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Physical and psychological harms of psychostimulant use

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EXECUTIVE SUMMARY

Introduction

The current review aims to examine the epidemiology of psychostimulant use and the nature of the harms associated with the use of these drugs. The review focuses on methamphetamine and cocaine, the two drugs in this class of the greatest clinical concern. Specifically, the current review examined:

i. The epidemiology of psychostimulant use;

ii. The major physical health effects of psychostimulant use;

iii. The major psychological effects of psychostimulant use; and

iv. The risk factors associated with such harm.

Epidemiology of Psychostimulant Use

There are estimated to be 26 million methamphetamine users and 14 million cocaine users worldwide. In Australia, lifetime methamphetamine use is estimated at 9.1% and past year use at 3.2%. Lifetime cocaine use is estimated at 4.7% and past year use at 1%. Males are more likely to report both lifetime and recent psychostimulant use.

Polydrug use, psychostimulant use and harm

Polydrug use is common amongst psychostimulant users, and has direct relations to increased levels of risk. The concomitant use of cocaine and alcohol produces cocaethylene, an active metabolite of cocaine which increases the toxicity of cocaine. Whilst the combination of methamphetamine and alcohol does not produce a third substance, it does increase heart rate and blood pressure beyond that seen for methamphetamine use alone. The concomitant use of psychostimulants and opioids increases myocardial oxygen demand with a simultaneous respiratory depression due to opioids. Combined methamphetamine and cocaine use has been demonstrated to substantially increase the vasoconstrictive and cardiotoxic effects of each drug.

Harms Associated With Psychostimulant Use

Physical harms

Toxicity and Mortality

Psychostimulant-related deaths are typically caused by seizures, cardiac arrhythmias, or respiratory failure, with cardiovascular complications accounting for the majority of deaths. Toxic reactions can occur irrespective of dose, frequency of use, or route of administration. Deaths have been reported

with small amounts of cocaine, and on the first occasion of use. In Australia, there were 68 fatal methamphetamine toxicity cases during 2005 and 15 cocaine toxicity deaths. Such deaths typically occur among experienced, male drug users aged in their mid-30s.

Cardiovascular and cerebrovascular pathology

Cocaine and amphetamine are cardiotoxic, place heavy demands upon the cardiovascular system, and can cause myocardial ischaemia and infarction. Consistent with this clinical profile, chest pains, palpitations, tachycardia and hypertension are the most common complaints among psychostimulants users presenting to accident and emergency departments. In addition to acute risks, psychostimulants are associated with the premature and accelerated development of coronary artery atherosclerosis, which increases the risk of myocardial infarction. There is also an increased the risk of cerebrovascular accidents.

Dependence

Dependence on psychostimulants is a substantial risk associated with their use. Recent Australian research reported half of methamphetamine and cocaine users to be dependent. An increased risk of psychostimulant dependence is associated with route of administration (injecting or smoking), more frequent psychostimulant use and the use of more potent forms of these drugs (e.g., crystalline methamphetamine and crack cocaine).

Blood borne virus transmission

Among injecting drug users, cocaine use is strongly associated with more frequent needle sharing, increased sexual risk-taking and a higher HIV seroprevalence**.** In contrast, rates of needle sharing amongst methamphetamine users appear comparable to those seen amongst opioid injectors. The ability of psychostimulant drugs to increase libido enhances the risk of sexual disease transmission among this group.

Psychopathology

Psychosis

Unlike opioids, psychostimulant drugs can induce psychosis. Research has demonstrated that psychostimulant users have higher levels of psychosis than users of opioids and sedative drugs. In recent Australian research, 13% of methamphetamine users screened positive for psychosis, and

23% had experienced psychotic symptoms. Similarly, amongst Australian cocaine users 38% had paranoid symptoms, and 12% had recently experienced hallucinations. Psychotic symptoms are associated with longer term use, heavier use, dependence, injecting and a pre-existing history of psychotic symptoms.

Depression, suicide and anxiety

Depression and suicide attempts are common amongst psychostimulant users. A third of methamphetamine users have received a diagnosis of depression at some point in their lives, and 11% have been diagnosed with an anxiety disorder. A quarter of psychostimulants users have a history of attempted suicide compared to 3.6% of the general population. Higher levels of depression, suicide and anxiety are associated with longer psychostimulant use careers, more frequent use, dependence and injecting.

Violent behaviours

Violent behaviours appear to be common among psychostimulant users, particularly among people who inject these drugs. Recent Australian data indicated that 12% of methamphetamine users and 21% of cocaine users had committed a violent crime in the preceding year. The relationship between psychostimulant use and violent behaviour is complex, but these drugs do appear to increase the risk of violence in certain situations.

Summary

Psychostimulant use is associated with a number of serious negative health effects. High profile consequences, such as psychosis, are given prominence in the public debate, but the sequelae extend far beyond this. These are a class of drugs that cause serious heart disease, have serious dependence liability and high rates of suicidal behaviours. The current public image of these drugs does not adequately portray the extensive, and in many cases insidious, harm that they cause.

