The Prevention and Treatment of Adolescent Stimulant and Methamphetamine Use

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Introduction

Stimulant use remains a significant public health concern despite decades of research on prevention and treatment efforts. The use of cocaine, amphetamine, and methamphetamine produces a range of problems for the individual, specifically, and society, broadly. These costs include premature mortality, crime and lost productivity, transmission of infectious diseases, medical complications such as cardiovascular problems, and exacerbation of mental health conditions (Cavazos-Rehg et al., 2009; Havakuk, Rezkalla, & Kloner, 2017; Pasic, Russo, Ries, & Roy-Byrne, 2007; Shoptaw, King, et al., 2009; Stein, 1999). Stimulant misuse is particularly worrisome for adolescent populations because substance use can alter developmental trajectories during a period of dramatic physiological and psychological growth (Crowley & Riggs, 1995). High-risk behaviors already prominent in adolescents, such as violence, aggression, and unprotected sexual encounters, are also likely to increase under the influence of drugs (Jessor & Jessor, 1977). The pervasive impact

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of illicit substance use underscores the need for evidence-based prevention and treatment strategies targeting adolescent stimulant use.

This chapter examines the history and characteristics of stimulant use and misuse, the pharmacology and clinical effects of stimulants, and expected clinical outcomes for stimulant-using adolescents. The literature is also reviewed for current primary prevention and treatment approaches targeting adolescent stimulant use. *Primary prevention* is defined to include planned actions of health promotion that help adolescents prevent predictable problems, protect existing states of health as well as healthy functioning, and promote desired goals for adolescents. *Treatment* is defined as activities that focus on helping adolescents reduce problems associated with ongoing stimulant use/misuse and that change individual stimulant use behavior. This chapter focuses on cocaine, amphetamine, and methamphetamine because these substances represent commonly used and studied psychomotor stimulants in adolescent as well as adult populations (Center for Behavioral Health Statistics and Quality, 2016; Johnston, O'Malley, Miech, Bachman, & Schulenberg, 2017).

History of Stimulant Misuse

Cocaine is an alkaloid compound derived from the naturally occurring coca plant. The leaves of the coca plant were historically used by indigenous cultures in South America for medicinal and religious purposes. Cocaine alkaloid was isolated from the coca leaf in 1800s and soon after widely utilized in medical tonics and other commercially available products (e.g., the original Coca-Cola® formulation; Grinspoon & Bakalar, 1981). Following concerns over the health effects of cocaine use, cocaine was classified as a narcotic and put under the control of the US federal government with the 1914 Harrison Narcotics Act. Today, cocaine remains a class II schedule substance in the USA regulated by the Drug Enforcement Agency and is medically used as a topical anesthetic in eye, mouth, and nasal surgery.

The amphetamines are a group of synthetic chemicals first formulated as amphetamine isomers from ephedrine in the late 1880s. The popularity of amphetamines rose throughout the early twentieth century when they were used to promote alertness, particularly among soldiers in World War II. The nonmedical use of amphetamines was outlawed following that war citing widespread misuse and their potential negative health impact. Amphetamine isomers (e.g., Dexedrine®, Adderall®) are today used medically primarily in the treatment of attention deficit disorder/attention deficit hyperactivity disorder (ADD/ADHD). However, diversion of these medications for recreational use remains a concern, particularly among adolescent populations (Garnier et al., 2010; McCabe, Teter, & Boyd, 2004; McCabe, West, Teter, & Boyd, 2014; Wilens et al., 2008).

More recently, methamphetamine has emerged as a widely misused stimulant. The rise of methamphetamine is due, in part, to the ability to simply, but dangerously, synthesize it using common household items through pseudoephedrine reduction.

Production is further simplified for manufacture by small clandestine laboratories in a process known as the "shake 'n' bake" method (Brzeczko, Leech, & Stark, 2013). These chemical reduction methods are relatively easy to learn and instructions readily accessible to adolescents through varied resources, including Internet message boards and other online forums (e.g., erowid.org; bluelight.com). Increases in domestic regulation of methamphetamine precursors and seizures of local laboratories have been offset by a corresponding growth in international methamphetamine production and trafficking into the USA (Cunningham, Finlay, & Stoecker, 2015; Shukla, Crump, & Chrisco, 2012).

Prevalence of Adolescent Stimulant Use

Stimulant use remains a significant concern for adolescents (see Fig. 1). Findings from the 2016 Monitoring the Future Study (Johnston et al., 2017) indicate that by eighth grade, 1.4% of students have tried cocaine, 5.7% have tried amphetamines not prescribed to them, and 0.6% have tried methamphetamine. These numbers grow by tenth grade to 2.1%, 8.8%, and 0.7%, respectively, and by twelfth grade to 4.0%, 10.0%, and 1.2%, respectively. Important to note is that these estimates represent a substantial decrease over the last decade (see Fig. 1), wherein 8.5% of twelfth graders reported trying cocaine, 12.4% reported trying amphetamines, and 4.4% reported trying methamphetamine in 2006. Such decreases are consistent with general trends observed for adolescent substance use across most drug classes (Johnston et al., 2017). However, the substantial number of adolescents still misusing stimulants and the potential negative health consequences of such use reinforces the need for primary prevention efforts and evidence-based treatments.

