

IMPLICATIONS OF RESEARCH FOR TREATMENT: **METHAMPHETAMINE**

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Amphetamine-type substances (ATS) come in different forms and with different names. “Speed” (“meth,” “crank,” “goey”) is a powdered methamphetamine of relatively low purity and sold in grams or ounces. It can be snorted or injected. “Pills” can be pharmaceutical grade stimulants such as dextroamphetamine (Dexedrine or Adderall) or they can be methamphetamine powder that has been pressed into tablets and sold as amphetamines or ecstasy. There is also a damp, sticky powder of higher purity than Speed that is known as “Base,” “Wax,” or “Peanut Butter.” “Ice,” also known as “Shard,” “Tina,” or “Crystal,” is methamphetamine that has been “washed” in a solvent such as denatured alcohol to remove impurities. Ice resembles glass shards or ice shavings, has longer-lasting physical effects and purity levels above 80% [1].

LATEST RESEARCH FINDINGS

One of the problems in monitoring use is that the distinctions between the different types of ATS and routes of administration are often not clear. This is partially due to the fact that toxicological screens identify the presence of ATS, but a confirmatory test such as gas chromatography and mass spectrometry (GC-MS) is necessary to differentiate methamphetamine or ecstasy from amphetamine [2].

Adverse Effects

Methamphetamine use in the short-term causes increases in heart rate, blood pressure, temperature, and rate of breathing, and in addition, constriction of blood vessels and cardiac arrhythmia. Over longer periods of time, methamphetamine use is associated with health problems such as stroke, cardiac valve thickening, decreases in lung function, pulmonary hypertension, changes to the brain, poorer cognitive functioning, and poorer mental health [3].

Methamphetamine abuse also adversely impacts social support and social networks and behavioral functioning [4]. It produces a variety of effects including irritability, physical aggression, hyperawareness, hypervigilance, and psychomotor agitation. Chronic intoxication can produce a psychotic paranoid state with frightening delusions that may result in aggressive acts. With increased dosage and duration of administration, amphetamines can produce delirium, which is manifested by disorientation, confusion, fear, and anxiety. During high-dose use, individuals can experience stimulant-induced psychosis characterized by delusions, paranoid thinking, and compulsive behavior. There is also substantial evidence to associate the effects of its use with violence [5].

The Methamphetamine Treatment Project in California found participants had high levels of psychiatric symptoms, particularly depression and attempted suicide, as well as anxiety and psychotic symptoms. They reported high levels of problems controlling anger and violent behavior, with a

correspondingly high frequency of assault and weapons charges [6]. Past and current interpersonal violence is a characteristic of the lifestyles of the majority entering treatment for methamphetamine dependence [7].

The motivations for using methamphetamine reported by 28% of clients admitted for treatment in Los Angeles County included the belief that methamphetamine was an alternative, better, cheaper, and safer stimulant than other stimulants they had been dependent on. An additional 28% used methamphetamine as a crutch to help them cope with mental illness, distress, or trauma so that they felt “normal.” Twenty-three percent primarily used the drug to stay awake longer and to gain strength and energy, while 11% used it to enhance sexual experience and performance. For 10%, it was used as a tool to lose weight [8].

And a comparison of patterns of methamphetamine and cocaine use found the typical methamphetamine user used more than 20 days a month. Use was evenly spaced throughout the day, stopped at night to sleep, and although the amount of drug used per day was not different, methamphetamine users used fewer times per day than did cocaine users. Cocaine users were more likely to use on fewer days, in the evenings, and to take more frequent doses per day, which fits a picture of recreational use, whereas the all-day-most-days methamphetamine pattern does not [9]. Besides this pattern of chronic and periodic administration of methamphetamine throughout the day, there is also a pattern of continuous use with increasing doses throughout several days and nights (a “binge” or “run”) [10].

The 2003 Australian Party Drug survey found that Ice users (as compared to users of Speed or Base) were significantly more likely to report that they had “binged” on stimulants in the past six months (i.e., used the drug continuously for more than 48 hours without sleep) and to report that drug use caused social, work, and financial problems [11]. Recent Ice injectors were significantly more likely to have sought treatment for mental health problems in the last six months, with the most common problems being depression and anxiety [12].

A sample of “crystal meth” users in Sydney found they reported benefits that included alertness, energy, aphrodisiac effects, sociability, euphoria, and loss of inhibitions. Although most did not have extensive experience with Ice, they reported high rates of physical and psychological side effects, including “comedown,” paranoia, inability to sleep, addiction, and aggression. Compared with a sample of longer-term, heavier, and predominately injecting amphetamine users, crystal meth users appeared more likely to experience significant harms after a much shorter and lower level of use [13].

Many methamphetamine users are at high risk of sexually transmitted and blood-borne diseases. A study of 139 HIV-negative heterosexuals who were dependent on methamphetamine found they used the drug to get high, to get more energy, and to party. They reused syringes, shared needles, drank alcohol daily, used other drugs, had unprotected sex, had multiple sex partners (average of 9.4 in the past two months), and engaged in marathon sex [14].