1.0 INTRODUCTION

In recent years, in Australia and internationally, there has been mounting concern about the increasing prevalence of psychostimulant use. Methamphetamine (including its chemical analogue amphetamine) and cocaine, in particular, are the two psychostimulants that have engendered the most clinical interest. The extent of the problem suggests the need for a comprehensive review of the major harms that are associated with the use of psychostimulants. The current review aims to examine the epidemiology of psychostimulant use and the nature of the harms associated with the use of these drugs. In particular, the current review aims to examine:

i. The epidemiology of psychostimulant use;
ii. The major physical health effects of psychostimulant use;
iii. The major psychological effects of psychostimulant use; and
iv. The risk factors associated with such harm.

The area of psychostimulant use is plagued by terminological ambiguities. This review will refer to methamphetamine to include both methamphetamine and its less potent analogue, amphetamine, which are sold under the street names of 'speed', 'base', 'ice', 'crystal meth' and 'amphetamines'. Indeed, drug seizure data indicate that methamphetamine is currently far more common than amphetamine both in Australia and internationally. Where appropriate, a distinction between methamphetamine and amphetamine will be made. Similarly, the term cocaine will be used to cover cocaine hydrochloride powder and its more powerful derivative "crack", with distinctions drawn where necessary.

2.0 EPIDEMIOLOGY OF PSYCHOSTIMULANT USE

2.1 International psychostimulant use

It is estimated that there are 26 million methamphetamine users globally (United Nations Office of Drug Control, 2005). In the United States, the lifetime prevalence of methamphetamine use is estimated at 8.3% (Substance Abuse and Mental Health Services Administration, 2005), whilst in European countries, lifetime prevalence typically ranges between 0.1% and 6%. Rates are higher in the United Kingdom, however, ranging up to 12% (European Monitoring Centre for Drugs and Drug Addiction, 2005).

Increases in methamphetamine use have been noted in recent years in many countries (United

Nations Office of Drug Control, 2005). Production and consumption of methamphetamine appears to have increased considerably, notably around the Pacific Rim (North America, South-East Asia and Oceania) (United Nations Office of Drug Control, 2005). Increased use of crystal methamphetamine was first noted in the Philippines, Korea, Taiwan and Japan (Laidler & Morgan, 1997; Matsumoto et al, 2000; Shaw, 1999), and later in the United States (Laidler & Morgan, 1997; Morgan & Beck, 1997; National Drug Intelligence Centre, 2003). In recent years, crystal methamphetamine use and availability have been increasing in Oceania (McKetin et al, 2005a; McKetin et al, 2005c; Topp et al, 2002; Wilkins, 2002).

It is estimated that there are 14 million cocaine users globally, two thirds are in the Americas (where cocaine production almost exclusively occurs) (United Nations Office of Drugs Control, 2005). The lifetime prevalence of cocaine use globally is estimated to be 0.3% (United Nations Office of Drugs Control, 2005), but is significantly higher in the United States, where 14 % of those aged 12 years or older report lifetime use and 2.4 % in the previous 12 months (Substance Abuse and Mental Health Services Administration, 2005).

Recent years may have seen an increase in the availability and use of cocaine in Europe, and increases in the use of "crack" cocaine in particular (Home Office, 2004). Recent population surveys estimate that between 0.5 % and 6 % of the European population have tried cocaine, with rates in the United Kingdom (6.8 %), Spain (4.9 %) and Italy (4.6 %) being the highest in Europe (European Monitoring Centre for Drugs and Drug Addiction, 2005).

2.2 Psychostimulant use in Australia

In Australia, lifetime methamphetamine is estimated at 9.1% of the population (Figure 1), and use in the past year at 3.2% (Figure 2) (Australian Institute of Health & Welfare, 2005a). The prevalence of methamphetamine use varies substantially across various demographic subgroups of the population, with the highest levels of both lifetime and recent use seen amongst those aged 20-29 years. Amongst this group, a fifth have used methamphetamine and a tenth have done so in the preceding 12 months. As with all illicit drugs, males are more likely than females to report both lifetime (11.0 v 7.3%) and recent use (4.0 v 2.5%) (Australian Institute of Health & Welfare, 2005a, 2005).

Whilst amphetamine use in Australia has a long history (Hall & Hando, 1994), the shift from amphetamine to methamphetamine supply in the mid-1990s, and subsequent increases in the purity of the drug, have had serious clinical ramifications (McKetin et al, 2005a). Of particular note was the emergence of imported high purity crystalline methamphetamine ('ice') in Australia in the late 1990s (Topp et al, 2002), which has been associated with an increase in smoking methamphetamine (McKetin et al, 2005a). Around the same time, domestically produced methamphetamine became marketed as a high purity damp or oily product called 'base' or 'paste' (McKetin et al, 2005a).

The prevalence of lifetime cocaine use is approximately half that of methamphetamine use (4.7%) (Figure 1), while 1% have used the drug in the preceding 12 months (Figure 2) (Australian Institute of Health and Welfare, 2005). As is the case with methamphetamine, these figures mask large demographic differences. Amongst those aged between 20 and 39 years, almost a tenth have used cocaine, whilst 3% of the 20-29 year group have used the drug in the past 12 month. Again, males are more likely than females to report both lifetime (5.8 v 3.7%) and recent use (1.3 v 0.8%).