Pharmacological and Clinical Characteristics of Stimulant Misuse

The primary pharmacological effects of stimulants are mediated by actions on the central nervous system and monoamine neurotransmitters (Elliott & Beveridge, 2005; Howell & Negus, 2014; Rocha, 2003; Rothman & Baumann, 2003; Uhl, Hall, & Sora, 2002). The following section reviews these pharmacological mechanisms, characteristic patterns of use, and the short- and long-term health consequences of cocaine, amphetamines, and methamphetamine use for adolescents and emerging adults.

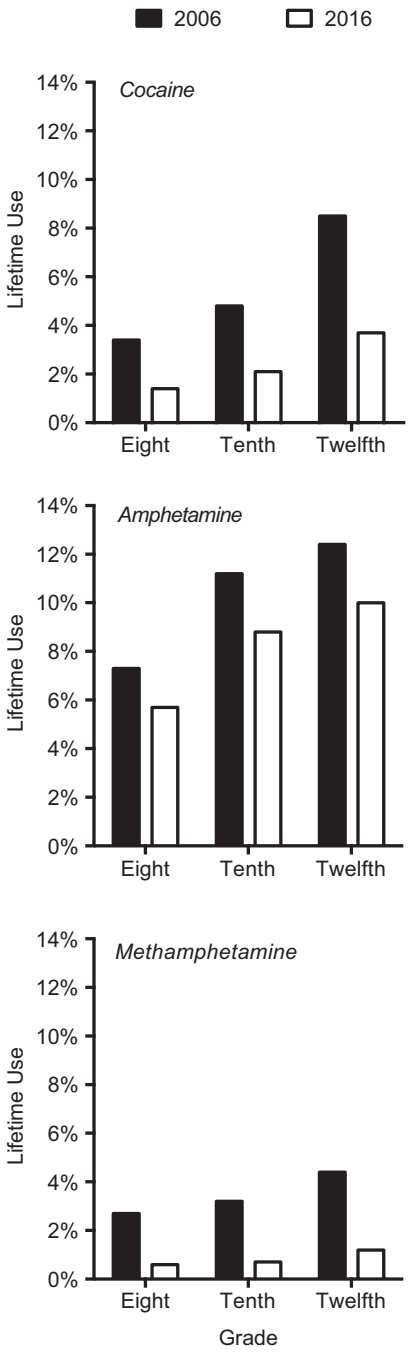

Fig. 1 Lifetime prevalence of illicit stimulant use by US adolescents. Depicted are 2006 (black bars) and 2016 (white bars) prevalence estimates of lifetime illicit cocaine (top), amphetamine (middle), and methamphetamine (bottom) use among adolescents in eight, tenth, and twelfth grade. Adapted from data in "*Monitoring the Future national survey results on drug use, 1975–2016: Overview, key findings on adolescent drug use*," by L. D. Johnston, P. M. O'Malley, R. A. Miech, J. G. Bachman, and J. E. Schulenberg, 2017, Ann Arbor, MI: Institute for Social Research, The University of Michigan

Receptor Pharmacology

Cocaine's primary mechanism of action is reuptake inhibition at monoamine transporters (i.e., dopamine, norepinephrine, and serotonin). The net effect of this reuptake inhibition is increased synaptic monoamine concentrations and sustained activation of corresponding neurotransmitter systems. Recent evidence also suggests that cocaine may produce additional passive outflow of dopamine by fixing the dopamine transporter in an outward facing confirmation (Heal, Gosden, & Smith, 2014). Cocaine acts in vitro with relative equal potency at each of the monoamine transporters (Rothman & Baumann, 2003). Research has historically focused on dopamine reuptake inhibition as the primary mediator of abuse-related effects (Nutt, Lingford-Hughes, Erritzoe, & Stokes, 2015; Wise & Bozarth, 1987). However, the last decade has witnessed an increasing focus on the importance of serotonergic systems (e.g., Cunningham & Anastasio, 2014; Howell & Cunningham, 2015; Müller, Carey, Huston, & De Souza Silva, 2007) and noradrenergic systems (e.g., Sofuoglu & Sewell, 2009; Weinshenker & Schroeder, 2007) as they relate to cocaine use and misuse.

Amphetamine and methamphetamine also act on the monoamine transporters. The primary mechanism of action for amphetamines is to encourage neurotransmitter release in contrast to the reuptake inhibition produced by cocaine (Rothman et al., 2001; Rothman & Baumann, 2003). Amphetamines brought into the cell can stimulate vesicular neurotransmitter release into the synaptic cleft through a reverse transporter mechanism. Amphetamines have high potency for dopamine and norepinephrine transporters, but are comparatively less potent at the serotonin transporter (Alexander et al., 2005; Rothman et al., 2001; Wee et al., 2005). The dextrorotary forms of amphetamines (D-amphetamine and D-methamphetamine) show greater potency for the dopamine transporter than the levorotary ones (l-amphetamine and l-methamphetamine) (Rothman et al., 2001; Rothman & Baumann, 2003) and many medical versions use varying racemic or combined formulations (e.g., Adderall® is 75% D-amphetamine and 25% L-amphetamine).

