV/AIDS and hepatitis B and C?

Increased HIV and hepatitis B and C transmission are consequences of increased methamphetamine abuse, not only in individuals who inject the drug, but also in noninjecting methamphetamine abusers. Among injection drug users,

infection with HIV and other infectious diseases is spread primarily through the re-use of contaminated syringes, needles, or other paraphernalia by more than one person. However, regardless of how it is taken, the intoxicating effects of methamphetamine can alter judgment and inhibition and lead people to engage in unsafe behaviors.

Methamphetamine has become associated with a culture of risky sexual behavior, both among men who have sex with men (MSM) and heterosexual populations. This link may be due to the fact that methamphetamine and related psychomotor stimulants can increase libido. Paradoxically, long-term methamphetamine abuse may be associated with decreased sexual functioning, at least in men. The combination of injection and sexual risk-taking may result in HIV becoming a greater problem among methamphetamine abusers than among opiate and other drug abusers, something that already seems to be occurring, according to some epidemiologic reports. For example, while the link between HIV infection and methamphetamine abuse has not yet been established for heterosexuals, data show an association between methamphetamine abuse and the spread of HIV among MSM.

Methamphetamine abuse may also worsen the progression of

HIV and its consequences. In animal studies, methamphetamine increased viral replication; in human methamphetamine abusers, HIV caused greater neuronal injury and cognitive impairment compared with nondrug abusers.

NIDA-funded research has found that, through drug abuse treatment, prevention, and community-based outreach programs, drug abusers can change their HIV risk behaviors. Drug abuse can be eliminated and drug-related risk behaviors, such as needle-sharing and unsafe sexual practices, can be reduced significantly, thus decreasing the risk of exposure to HIV and other infectious diseases. Therefore, drug abuse treatment *is* HIV prevention.

What treatments are effective for methamphetamine abusers?

At this time, the most effective treatments for methamphetamine addiction are behavioral therapies such as cognitive behavioral and contingency management interventions. For example, the Matrix Model, a comprehensive behavioral treatment approach that combines behavioral therapy, family education, individual counseling, 12-Step support, drug testing, and encouragement

for nondrug-related activities, has been shown to be effective in reducing methamphetamine abuse. Contingency management interventions, which provide tangible incentives in exchange for engaging in treatment and maintaining abstinence, have also been shown to be effective.

There are currently no specific medications that counteract the effects of methamphetamine or that prolong abstinence from and reduce the abuse of methamphetamine by an individual addicted to the drug. However, there are a number of medications that are FDA-approved for other illnesses that might also be useful in treating methamphetamine addiction. Recent study findings reveal that bupropion, the anti-depressant marketed as Wellbutrin, reduced the methamphetamine-induced “high” as well as drug cravings elicited by drug-related cues. This medication and others are currently in clinical trials, while new compounds are being developed and studied in preclinical models.

Where can I get further scientific information about methamphetamine abuse?

To learn more about methamphetamine and other drugs of abuse, contact the National Clearing-

house for Alcohol and Drug Information (NCADI) at 800-729-6686. Information specialists are available to help you locate information and resources.

Fact sheets, including *InfoFacts*, on the health effects of methamphetamine, other drugs of abuse, and other drug abuse topics are available on the NIDA Web site (www.drugabuse.gov), and can be ordered free of charge in English and Spanish from NCADI at www.health.org.

Access information on the Internet

- What’s new on the NIDA Web site
- Information on drugs of abuse
- Publications and communications (including *NIDA Notes*)
- Calendar of events
- Links to NIDA organizational units
- Funding information (including program announcements and deadlines)
- International activities
- Links to related Web sites (access to Web sites of many other organizations in the field)

NIDA Web Sites

www.drugabuse.gov
www.steroidabuse.gov
www.clubdrugs.gov
www.hiv.drugabuse.gov
www.inhalant.drugabuse.gov

NCADI

Web Site: www.health.org
 Phone No.: 800-729-6686

Glossary

Addiction: A chronic, relapsing disease, characterized by compulsive drug seeking and drug use and by neurochemical and molecular changes in the brain.

Attention deficit hyperactivity disorder: A disorder that often presents in early childhood, characterized by inattention, hyperactivity, and impulsivity.

Central nervous system (CNS): The brain and spinal cord.

Craving: A powerful, often uncontrollable desire for drugs.

Dopamine: A neurotransmitter present in regions of the brain that regulate movement, emotion, motivation, and feelings of pleasure.

Narcolepsy: A disorder characterized by uncontrollable attacks of deep sleep.

Psychomotor stimulants (psychostimulants): Drugs that increase or enhance the activity of monoamines (such as dopamine and norepinephrine) in the brain. Psychostimulants increase arousal and activity, as well as heart rate, blood pressure, and respiration.

Psychosis: A mental disorder characterized by symptoms such as delusions or hallucinations and disordered thinking.

Rush: A surge of euphoric pleasure that rapidly follows administration of a drug.

Tolerance: A condition in which higher doses of a drug are required to produce the same effect as experienced initially.

Toxic: Damage to an organ or group of organs.

Withdrawal: A variety of symptoms that occur after chronic abuse of an addictive drug is reduced or stopped.

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