The form of cocaine used in Australia is overwhelmingly cocaine hydrochloride powder, with the use of crack cocaine being rare (Darke et al, 2002; Stafford et al, 2006). There are major geographical differences in the use of cocaine in Australia, with use being far more prevalent in NSW (Stafford et al, 2006). Sharp increases in the use of cocaine in NSW were recorded in 1998 and 2001, with a strong association to injecting drug use, and existing heroin injectors in particular (Darke et al, 2002).

Figure 1
Lifetime prevalence of methamphetamine and cocaine use in Australia, 2004

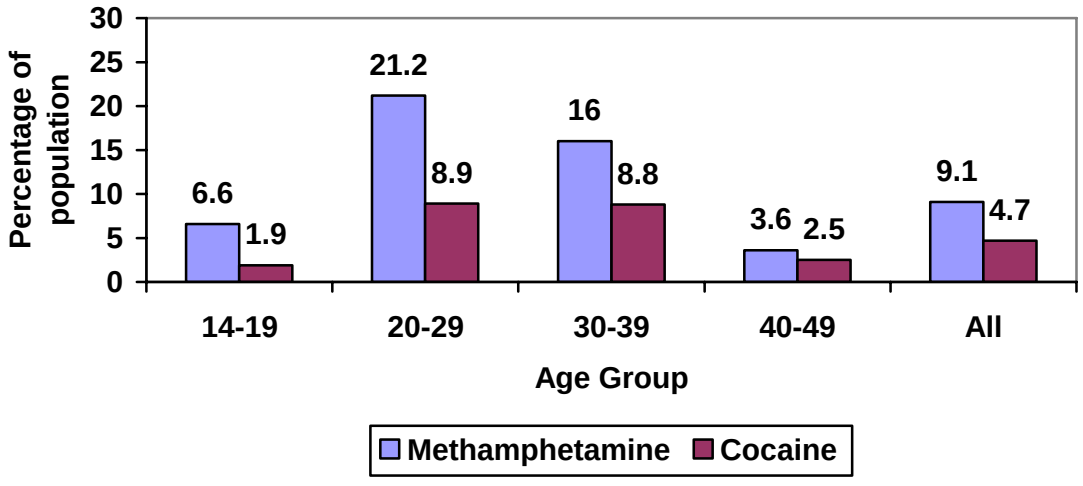
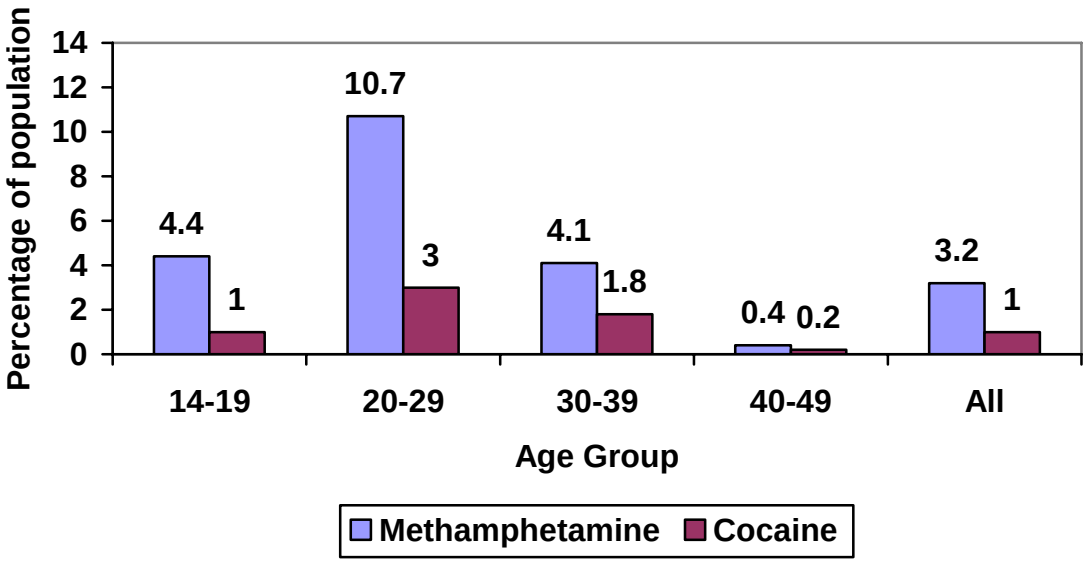


Figure 2
Past year prevalence of methamphetamine and cocaine use in Australia, 2004



2.3 Polydrug use, psychostimulant use and harm

As is the case with all illicit drugs, psychostimulant users consume a variety of drugs other than their primary drug of choice. The two drugs most commonly associated with cocaine use are alcohol and heroin (Darke et al, 2002; Gossop et al, 2006; Hall & Darke, 1995; Kaye & Darke, 2004a,b; Shearer et al, 2005; Williamson et al, 2006a, 2006b). The type of concomitant drug use associated with cocaine use, however, varies according to route of administration. Injecting cocaine users, who are often existing heroin users, typically use heroin, cannabis, benzodiazepines and alcohol, while non-injecting cocaine users typically use ecstasy, methamphetamine, cannabis and alcohol with cocaine (Kaye & Darke, 2004a,b; Shearer et al, 2005).