Use of methamphetamine, and particularly Ice, has increased among men who have sex with men. Ice appears to be especially sexually arousing and disinhibitory and is strongly associated with sexual behaviors that put users at risk for HIV infection [15] because it is used to initiate, enhance, and prolong sexual encounters and intoxication can lead to lapses in judgment with regard to safe sex [16]. Methamphetamine and sex are not only integrally connected, but participants report sex on methamphetamine as “compulsive” and “obsessive,” with loss of control over their sexual expression [17].

In addition, methamphetamine can be used in combination with a wide variety of other drugs including alcohol, cocaine, ecstasy, ketamine, and GHB, which increases the risk of overdose and other adverse events [18]. Medical complications for methamphetamine abuse in HIV-infected patients include hypertension, hyperthermia, rhabdomyolysis, and stroke, and some researchers suggest that dopaminergic systems are vulnerable to the combined neurotoxicity of HIV infection and methamphetamine [16].

Methamphetamine use during pregnancy may affect the developing fetus [19]. Human studies are limited, but the findings suggest that children may be at risk developmentally due to both the direct effects of prenatal drug exposure and the care giving environment associated with that drug use. Maternal drug use is associated with risk factors such as poverty, chaotic and dangerous lifestyles, symptoms of psychopathology, history of childhood sexual abuse, and involvement in difficult or abusive relationships with male partners [20].

Children are frequently found at the scene of a meth laboratory and are exposed to toxic chemicals and fumes through absorption, inhalation, or ingestion, as well as being in homes with poor sanitation, hygiene, and nutrition. There can also be a high incidence of developmental delays. In these instances, the child welfare system often becomes involved and child protective services and other social work agencies need protocols to address the needs of the children and their parents, as well as those of the legal system [21].

Cognitive/Psychiatric Associations

One study of methamphetamine users found pre-morbid schizoid/schizotypal personality predisposed methamphetamine users to develop psychoses. Those with psychosis were younger at first use, used larger amounts, had significantly higher mean Premorbid Schizoid and Schizotypal Trait scores, and higher rates of depressive disorder, alcohol dependence, and antisocial personality disorders [22].

Methamphetamine-dependent individuals who were abstinent 5 to 14 days performed significantly worse than control subjects on neurocognitive measures sensitive to attention/psychomotor speed, on measures of verbal learning and memory, and on executive systems measures sensitive to fluency [23]. And recently abstinent methamphetamine-dependent subjects demonstrated quantitative EEG abnormalities that are consistent with a generalized encephalopathy. These changes in brain electrical activity are frequently associated with a range of

cognitive and psychiatric abnormalities, suggesting further avenues of investigation [24].

Preliminary evidence suggests that methamphetamine dependence may cause long-term neuronal damage and deleterious effects on cognitive processes such as memory and attention [25]. Methamphetamine abusers who remain abstinent for 9 months or longer show modest improvement in performance on some tests of motor skill and memory and they appear to recover from some of the drug's damaging effects on metabolism in the thalamus. Drug-related deficits appear to persist longer, however, in the striatum. Persistent decreases in striatal metabolism in methamphetamine abusers could reflect long-lasting changes in dopamine cell activity and decreases in the nucleus accumbens could account for the persistence of amotivation and anhedonia in detoxified patients. The recovery of thalamic metabolism could reflect adaptation responses to compensate for the dopamine deficits, and the associated improvement in neuropsychological performance further indicates its functional significance [26].

Using magnetic resonance imaging (MRI) and new computational brain mapping techniques, Thompson et al. [27] demonstrated systematic brain structural deficits with chronic methamphetamine abuse in human subjects and related these deficits to cognitive impairment. MRI-based maps suggest that chronic methamphetamine abuse causes a selective pattern of cerebral deterioration that contributes to impaired memory performance.

TREATMENT IMPLICATIONS

Treatment for methamphetamine abuse is a recent phenomenon and, for the most part, is based on previous treatment approaches for cocaine abuse [4]. But there are some aspects of methamphetamine-related disorders that are specific to the consequences of using the drug. A study comparing cognitive performance of methamphetamine and cocaine abusers found methamphetamine abusers have trouble organizing information from more than one source and have

difficulty switching points of view (set), as well as comprehension deficits. Law enforcement agencies and treatment providers should make extra efforts with methamphetamine users to determine that they understand what counts as compliance, what help is available, and the consequences for failing to comply. Physicians and other health professionals should ensure that medical advice is not only understood, but that the patient will have a method for remembering to take medications and to follow suggested medical procedures. Treatment providers need to provide concrete and specific information [28].