Routes of Administration and Use Patterns

Cocaine is typically administered by insufflation ("snorting") or inhalation ("smoking") when used recreationally, but is also used by oral and intravenous routes under some circumstances. Cocaine hydrochloride is a white powder salt that is water-soluble and thus may be insufflated and absorbed through the vascular region of the nasal cavity or dissolved for intravenous use. "Crack cocaine" is a freebase preparation of cocaine with a hard, rocklike appearance. The low melting point of these rock crystals means that crack cocaine may be heated and the vapors inhaled for smoked use. Cocaine is readily absorbed in the bloodstream and produces its peaks effects within 10–20 min when insufflated and within minutes when inhaled or

injected (Volkow et al., 2000). Cocaine is metabolized quickly with a half-life of 30–90 min and apparent effects that diminish within an hour following administration (Isenschmid, Fischman, Foltin, & Caplan, 1992; Jeffcoat, Perez-Reyes, Hill, Sadler, & Cook, 1989; Newton, De La Garza II, Kalechstein, & Nestor, 2005). This rapid onset–offset means that recreational use may progress to binge patterns of use characterized by excessive and escalating drug intake over short periods of time (Gawin, 1991; Gawin & Kleber, 1985).

Amphetamines are typically administered for medical use by the oral route (e.g., Adderall® for ADHD). Recreationally, however, amphetamines are commonly insufflated or injected. A pure form of D-methamphetamine hydrochloride known as "crystal meth" or "ice" is also commonly used and may be melted and its vapors inhaled similar to crack cocaine. Amphetamines, and D-methamphetamine in particular, have a long duration of action due to slower metabolism and a half-life of 8–12 h depending on the compound formulation (Angrist, Corwin, Bartlik, & Cooper, 1987; Cruickshank & Dyer, 2009; Harris et al., 2003). Binge patterns exemplified by continuous intake and no sleep for multiple days are also typical for methamphetamine use (Cruickshank & Dyer, 2009; Simon et al., 2002).

Short-Term Effects

Cocaine and the amphetamines produce robust effects on the cardiovascular system, including increased heart rate, blood pressure, and respiration rate (Foltin & Fischman, 1990; Foltin, Fischman, Pedroso, & Pearlson, 1988; Marks et al., 2016; Mendelson et al., 2006; Stoops, Pike, Hays, Glaser, & Rush, 2015). Acute high doses also carry the risk of acute overdose primarily due to respiratory collapse from seizures and convulsions, stroke, or myocardial infarction. Anorectic or appetite-suppressant effects also accompany the acute administration of cocaine and amphetamines.

Acute stimulant administration also produces dose-dependent positive subjective effects, including improved mood, increased talkativeness, and decreased fatigue (Foltin & Fischman, 1991; Hart, Ward, Haney, Foltin, & Fischman, 2001; Hart et al., 2008; Kirkpatrick et al., 2012; Rush, Baker, & Wright, 1999; Stoops, Glaser, Fillmore, & Rush, 2004). Stimulants can improve performance on physical endurance and cognitive-performance tasks, although these effects often depend on the dose administered. Desirable effects related to arousal and/or cognitive-performance are a primary reason that adolescent populations report seeking out diverted stimulant medications as "study aids" (Teter, McCabe, Cranford, Boyd, & Guthrie, 2005; Vrecko, 2015; Wilens et al., 2008). Higher acute doses can also produce untoward psychotic effects, including hallucinations, paranoid delusions, and stereotyped behaviors.

Long-Term Effects

Chronic stimulant administration can result in tolerance and withdrawal upon cessation of use. Acute tolerance following repeated administration over short periods of time has also been observed for cocaine and methamphetamine (Comer et al., 2001; Ward, Haney, Fischman, & Foltin, 1997). Such tolerance to the positive subjective effects of stimulants can result in heavier and more frequent use, which exacerbates the negative effects of cardiovascular and brain function. Although withdrawal symptoms are not readily apparent compared to other substances such as opioids or alcohol, withdrawal from cocaine or amphetamine use can result in depression, anxiety, and sleep and appetite disturbances (Gossop, Bradley, & Brewis, 1982; Shoptaw, Kao, Heinzerling, & Ling, 2009). As noted earlier in this section, tolerance and withdrawal may reinforce the "crash-binge" use pattern characterized by bouts of intense and heavy use followed by several days of depressed mood and increased sleep and food intake (Cruickshank & Dyer, 2009; McGregor et al., 2005; Simon et al., 2002).

Long-term stimulant use can also disrupt physical health, particularly in adolescent populations (e.g., Mone, Gillman, Miller, Herman, & Lipshultz, 2004; Rawson, Gonzales, McCann, & Ling, 2007). Chronic cocaine and amphetamine misuse causes damage to the cardiovascular and related organ systems, including heart muscle inflammation and aortic ruptures, and increased risk of myocardial ischemia or infarction (Havakuk et al., 2017). Regular stimulant insufflation also damages the nasal vasculature and can result in the loss of smell and nasal septum inflammation (Glauser & Queen, 2007; Valencia & Castillo, 2008). Similarly, chronic inhalation of cocaine or methamphetamine can cause lung damage and aggravate existing pulmonary problems (Drent, Wijnen, & Bast, 2012; Susskind, Weber, Volkow, & Hitzemann, 1991; Tashkin et al., 1992; Wells et al., 2010). The anorexic effects of stimulants may also result in the chronic appetite loss and malnourishment. This concern is particularly troubling for adolescents who may use stimulants to engage in unhealthy weight loss behaviors or whose use may disrupt natural growth and development (e.g., Berman, Kuczenski, McCracken, & London, 2009; Dutta et al., 2006; Neale, Abraham, & Russell, 2009).