Extensive polydrug use is associated with poorer clinical profiles and increased levels of harm (Darke & Hall, 1995; Williamson et al, 2006a, 2006b). There are, however, specific harms that arise from the concomitant use of cocaine with other drugs. As with opioid overdose, there is a strong association between alcohol and cocaine overdose (Darke et al, 2007). The reasons for this association, however, differ from the association between opioids and alcohol (which is due to the combined CNS depression effects on respiration). By contrast, concomitant ingestion of cocaine and alcohol produces cocaethylene, an active metabolite of cocaine which is not only more toxic

than cocaine itself, but which has a synergistic effect in increasing the toxicity of cocaine (Brookoff et al, 1996; Harris et al 2003; Karch, 2002). Increased risk here is thus due to the production of a *third* psychoactive substance, rather than their interaction *per se*.

Cocaine users, and injectors in particular, often combine heroin with cocaine, with the resultant mixture referred to as a 'CC (cocaine cocktail)' or 'speedball'. The rapid sequential injection of heroin and cocaine is also common (Darke et al, 2002). The combination of cocaine and heroin is more dangerous than when either drug is used alone, as cocaine potentiates the tendency of opioids to depress respiration (Darke et al 2007; Platt, 1997). It may also be speculated that respiratory depression may induce cardiac failure, particularly among people where cardiac disease is present, due to increased myocardial oxygen from the effects of cocaine in the presence of respiratory depression from the effects of heroin (Darke et al, 2005, 2006, 2007). Consistent with this, in the United States non-fatal overdoses are more often associated with the concomitant use of these two drugs than with either drug alone (Ochoa et al, 2001).

The influence of concomitant drug use is particularly pronounced amongst cocaine overdose fatalities. Multiple drugs are typically detected among cocaine-related fatalities, most commonly heroin in over half of cases and alcohol in over a fifth (Coffin et al, 2003; Darke et al, 2005; Tardiff et al, 1996; Wetli & Wright, 1979). The role of polydrug use is illustrated by Coffin et al (2003). Changes in both cocaine and heroin overdoses rates were related to changes in the rate of polydrug deaths, whilst the rate of single drug deaths remained stable. Similarly, non-fatal cocaine overdose has been strongly related to concomitant drug use (Kaye & Darke, 2004a).

Amongst methamphetamine users, heavy cannabis use is particularly common (McKetin et al*,* 2005a; McKetin et al*,* 2005b). The majority also drink alcohol, although only a small proportion drink heavily. Importantly, a substantial proportion have a history of heroin use, and the use of other psychostimulants is also common (McKetin et al*,* 2005a). The importance of concomitant use of other substances with methamphetamine is that when combined with alcohol, cocaine or opiates, methamphetamine toxicity is increased (Albertson et al, 1999; Mendelson et al, 1995). Unlike cocaine, the combination of alcohol and methamphetamine does not produce a new psychoactive substance. The combination does, however, increase heart rate and blood pressure beyond that seen for methamphetamine alone (Darke et al, 2007; Mendelson et al, 1995). As is the case for cocaine,

the combination of heroin and methamphetamine may produce a situation where there is increased myocardial oxygen demand due to methamphetamine with a contiguous depression of respiration due to heroin. Multiple psychostimulant use is also cause for concern. The combination of methamphetamine and cocaine has been demonstrated to substantially increase the vasoconstrictive and cardiotoxic effects of both drugs (Welder, 1992). Given the cardiotoxic effects of methamphetamine (cf. Section 3.1.2), it is reasonable to speculate that the concomitant use of alcohol or cocaine with methamphetamine may increase the risk of a toxic reaction.

Compared to the data for cocaine, little data are available examining the role of polydrug use in fatal methamphetamine toxicity. Consistent with what is known and speculated about drug interactions, where toxicology has been reported multiple substances are detected in approximately half of cases, most commonly alcohol (10-25%), cocaine (12-25%) and morphine (20-30%) (Karch et al, 1999; Logan et al, 1998).

2.4 Summary of epidemiology of psychostimulant use

There are estimated to be 26 million methamphetamine users and 14 million cocaine users worldwide. In Australia, lifetime methamphetamine use is estimated at 9.1% and past year use at 3.2%. Lifetime cocaine use is estimated at 4.7% and past year use at 1%. Males are more likely to report both lifetime and recent psychostimulant use.

Polydrug use is common amongst psychostimulant users, and has direct relations to increased levels of risk, although by different mechanisms. The concomitant use of cocaine and alcohol produces cocaethylene, an active metabolite of cocaine which increases the toxicity of cocaine. Whilst the combination of methamphetamine and alcohol does not produce a third substance, it does increase heart rate and blood pressure beyond that seen for methamphetamine use alone. The concomitant use of psychostimulants and opioids increases myocardial oxygen demand due to psychostimulants with a simultaneous respiratory depression due to opioids. Combined methamphetamine and cocaine use has been demonstrated to substantially increase the vasoconstrictive and cardiotoxic effects of these drugs.