The development of treatments is particularly critical for a number of user groups including those who experience persistent psychosis, pregnant women and women with children, gay and bisexual men, and users involved in the criminal justice system [29] as well as for rural populations, Hispanics, and youths. A randomized controlled trial of methamphetamine-dependent gay and bisexual males found that treatment that focused on both drug use and risky sexual behaviors in a gay-friendly setting produced significant reductions in methamphetamine use and sexual risk behaviors [30]. Drug treatment merits consideration as a primary HIV prevention strategy for this population [17].

Brief interventions consisting of motivational interviewing and cognitive-behavior therapy (CBT) have been shown to increase the likelihood of abstinence from amphetamines. Regular users in non-treatment settings should receive a structured assessment, self-help material, and regular monitoring of amphetamine use and related harms. Users who present to treatment setting could be offered two sessions of CBT and those with moderate to severe levels of depression may best be offered four sessions of CBT, with further treatment for amphetamine use and/or depression depending on response [31].

Psychosocial and behavioral approaches currently constitute the primary treatments for methamphetamine-dependent individuals, although

research continues on replacement pharmacotherapies. The Center for Substance Abuse Treatment's *Tip #33, Treatment of Stimulant Abuse* [32] remains a basic guide for clinicians. The Matrix Model, a manualized 16-week outpatient treatment approach for treating stimulant disorders, combines techniques and materials from the cognitive behavioral therapy literature to include accurate information on the effects of stimulants, family education, Twelve-Step program participation, and positive reinforcement for behavior change and treatment compliance. It has been assessed in several large groups and outcomes have demonstrated that, in general, the treatment response of methamphetamine-dependent individuals was positive [33]. Findings of the Methamphetamine Treatment Project continue to support the value of integrated treatment for co-occurring conditions, and especially the importance of training counseling staff to handle psychotic symptoms when needed [6].

While specific behavioral interventions are useful in treatment of substance use disorders, medications also have an important role in treatment and promising results are emerging for an agonist-type or "replacement" strategy paralleling that for nicotine and opioid dependence. In a detailed review, Grabowski and colleagues [34] examined the current status of preclinical research agonist and antagonist pharmacotherapy strategies, and in particular, the use of stimulant medications in replacement strategies for amphetamine and cocaine dependence. They concluded the risks in a replacement/agonist-like strategy for stimulant dependence are manageable. Joint application of quality behavioral therapy and a potent stimulant, with appropriate monitoring procedures should produce benefit and a reduction in risk compared to continuation of the usual patterns of stimulant abuse and dependence. Collaborative efforts of preclinical and clinical researchers will be important in the development of specific medications and conceptualization of optimal strategies and regimens.

GLOSSARY

- agonist—a drug or other chemical that can combine with a receptor on a cell to produce a physiologic reaction typical of a naturally occurring substance.
- antagonist—a chemical substance that interferes with the physiological action of another, especially by combining with and blocking its nerve receptor.
- antiretrovirals—substances used to kill or inhibit the multiplication of retroviruses such as HIV; antiretroviral drugs attack HIV, which is a retrovirus.
- cardiac arrhythmia—an irregularity in the force or rhythm of the heartbeat.
- dependence—a pattern of substance misuse characterized by a combination of factors, such as withdrawal, tolerance, cravings, out-control use, and use despite negative effects.
- depression—a mood disorder characterized by poor appetite or overeating, sleeplessness or hypersomnia, low energy or fatigue, low self-esteem, feelings of hopelessness, and difficulty concentrating or making decisions.
- executive functioning—associated with mental operations such as planning, working memory, and initiation and self-regulation of goal-directed behavior.
- gray matter—neural tissue, especially of the brain and spinal cord, that contains cell bodies as well as nerve fibers, has a brownish gray color, and forms most of the cortex and nuclei of the brain, the columns of the spinal cord, and the bodies of ganglia.
- hippocampus—a curved elongated ridge that is an important part of the limbic system, extends over the floor of the descending horn of each lateral ventricle of the brain, and consists of gray matter covered on the ventricular surface with white matter.
- hypertension—high blood pressure.
- hyperthermia—exceptionally high fever.
- hypervigilance—the condition of maintaining an abnormal awareness of environmental stimuli
- psychosis—a thought disorder in which reality is grossly distorted. Symptoms can include seeing, hearing, smelling, or tasting things that are not there; paranoia; delusions. Psychosis can occur as a result of brain injury or disease, and is seen particularly in schizophrenia and bipolar disorders.
- rhabdomyolysis—the breakdown of muscle fibers with leakage of potentially toxic cellular contents into the systemic circulation.
- schizophrenia—a severe mental illnesses whose symptoms may include loss of personality (flat affect), agitation, catatonia, confusion, psychosis, unusual behavior, and withdrawal. The illness begins in early adulthood in many cases.
- tachycardia—relatively rapid heart action whether physiological (as after exercise) or pathological.
- verbal fluency letter generation—a classic neuropsychological test of language production which involves subjects generating and articulating a word in response to a cue the Verbal Fluency Task. As an example, in the letter category, participants are asked to produce as many words as possible beginning with a specified letter in one minute.

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