Likewise, the chronic use of stimulants during adolescents can result in neurobiological damage and changes in those brain systems associated with an increased susceptibility to other substance misuse, physical health problems, and mental health concerns (e.g., Lyoo et al., 2015; Pianca et al., 2017). Adolescent methamphetamine users exhibit greater and more widespread damage to gray and white matter, particularly in the frontostriatal region, as compared to adult users (Lyoo et al., 2015). Cocaine use during adolescence is also associated with elevated serum levels of interleukin (IL) inflammatory markers IL-6 and IL-10 as well as oxidative stress markers (Pianca et al., 2017). Notably, one study found that these increases in IL-6 and IL-10 were reduced following 20 days of abstinence suggesting possible remediation of this inflammatory damage upon treatment and use cessation (Pianca et al., 2017). Changes in central nervous and immune systems function may worsen

Table 1 Primary prevention efforts for adolescent stimulant use

Method	Description	Example(s)	Evidence
Regulation and Law Enforcement	Actions designed to reduce the supply of and/or demand for drugs through laws and policies	*United Nations Single Convention on Narcotic Drugs*	*Weak Evidence*
Mass Media Campaigns	Campaigns typically focused on preventing illicit substance use through printed, televised, or online public service announcements (PSAs).	*The Meth Project*	*Weak Evidence*
School-Based Programs	Programs delivered in the school setting. May include didactic teaching and education and/or interactive methods (skill building, role-playing)	*Drug Abuse Resistance Education (D.A.R.E.); Project Towards No Drug Abuse (Project TND)*	*Weak Evidence (Didactic Programs) Good Evidence (Interactive Programs)*
Family-Based Programs	Family involvement to reduce pathways to initiation and improve the psychosocial development of the child	*Preparing for the Drug Free Years; Strengthening Families Program; Family Empowerment Intervention*	*Mixed Evidence/ Limited Data for Stimulant-Specific Outcomes*

Note. All evaluations represent the authors' perspective after review of the literature
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already ongoing high rates of comorbidity between substance misuse and mental health problems in adolescents. Prospective studies, such as the ongoing Adolescent Brain Cognitive Development study (abcdstudy.org), will be essential for investigating the neurobiological mechanisms that are antecedent to and consequence of adolescent cocaine and amphetamine use.

Primary Prevention Efforts

The following section reviews primary prevention efforts designed to promote the desired goal of preventing stimulant use initiation in adolescents (see Table 1). Compared to alcohol and tobacco use, there are few studies with a primary focus on adolescent stimulant use. However, in several cases those approaches targeting alcohol or tobacco prevention have shown similar positive outcomes for preventing stimulant use.

Population and Community-Level Efforts: Regulation and Media Campaigns

Regulatory efforts include actions designed to reduce the supply of and/or demand for drugs through the laws, policies, and other enforcement measures. The nonmedical use of stimulants is prohibited under the United Nations Single Convention on Narcotic Drugs resulting in the prohibition of use in many countries, including the USA. Although strict enforcement of drug laws and sanctions is frequently noted as a primary prevention mechanism, the evidence is mixed for the utility of these policies for reducing substance use and may have the untoward effect of increasing public health harms such as market violence and risky injection practices (Kerr, Small, & Wood, 2005; Strang et al., 2012; Werb et al., 2011). Other regulatory strategies, such as minimum drinking or smoking ages and taxation efforts, have shown some positive effects for deterring alcohol and tobacco use and harms among adolescents (Botello-Harbaum et al., 2009; DiFranza, Savageau, & Fletcher, 2009; Lewit, Hyland, Kerrebrock, & Cummings, 1997; McCartt, Hellinga, & Kirley, 2010; Voas, Tippetts, & Fell, 2003). Many of those strategies (e.g., advertising regulations or bans) cannot be applied to curtail stimulant use, however, given that these drugs are only legally available through prescription and not on the commercial market.

Another commonly noted approach to prevent adolescent stimulant use is mass media campaigns (Ferri, Allara, Bo, Gasparrini, & Faggiano, 2013). These campaigns typically focus on preventing illicit substance use through printed, televised, or online public service announcements (PSAs). Some of these campaigns have specifically targeted adolescent stimulant misuse, one of the most notable being *The Montana Meth Project* and later *The Meth Project* (Siebel & Mange, 2009). Initiated in Montana and then expanded to seven other states after an apparent success, this campaign utilized a marketing strategy of television, radio, print, and social media advertising combined with community outreach to highlight the risks of methamphetamine through shocking images and slogans of use and users (e.g., "15 bucks for sex isn't normal. But on meth it is"). Minimal reductions in methamphetamine use were observed across each of the eight states adopting the program, however, after adjusting for preexisting downward trends in use (Anderson, 2010; Anderson & Elsea, 2015; Erceg-Hurn, 2008; Marsh, Copes, & Linnemann, 2017). A recent qualitative study with current and former methamphetamine users also reported that individuals found the dramatized images to be ineffective at curtailing their own drug use and that such depictions represented an inauthentic "worst-case" scenario that was not relevant to and symbolically distant from their experience (Marsh et al., 2017). These and similar depictions of substance-using populations as weak, lacking control, or "a junky" can impede recovery efforts by stigmatizing substance use or creating a symbolic boundary between oneself and a problematic user in need of help (e.g., Marsh et al., 2017; Radcliffe & Stevens, 2008; Rodner, 2005). Findings from *The Meth Project* are consistent with at least two recent systematic reviews on mass media campaigns for preventing illicit

adolescent substance use (Allara, Ferri, Bo, Gasparrini, & Faggiano, 2015; Ferri et al., 2013). These reviews concluded that mass media campaigns have minimal effect on adolescent illicit substance use. They also exhort that caution should be taken for future campaign development given the potential for adverse effects, such stigmatizing substance users and/or increasing awareness of and interest in illicit substance use (i.e., the "boomerang effect" or iatrogenic effects) (e.g., Allara et al., 2015; Hornik, 2006; Marsh et al., 2017; Scheier & Grenard, 2010).