Table 1

Summary of epidemiology of psychostimulant use

Key Points

- There are estimated to be 26 million methamphetamine users and 14 million cocaine users worldwide.
- Lifetime methamphetamine use is estimated at 9.1% of the Australian population and past year use at 3.2%.
- Lifetime cocaine use is estimated at 4.7% of the Australian population and past year use at 1%.
- Males are more likely to report both lifetime and recent psychostimulant use.
- Polydrug use is common amongst psychostimulant users, and has direct relations to increased levels of risk.
- Concomitant use of cocaine and alcohol produces cocaethylene, an active metabolite of cocaine which increases the toxicity of cocaine.
- The combination of methamphetamine and alcohol increases heart rate and blood pressure beyond that seen for methamphetamine use alone.
- The concomitant use of psychostimulants and opioids increases myocardial oxygen demand due to psychostimulants with a simultaneous respiratory depression due to opioids.
- Combined methamphetamine and cocaine use has been demonstrated to substantially increase the vasoconstrictive and cardiotoxic effects of these drugs.

3.0 HARMS ASSOCIATED WITH PSYCHOSTIMULANT USE

3.1 Physical harms

3.1.1 Toxicity and Mortality

Whereas heroin overdose is indicated by a specific diagnostic triad of signs (reduced level of consciousness, miosis, respiratory depression) (Hardman et al, 1996), psychostimulant overdose is less clearly defined. Psychostimulant toxicity may manifest as a variety of acute physical and psychological symptoms. The presentation of a psychostimulant overdose can vary among individuals and does not necessarily entail loss of consciousness. Indeed, overdose signs such as excited delirium, which may result in cardiac arrest and death, by definition preclude loss of consciousness. Physical symptoms of psychostimulant overdose include nausea and vomiting, chest pain, tremors, increased body temperature, increased heart rate, breathing irregularities, and seizures. Psychological symptoms such as extreme anxiety, panic, extreme agitation, extreme paranoia, hallucinations, and excited delirium are also indicative of psychostimulant overdose (Brands et al, 1998; Karch, 2002).

Psychostimulant-related deaths are typically caused by seizures, cardiac arrhythmias, or respiratory failure, with cardiovascular complications accounting for the majority of deaths (Karch, 2002; Kaye et al, in press). Fatal overdose has also occurred due to brain haemorrhage, ischaemic stroke and kidney failure (Karch, 2002; Petitti et al, 1998, Richards et al, 1999). Hyperthermia may also contribute to mortality, with research demonstrating an increase in cocaine overdose fatalities during hot weather (Marzuk et al, 1998).

While dose and frequency of use may influence the likelihood of coronary and cerebrovascular complications, the threshold over which potentially fatal reactions occur varies widely. Toxic reactions can occur irrespective of dose, frequency of use, or route of administration, and have been reported with small amounts of cocaine and on the first occasion of use (Karch, 2002, Kaye et al, in press; Lange & Hillis, 2001; Platt, 1997). Overall there appears to be no well delineated dose response (Karch, 2002; Karch et al, 1998, 1999; Lange & Hillis, 2001; Zhu et al, 2000).

Over the preceding two decades cocaine has emerged to become a major cause of mortality (Coffin et al, 2003; Department of Health and Human Services, 2005; European Monitoring Centre for Drugs and Drug Addiction, 2005; Sanchez et al, 1995; Tardiff et al, 1996;). This is particularly true of

the United States, where cocaine is implicated in the majority of drug overdose deaths (Coffin et al, 2003). Cocaine-related deaths have also increased substantially in Europe (European Monitoring Centre for Drugs and Drug Addiction, 2005). Significant numbers of hospital admissions and deaths attributable to methamphetamine toxicity also occur, and appear to be increasing, reflecting the renewed popularity of methamphetamine worldwide (Department of Health and Humans Services, 2005; European Monitoring Centre for Drugs and Drug Addiction, 2005; Karch, 2002; Karch et al, 1999; National Institute on Drug Abuse, 2003).

In Australia, psychostimulant-related fatalities are less common than opioid toxicity deaths. This is consistent with worldwide data, which repeatedly demonstrates that the highest rates of mortality are associated with the opioids (Darke et al, 2007). According to ABS figures, there were 68 fatal methamphetamine toxicity cases in Australia during 2005 and 15 cocaine toxicity deaths (i.e. cases where methamphetamine or cocaine was mentioned as either the primary cause of death or noted in "toxic quantities" where another drug was listed the primary cause of death) (Degenhardt et al, 2007a). By comparison, in 2005 there were 374 deaths attributed to opioid toxicity in Australia (Degenhardt et al, 2007b).

In discussing toxicity, it is essential to bear in mind that fatalities form only a proportion of overdose cases, and that the harms associated with overdose extend far beyond death *per se*. In the case of heroin, it is estimated that the proportion of overdoses that results in death is 2-4% (Darke et al, 2003). To date, there are no comparable data on methamphetamine toxicity, but one Australian study has been conducted on non-fatal cocaine overdose (Kaye et al, 2004). This found that 13% of regular cocaine users had overdosed on cocaine, 7% having done so in the preceding 12 months.

Deaths due to psychostimulant toxicity typically occur among male, experienced drug users aged, on average, in their mid-30s (Darke et al, 2007; Darke et al, 2005; Huang et al, 2003; Kaye et al, in press; Karch et al, 1999; Tardiff et al, 1996; Waksman et al, 2001; Zhu et al, 2000). The older age profile of fatalities may simply reflect the cumulative risk exposure of repeated use. The effects of repeated psychostimulant administration are, however, quite distinct from those seen in the use of opioids. Repeated administration of cocaine or methamphetamine results in cumulative risk of cardiac and coronary artery disease, most commonly ventricular hypertrophy and coronary artery atherosclerosis (Darke et al, 2007; Karch, 2002) (See below). The accumulated damage from long-term

psychostimulant use may substantially increase risk of myocardial infarction as the user ages, and substantially increase the risk for each individual use episode over time.

3.1.2 Cardiovascular and cerebrovascular pathology

Both cocaine and methamphetamine are distinguishable from opioids in that both are known to be cardiotoxic, and place heavy demands upon the cardiovascular system, increasing heart rate and blood pressure (Karch 2002). As such, two of the most serious sequelae of psychostimulant use are cardiovascular and cerebrovascular complications, both of which occur regardless of route of administration (Karch, 2002). While much has been written about the cardiotoxicity of cocaine (Darke et al, 2005, Kontos, 2003; Lange & Hillis, 2001), the pathological effects of methamphetamine are similar to, or indistinguishable from, those attributable to cocaine (Julien, 2001; Sztajnkryier, 2002).

Psychostimulants can cause myocardial ischaemia and infarction via several mechanisms: an increase in myocardial oxygen demand, vasoconstriction of the coronary arteries and coronary thrombosis (Hollander et al, 1997; Karch, 2002; Kontos et al, 2003; Lange & Hillis, 2001; Moliterno et al, 1994; Rump et al, 1995; Swalwell & Davis, 1999; Wijetunga et al, 2003; Zhu et al, 2000). Importantly, coronary vasospasm may occur where there is no underlying coronary artery disease (Karch, 2002; Kaye et al, in press; Lange & Hillis, 2001).

Although psychostimulants can induce cardiovascular complications in users with normal coronary arteries (Mittleman et al, 1999; Lange & Hillis, 2001; Vasica & Tennant, 2002), underlying atherosclerosis (particularly of the left coronary arteries) has been consistently demonstrated (Darke et al, 2005, 2006; Hollander et al, 1997; Kontos et al, 2003; Mittleman et al, 1999; Karch, 2002; Pavon-Jimanez, 1999; Rump et al, 1995; Vasica & Tennant, 2002). The premature and accelerated development of coronary artery atherosclerosis, which increases the risk of myocardial infarction, has been associated with the chronic use of psychostimulants (Benzaquen et al, 2001; Darke et al, 2005, 2006; Hollander et al, 1997; Karch 2002; Karch et al, 1999, Kaye & McKetin, 2005; Kontos et al, 2003; Lange & Hillis, 2001; Logan et al, 1998; Mittleman et al, 1999; Wijetunga et al, 2004). Chronic use is also associated with ventricular hypertrophy, a condition that can predispose to cocaine-induced myocardial ischaemia and/or arrhythmia (Benzaquen et al, 2001; Karch, 2002; Om et al, 1993).

Two recent Australian studies of cocaine-related fatalities have specifically examined cardiac pathology amongst cases of cocaine-related deaths (Darke et al, 2005, 2006). Consistent with the international literature, rates of pathology were extremely high. Cardiac pathology was noted in 57% of cases, most commonly coronary artery atherosclerosis and cardiac hypertrophy (Darke et al, 2005). Importantly, rates amongst these cases were significantly higher than those seen amongst opioid toxicity overdoses (Darke et al, 2006). Cocaine cases had significantly higher proportions of left ventricular hypertrophy and ischaemic heart disease than opioid cases. Coronary artery atherosclerosis also was detected in a significantly higher proportion of cocaine cases. Cocaine cases were more likely to have atherosclerosis of the left anterior descending coronary artery, right coronary artery and circumflex artery. The high levels of cardiac pathology seen amongst cocaine cases were thus not artefacts of a drug dependent lifestyle, but related specifically to cocaine. Work on the prevalence of cardiac morbidity among methamphetamine-related deaths is currently in progress at the National Drug and Alcohol Research Centre.

Consistent with the cardiotoxic profile of psychostimulants, chest pains, palpitations, tachycardia and hypertension are among the most common complaints among psychostimulants users presenting to accident and emergency departments (Kontos et al, 2003; Lange & Hillis, 2001; Lan et al, 1998; Richards et al, 1999; Turnipseed et al, 2003). In Australia, palpitations are among the most common physical side effect reported by cocaine users (Kaye & Darke, 2004a,b).

Psychostimulant-induced cerebrovascular accidents are also well recognised (Darke et al, 2005, 2006; Pettiti et al, 1998; Westover et al, 2007). In a recent US study there was a 14 fold increase in the risk of ischaemic or haemorrhagic stroke among cocaine users compared to matched controls, and a 4-fold increased risk for methamphetamine (Pettiti et al, 1998). In the recently published Australian work on cocaine-related deaths, cerebrovascular pathology was noted in 22% of cases, most commonly cerebrovascular atherosclerosis (10%) (Darke et al, 2005). As with cardiac pathology, cocaine cases also had significantly higher levels of cerebrovascular atherosclerosis than opioid toxicity cases, indicating that the effects were related to cocaine use (Darke et al, 2006). Work on comparative rates of cerebrovascular pathology amongst Australian methamphetamine-related deaths is currently in progress at the National Drug and Alcohol Research Centre.