School-Based Programs

School-based interventions have received extensive attention for preventing adolescent substance and stimulant use (Carney, Myers, Louw, & Okwundu, 2016; Faggiano, Minozzi, Versino, & Buscemi, 2014). Although these interventions are limited by their inability to reach at-risk adolescents who frequently miss or have left school, they do represent a straightforward and potentially useful venue for prevention (and treatment) delivery. Many of these programs use didactic teaching and education regarding drug use and consequences. Despite the popularity of such an approach, negative outcomes have generally been reported for reducing substance use among adolescents (Paglia & Room, 1999; Tobler et al., 2000). For example, *Drug Abuse Resistance Education* (*D.A.R.E.*) is a school-based program providing information about the dangers of recreational drug use by local police officers. *D.A.R.E.* remains a popular and widely used program in the educational setting despite numerous studies and meta-analytic reviews demonstrating limited effects on long-term adolescent drug use (Clayton, Cattarello, & Johnstone, 1996; Lynam et al., 1999; Pan & Bai, 2009; West & O'Neal, 2004). Clinically useful school-based programs require varied, interactive teaching methods to enhance important life skills, including communication, coping, and assertiveness (Tobler et al., 2000). In fact, a modified version of *D.A.R.E. (D.A.R.E. Plus)* incorporating parental participation, skill building, and extracurricular activities resulted in better prevention of adolescent substance use (Perry et al., 2003). A meta-analysis of 207 studies found that inclusion of interactive components significantly predicted positive outcomes for school-based preventive efforts (Tobler et al., 2000). In contrast, non-interactive lectures delivering only affective development or drug knowledge demonstrated small effects.

In this respect, social competence and social norms approaches have demonstrated positive outcomes for preventing adolescent substance drug use (Faggiano et al., 2014; Thomas, McLellan, & Perera, 2013). Social competence programs are grounded in social learning theory, which posits that adolescents learn drug-use behaviors through modeling, imitation, and selective reinforcement and punishment by substance-using peers. Social norm efforts target substance use through self-management skills designed to correct incorrect beliefs about peer substance use (e.g., overestimation) and to teach skills associated with recognizing high-risk situations and refusal skills. A recent meta-analysis indicated that these programs

alone and combined produce small, but consistent, protective effects for illicit drug use compared to usual curriculum (Faggiano et al., 2014). Little research exists specifically evaluating stimulant use. However, some studies have revealed positive effects on "hard drug" use (e.g., combined cocaine, hallucinogens, inhalants, stimulants, ecstasy, and "other"). For example, *Project Towards No Drug Abuse* (*Project TND*) is a classroom-based prevention program combining social competence and norm approaches to improve motivation/listening skills, provide information about the negative consequences of substance use and correct misperceptions, and teach coping, decision-making, and refusal skills to encourage health-promoting behavior. *Project TND* has shown small, but positive effects across seven cluster-randomized controlled trials for reducing and preventing "hard drug" initiation (e.g., Rohrbach, Sun, & Sussman, 2010; Sun, Skara, Sun, Dent, & Sussman, 2006; see review by Sussman, Valente, Rohrbach, Dent, & Sun, 2014). Some debate does exist, however, concerning the veracity of these findings due to inconsistent measurement and potential data analytic problems (Gorman, 2014).

Family-Based Programs

Family participation is a critical component of many successful prevention efforts. These approaches often strive to reduce pathways to drug initiation and improve the psychosocial development of the child. Successful family prevention programs typically enhance familial protective factors associated with adolescent substance use (e.g., supportive relationships with family members), provide skills training for parents, and target improvements in familial risk factors, such as poor communication or substance use among family members (Ary et al., 1999). The National Institute on Drug Abuse endorses family-based programs given this importance of family relationships as risk/protective factors and mediators of adolescent substance use (Swadi, 1999).

Some common examples of family-based programs include *Preparing for the Drug Free Years* (Park et al., 2000), *Strengthening Families Program* (Kumpfer, Alvarado, & Whiteside, 2003), and the *Family Empowerment Intervention* (Dembo, Wothke, Livingston, & Schmeidler, 2002). To this end, family-based interventions have shown good evidence for enhancing parenting skills, reducing family conflict, and improving communication across varied demographic groups (Aktan, Kumpfer, & Turner, 1996). Like other prevention efforts, the majority of family interventions targeting illicit drug use have focused on cannabis use. A recent meta-analysis supported parent–child targeted interventions for preventing the initiation of adolescent marijuana use (Vermeulen-Smit, Verdurmen, & Engels, 2015). Less support was reported for other illicit substance use, with the limited literature indicating generally small or no effect on adolescent stimulant use (e.g., Catalano, Gainey, Fleming, Haggerty, & Johnson, 1999; Haggerty, Skinner, Fleming, Gainey, & Catalano, 2008; Wu et al., 2003). However, additional and larger randomized

clinical trials are needed before conclusions about the impact of family-based programs on adolescent stimulant prevention may be made.

Summary of Evidence-Based Primary Prevention Efforts

We reviewed the relative impact of population/community, school, and family-based primary prevention programs for curtailing the initiation of stimulant use in adolescent populations. Few studies have evaluated programs or outcome measures specifically targeting adolescent stimulant use despite extensive study for alcohol, cigarette, and cannabis use. The broader literature suggests that the most successful programs will likely be comprehensive ones targeting multiple dimensions of adolescent stimulant use through combinations of the methods reviewed. For example, the *Midwestern Prevention Project* was a comprehensive multi-component program targeting adolescent drug use prevention through mass media campaigns, school-based skills training, parent programming, school policy changes, and community organization to address changing local policy. Reduced rates of alcohol, cigarette, and cannabis initiation and use were observed in program relative to control students (e.g., Johnson et al., 1990; Pentz et al., 1989). Promising results were also recently reported for amphetamine and methamphetamine use with reductions in use initiation that were sustained into adulthood (Riggs, Chou, & Pentz, 2009). Such findings provide support for the continued study and implementation of multi-component prevention efforts incorporating elements from community, school, and family-level focused programs.

Evidence-Based Treatments

Treatment efforts have historically focused on adolescent alcohol, tobacco, and cannabis use much like primary prevention efforts. Recent years, however, have seen an increase in the adaptation of these evidence-based interventions for stimulant use outcomes. The following section reviews treatment strategies for managing adolescent stimulant use, including brief interventions, cognitive-behavioral therapy, contingency management, family-based approaches, and pharmacotherapies (see Table 2).

Screening and Brief Interventions

Screening and brief interventions often represent a “first-line of defense” for intervening in adolescent stimulant use disorder (Pilowsky & Wu, 2013). This strategy fits within the broader model of “Screening, Brief Interventions, and Referral to

Table 2 Evidence-based interventions for adolescent stimulant use

Method	Description	Example(s)	Evidence
Screening and Brief Interventions	Integrated identification and treatment linkage for at risk individuals. Often designed to enhance motivation for change and treatment engagement	Motivational Interviewing (MI); Motivational Enhancement Therapy (MET)	*Mixed Evidence/ Limited Data for Stimulant-Specific Outcomes*
Cognitive-Behavioral Therapy	Designed to build coping skills for craving and other temptations to use drugs, improve interpersonal relationships, and reduce risk behaviors associated with drug use (e.g., driving while intoxicated)	N/A	*Good Evidence/ Limited Data for Stimulant-Specific Outcomes*
Contingency Management	Patients are provided a non-drug reinforcer, such as money or a voucher redeemable for material items, contingent upon a clinical response, such as drug abstinence	N/A	*Good Evidence*
Family-Based Interventions	Focuses on improving adolescent social functioning in the family and other contexts, enhancing communication within the family and social system, and providing parental monitoring and other adult skills	Multidimensional Family Therapy, Functional Family Therapy, Brief Strategic Family Therapy, and Adolescent Community Reinforcement	*Good Evidence/ Limited Data for Stimulant-Specific Outcomes*
Pharmacotherapy: Substance Use	Use of pharmacological agent delivered acutely or chronically to reduce stimulant use	None successful; Bupropion tested	*Limited Data for Stimulant-Specific Outcomes*
Pharmacotherapy: Psychiatric Comorbidities	Use of pharmacological agent delivered acutely or chronically to address psychiatric comorbidity	Extended-Release Methylphenidate for ADHD	*Good Evidence for Comorbidities/ Weak Evidence for Substance Use Outcomes*

Note. All evaluations represent the authors' perspective after review of the literature
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Treatment" or SBIRT (Babor et al., 2007; Madras et al., 2009). SBIRT proposes a comprehensive and integrated identification and treatment linkage for individuals at risk for or suffering from a substance use disorder. Although SBIRT has only recently been applied to adolescent substance use, preliminary evidence supports its potential utility and justification for further evaluation (Mitchell et al., 2012;

Mitchell, Gryczynski, O'Grady, & Schwartz, 2013; Ozechowski, Becker, & Hogue, 2016; Sterling et al., 2015).

The most extensively researched and validated screening measure to identity substance-related problems in adolescents is the CRAFFT (named after the first letter of key words in the questionnaire; CAR, RELAX, ALONE, FORGET, FRIENDS, and TROUBLE) (Knight et al., 1999; Knight, Sherritt, Shrier, Harris, & Chang, 2002; Knight, Sherritt, Harris, Gates, & Chang, 2003; Pilowsky & Wu, 2013). The CRAFFT consists of six yes/no questions addressing potential problematic alcohol or drug use (e.g., "Do you ever use alcohol or drugs to relax, feel better about yourself, or fit in?"). Endorsing two or more items is suggestive of a substance use disorder with several studies demonstrating high specificity and sensitivity when using this cut off (Knight et al., 1999, 2002; Mitchell et al., 2014). Strong psychometric properties combined with the ease of administration (1–2 min) make it an ideal tool for rapid screening by health care professionals and primary care physicians during routine medical visits. The majority of research has evaluated the benefits of the CRAFFT in alcohol use disorder. However, some evidence indicates the utility of the CRAFFT for identifying non-medical prescription opioid use (McCabe et al., 2012) and cannabis use (Oesterle, Hitschfeld, Lineberry, & Schneekloth, 2015). Future research is needed before the ultimate utility for screening stimulant use disorders can be determined.