While both cocaine and methamphetamine are both cardiotoxic, the incidence of serious pathological effects of methamphetamine appears less common than those associated with cocaine (Derlet & Horowitz, 1995; Karch, 2002, Petitti et al, 1998; Wijetunga et al, 2004). This may explain why cocaine constitutes a larger proportion of overdose fatalities than does methamphetamine (e.g. Coffin et al, 2003), despite the widespread use of methamphetamine. This observation must, however, be tempered by the fact that substantially less research has been conducted into methamphetamine-related death than is the case with cocaine.

3.1.3 Dependence

Dependence on psychostimulants, like all psychoactive drugs, is defined by tolerance, withdrawal, pre-occupation with the drug, not being able to reduce use, and using the drug despite significant social, health or psychological impairment (American Psychiatric Association, 2000). Tolerance and withdrawal are clearly marked in the case of substances such as alcohol and the opioids, with clearly defined withdrawal syndromes.

Despite being a less marked syndrome, tolerance and withdrawal symptoms are a key feature of both the cocaine and methamphetamine dependence syndrome (American Psychiatric Association, 2000; Topp & Mattick, 1997). Withdrawal symptoms consist of fatigue, lethargy, sleep disturbances, appetite disturbances, depressed mood, irritability, psychomotor retardation or agitation, and strong cravings for the drug (American Psychiatric Association, 2000; McGregor et al, 2005; Topp & Mattick, 1997). Tolerance may be demonstrated by a transition from non-injecting routes of administration to injecting methamphetamine or cocaine use, using higher doses of the drug per use episode, more frequent use and a preference for more potent forms of these drugs. Thus, in the case of methamphetamine, for high purity crystalline methamphetamine rather than powder. In the case of cocaine this may be reflected in a preference for crack rather than powder, due to its higher potency. This, however, does not currently apply to the Australian setting, where crack use remains rare (Darke et al, 2002; Darke et al, 2005; Stafford et al, 2006).

Given its short half-life and powerful reinforcing effects, cocaine is regarded as having a high dependence liability, which can develop after a relatively short history of use (American Psychiatric Association, 2000; Dackis & O'Brien, 2001; Jacobs & Fehr, 1987). Problematic use may be chronic, such that cocaine is used on a daily, or almost daily, basis, or it may be episodic, where the pattern

may be to binge on cocaine over a period of hours or days and then abstain for several days. Smoking and injecting cocaine are associated with a greater dependence liability than intranasal use, with use often progressing to dependence in a matter of weeks or months (Chen & Kandel, 2002; Darke & Kaye, 2004; Gossop et al, 1994; Hatsukami & Fischman, 1996). The onset of dependence as a consequence of intranasal use is much more gradual, typically taking months or even years (American Psychiatric Association, 2000). The dependence liability of cocaine is clearly demonstrated by recent Australian research in which a half of current cocaine users were dependent (Kaye & Darke, 2004b; Darke & Kaye 2004). Consistent with international research, there was a strong association between route of administration and dependence. Two thirds of cocaine injectors were dependent on the drug, compared to 9% of intranasal users (Kaye & Darke, 2004b). As would be expected from these figures, cocaine use was far more frequent amongst injectors.

The patterns and course of methamphetamine dependence are similar to that seen with cocaine (American Psychiatric Association, 2000). This is not surprising as both drugs are psychostimulants with similar psychoactive and sympathomimetic effects. As is the case with cocaine dependence, methamphetamine dependence may be chronic or involve bingeing with brief drug-free periods. Methamphetamine dependence is strongly associated with injecting and smoking of the drug (McKetin et al*,* 2006a). The extent of methamphetamine dependence is illustrated by a recent study of Australian methamphetamine users, in which approximately half were methamphetamine dependent (McKetin et al, 2006a). As seen in relation to Australian cocaine users, dependence was strongly related to route of administration. Thus, two thirds of methamphetamine injectors were dependent, as were 58% of smokers of the drug. Substantially lower levels of dependence were seen amongst intranasal (33%) and oral (22%) users. The patterns are remarkably similar to that reported for cocaine. As with cocaine dependence, those who were methamphetamine dependent used the drug more frequently. Importantly, the use of "ice" was independently associated with dependence. It is not only frequency of use, but the potency of the drug that appears to increase the liability to dependence amongst Australian methamphetamine users.

Thus, for psychostimulants as a class, dependence is a substantial risk, a risk that is exacerbated by route of administration (in particular injecting and smoking), more frequent use and the use of more potent forms of the drugs.

3.1.4 Blood borne virus transmission

Amongst injecting drug users, the injection of cocaine (both independently and in combination with heroin, `*speedballs*'), has been strongly associated with more frequent injections, more frequent needle sharing, increased sexual risk-taking, more frequent use of shooting galleries, and a higher seroprevalence of HIV (Bux et al, 1995; Chaisson et al, 1989; Darke et al, 1992; Doherty et al, 2000; Schoembaum et al, 1989; Torrens et al, 1991; Tyndall et al, 2001). It is important to note that the link between cocaine use and risk is not restricted to parenteral use. Crack smoking has been independently linked to higher levels of needle risk in crack users who also inject, to sexual risk-taking and to increased risk of being HIV positive (Chiasson et al, 1991; Chirgwin et al, 1991; DesJarlais et al, 1992; Doherty et al, 2000; Grella et al, 1995).