Brief interventions may be combined with screening assessments to provide immediate linkage to treatment and initial harm reduction. Motivational interviewing is a widely-used brief intervention characterized by short patient-centered interviewing to enhance motivation for treatment, encourage positive behavior change, and set realistic goals for recovery (Miller & Rollnick, 1991). Motivational Enhancement Therapy (MET) also uses this motivational interviewing counseling style delivery over a slightly longer intervention period (e.g., 2–4 individual treatment sessions). Patients are similarly encouraged in MET to develop internal motivation for change through a patient-oriented, non-judgmental, and non-confrontational approach. These strategies can be delivered by health care professionals in one-to-one meetings following screening and identification of a potential stimulant or other substance use disorder. Brief motivational interviewing or MET is also common prior to longer and more intense interventions (e.g., CBT) to enhance motivation for change and treatment engagement. A meta-analysis of 21 studies evaluating MI in adolescents observed small, but significant, effects sizes post-treatment as well as at 6-month or longer follow-ups (Jensen et al., 2011). Although the only study targeting stimulant use reported negative findings (Marsden et al., 2006), the positive outcomes observed for other substances and the relatively low cost and effort required for these procedures supports the continued study of MI for adolescent stimulant use.

Cognitive-Behavioral Therapy

Cognitive-behavioral therapy (CBT) is a frequently used and evidence-based psychosocial intervention for adolescent and adult substance use disorder (Carroll & Onken, 2005; Dutra et al., 2008; Waldron & Turner, 2008). CBT is designed to build coping skills for craving and other temptations to use drugs, improve interpersonal relationships, and reduce risk behaviors associated with drug use (e.g., driving while intoxicated). Modules can be selected based on the individual's needs and include teaching practice skills through individual or group therapy, behavioral modeling, and role-play. The flexibility of CBT means that it is easily incorporated into inpatient or outpatient programs and often combined with other behavioral and pharmacological interventions. One study found that adolescents with methamphetamine use history showed higher rates of substance use at treatment discharge from CBT relative to non-methamphetamine using youth (Rawson, Gonzales, Obert, McCann, & Brethen, 2005). This finding implies that adolescents presenting with methamphetamine use may need additional components or services to encourage drug use cessation. Encouragingly, similar retention rates in a 28-day inpatient CBT program were reported for youth indicating methamphetamine as their primary substance of choice and those indicating another primary substance (Callaghan, Brands, Taylor, & Lentz, 2007). Readmission patterns also did not differ between methamphetamine and cocaine-using adolescents in another study (Callaghan, Taylor, Victor, & Lentz, 2007). These findings indicate the feasibility, albeit uncertain clinical utility, of CBT for adolescent stimulant use disorders.

Contingency Management

Contingency management (CM), also known as voucher-based reinforcement therapy, is a set of procedures that encourage behavioral change through principles derived from operant psychology (see reviews by Higgins & Petry, 1999; Stitzer & Petry, 2006). Patients are provided a non-drug reinforcer, such as money or a voucher redeemable for material items, contingent upon a predetermined clinical response, such as drug abstinence. Studies in adult populations have demonstrated the robust clinical utility of CM for initiating abstinence across a range of pharmacological classes, including stimulant drugs (e.g., Farronato, Dursteler-Macfarland, Wiesbeck, & Petitjean, 2013; Lee & Rawson, 2008; Prendergast, Podus, Finney, Greenwell, & Roll, 2006; Shoptaw et al., 2006). Fewer studies have been conducted in adolescent populations, but they have generally demonstrated positive effects on health behavior change (Stanger, Lansing, & Budney, 2016; Yu et al., 2016). For example, adolescents participating in a community-based CM program showed significant reductions in illicit drug use, generally, as well as cocaine use, specifically, when compared to adolescents receiving treatment as usual (Lott & Jencius, 2009). This trial was particularly noteworthy because it used

a community setting and a payment schedule that dramatically reduced direct expenditures for the program ($0.39/participant/day). Such low-cost procedures are important because perceived increases in monetary expenses are one of the greatest barriers to the widespread dissemination of CM.

Family-Based Approaches

Family participation has generally held a central role in treatment efforts consistent with its importance in prevention efforts. Commonly used programs include Multidimensional Family Therapy, Functional Family Therapy, Brief Strategic Family Therapy, and Adolescent Community Reinforcement Approach (Alexander & Parsons, 1982; Baldwin, Christian, Berkeljon, & Shadish, 2012; Godley, Godley, Dennis, Funk, & Passetti, 2002; Liddle, Rowe, Dakof, Henderson, & Greenbaum, 2009; Lindstrom, Filges, & Jorgensen, 2015; Rowe, 2012). Specific programs may differ in the extent to which the family is involved (e.g., the number of child-parent or parent only sessions). Consistent skills are provided, however, often focusing on improving adolescent social functioning in the family and other contexts, enhancing communication within the family and social system, and providing parental monitoring and other adult skills.

There is a paucity of data evaluating family-based interventions for stimulant use in adolescents, but one pilot clinical trial is of particular note. This study evaluated the Culturally Informed and Flexible Family-Based Treatment for Adolescents (CIFFTA) in Hispanic adolescents with substance use disorder (Santisteban, Mena, & McCabe, 2011). This culturally informed program was an adaptive one with flexible treatment components and manual. Adolescents assigned to the CIFFTA condition showed significant reductions in illicit drug use at an 8-month follow-up compared to those assigned to traditional family therapy. Similar, albeit not statistically significant, reductions were observed when evaluating cocaine use specifically. It is possible that this trend level for statistical significance was due to the pilot nature of the study, small sample size (n = 14/group), and/or strong comparator group (i.e., Family-Based Treatment as usual). Taken together, these findings highlight the importance of culturally informed practices in adolescent stimulant treatment.

Pharmacotherapy

Little research has evaluated pharmacological approaches for stimulant use in adolescents, particular when compared to the sizable extant literature in adult populations (Belendiuk & Riggs, 2014). To our knowledge, only one study has targeted adolescent methamphetamine use via a pharmacotherapy (Heinzerling et al., 2013). Adolescents in this parallel group study were randomly assigned to receive 150 mg

bupropion SR ($n = 12$) or placebo ($n = 7$) as a part of an 8-week outpatient substance use program. Bupropion is a weak dopamine reuptake inhibitor with limited abuse potential currently indicated for depression and smoking cessation (Foley, DeSanty, & Kast, 2006; Rush, Kollins, & Pazzaglia, 1998). Adolescents receiving bupropion provided significantly fewer methamphetamine-negative urine samples (i.e., poorer treatment outcomes) and showed a trend towards poorer treatment retention. These findings are consistent with human laboratory and clinical trials of bupropion in adults that have generally reported negative findings or subgroup specific effects (i.e., individuals with lower baseline levels of methamphetamine use) as well as high rates of non-adherence (e.g., Anderson et al., 2015; Elkashef et al., 2008; Shoptaw et al., 2008; Stoops et al., 2015).

An alternative approach for addressing adolescent stimulant use is to first address psychiatric comorbidities. The majority of adolescents with substance use disorder present with at least one comorbid psychiatric condition, such as ADHD and depression. Addressing these comorbidities can improve intervention efforts because reductions in adolescent treatment retention and worse outcomes are often observed in individuals with comorbid mental illness (Warden et al., 2012). ADHD poses a particularly salient concern for adolescents with a stimulant use disorder given the high rates of comorbidity (Bukstein, 2008; Upadhyaya, 2008). Other evidence also indicates that the lifetime risk of substance use disorder is increased to over 50% in children whose ADHD persists into adulthood (Biederman et al., 1995). Symptoms may also be hard to manage because physicians are sometimes reluctant to prescribe psychostimulant medications to these comorbid populations due to potential diversion and misuse.

Other approaches, including extended-release formulations and non-stimulant medications, have been evaluated for comorbid ADHD and substance use disorder (Zaso, Park, & Antshel, 2015). Some reductions in ADHD symptoms have been reported for extended-release methylphenidate (Szobot et al., 2008; but see Riggs et al., 2011) and bupropion (Riggs, Leon, Mikulich, & Pottle, 1998; Solhkhah et al., 2005). In one crossover study, adolescents with comorbid ADHD and substance use disorder ($n = 16$) were assigned to receive ascending doses of spheroidal oral drug absorption system methylphenidate (0.3, 0.7, 1.2 mg/kg/day ascending each week) or placebo over 3-week periods (Szobot et al., 2008). Improvements in ADHD symptoms were observed, but changes in substance use outcomes were not observed, potentially due to the short window of treatment for each study dose. Another study evaluated an alternative formulation of extended release methylphenidate (osmotic-release) on ADHD and substance use outcomes (Riggs et al., 2011). Adolescents were assigned to receive 72 mg of osmotic-release methylphenidate/day ($n = 151$) and CBT or matched placebo and CBT ($n = 152$). Methylphenidate was well tolerated, but did not produce greater reductions in ADHD or substance use outcomes than CBT alone. The reasons for the discrepancies between these studies are unclear, but could be due to the differences in dosing regimens or treatment delivery (e.g., psychosocial intervention inclusion). The limited number of studies in this extant literature and the modest reductions observed in some studies highlights the importance of future research for this and other comorbid adolescent populations.

Summary of Evidence-Based Interventions

Consistent with prevention efforts, the ultimate impact of evidence-based treatments for stimulant use disorders will rely on the integration of multiple approaches tailored to the individual needs of the patient. Unfortunately, few studies have examined the specific effects on adolescent stimulant use for evidence-based treatments commonly used in outpatient and inpatient settings. Further research evaluating the psychosocial and pharmacological interventions noted above as well as novel formats is needed before definitive clinical recommendations may be made.

Conclusions

Cocaine, amphetamine, and methamphetamine remain a significant public health concern associated with a range of physical, psychological, and social health complications. Stimulant misuse continues to pose a particular problem for adolescents given the remaining high rates of use and potential impact on developmental trajectories during a period of dramatic physiological and psychological growth. Moreover, stimulant use has received relatively little attention in the primary prevention and treatment literature when compared to adolescent alcohol, tobacco, and cannabis use. The available literature suggests that many of those prevention and treatment efforts developed for other substance use may help deter the initiation and reduce the misuse of stimulants in adolescents. Clinically useful prevention and treatment will likely incorporate multiple approaches tailored to the individual and addressing factors at the level of the individual, peer, family, and community. More work is needed, however, to understand the ultimate utility of evidence-based and novel methods for preventing and treating adolescent stimulant use disorder.

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