Why is cocaine so strongly associated with increased levels of risk? Two mechanisms may underlie this relationship. Firstly, the relatively short half-life of cocaine results in a greater frequency of injecting than that typically seen for heroin, and more frequent injecting is strongly associated with needle sharing. Indeed, cocaine injection binges are common (Kaye & Darke, 2004b). Secondly, disinhibition resulting from cocaine use may lead to higher levels of risky sexual activity and needle use, whether the cocaine is smoked or injected.

By contrast, needle sharing behaviour among methamphetamine injectors appears to be similar to that seen among opioid injectors (Kaye & Darke, 2000; McKetin et al*,* 2005a), and does not appear to be associated with an increased risk of HIV infection (Doherty et al, 2000). As with cocaine users, however, methamphetamine users appear at greater risk than opioid users of sexual disease transmission (Molitor et al*,* 1999; Zule & Desmond, 1999). Methamphetamine users are a younger and more sexually active population than opioid injectors, and it has been argued that the drug's ability to increase libido further enhances the risk of sexual disease transmission among this group (Rawson et al*,* 2002).

3.1.5 Summary of physical harms associated with psychostimulant use

Psychostimulant-related deaths are typically caused by seizures, cardiac arrhythmias, or respiratory failure, with cardiovascular complications accounting for the majority of deaths. Toxic reactions can occur irrespective of dose, frequency of use, or route of administration. Deaths have been reported with small amounts of cocaine, and on the first occasion of use. In Australia, there were 68 fatal

methamphetamine toxicity cases during 2005 and 15 cocaine toxicity deaths. Such deaths typically occur among experienced, male drug users aged in their mid-30s.

Cocaine and methamphetamine are cardiotoxic, place heavy demands upon the cardiovascular system, and can cause myocardial ischaemia and infarction. Consistent with this clinical profile, chest pains, palpitations, tachycardia and hypertension are the most common complaints among psychostimulants users presenting to accident and emergency departments. In addition to acute risks, psychostimulants are associated with the premature and accelerated development of coronary artery atherosclerosis, which increases the risk of myocardial infarction. There is also an increased risk of cerebrovascular accidents.

Apart from cardiovascular pathology, psychostimulant dependence is a substantial risk. Recent Australian research reported half of methamphetamine and cocaine users to be dependent. An increased risk of psychostimulant dependence is associated with route of administration (injecting or smoking), more frequent psychostimulant use and the use of more potent forms of these drugs.
Cocaine use is strongly associated with more frequent needle sharing, increased sexual risk-taking and a higher HIV seroprevalence**.** The ability of psychostimulants to increase libido also enhances the risk of sexual disease transmission among cocaine and methamphetamine users.

Table 2

Summary of physical harms and psychostimulant use

Key Points

- Psychostimulant-related deaths are typically caused by seizures, cardiac arrhythmias, or respiratory failure, with cardiovascular complications accounting for the majority of deaths.
- Toxic reactions can occur irrespective of dose, frequency of use, or route of administration, and have been reported on the first occasion of use.
- According to ABS figures, there were 68 fatal methamphetamine toxicity cases in Australia during 2005 and 15 cocaine toxicity deaths.
- Deaths due to psychostimulant toxicity typically occur among male, experienced drug users aged, on average, in their mid-30s.
- Cocaine and methamphetamine are cardiotoxic, and place heavy demands upon the cardiovascular system. These drugs can cause myocardial ischaemia and infarction.
- Chest pains, palpitations, tachycardia and hypertension are the most common complaints among psychostimulants users presenting to accident and emergency departments.
- Psychostimulants are associated with premature and accelerated development of coronary artery atherosclerosis, which increases the risk of myocardial infarction.
- Psychostimulant use increases the risk of cerebrovascular accidents.
- Psychostimulant dependence is a substantial risk. Recent Australian research reported half of methamphetamine and cocaine users to be dependent.
- Risk of dependence is exacerbated by route of administration (injecting or smoking), more frequent use and the use of more potent forms
- Cocaine use is strongly associated with more frequent needle sharing, increased sexual risk-taking and a higher HIV seroprevalence.
- The ability of psychostimulants to increase libido enhances the risk of sexual disease transmission among users of these drugs.

3.2 *Psychopathology*

Psychostimulant use is associated with a substantial burden of psychopathology, that includes elevated rates of psychosis, mood and anxiety disorders. The extent of this burden is illustrated in Zweben et al (2004), where a quarter of methamphetamine users had psychiatric symptoms severe enough to warrant hospitalisation, and a third had a history of having been prescribed psychiatric medications. McKetin et al (2005a) reported that among a sample of current Australian methamphetamine users one quarter were experiencing severe disability in their mental health functioning. Similarly, amongst Australian cocaine users, two thirds had at least one current psychiatric symptom (Kaye & Darke, 2004b).

3.2.1 Psychosis

One of the key clinical differences between psychostimulant drugs and other illicit drugs, such as the opioids, is that psychostimulant use can induce psychosis. Case-control studies have demonstrated that psychostimulant users have higher levels of psychosis compared to users of opioids, benzodiazepines and barbiturates (Curran et al, 2004; Dalmau et al, 1999; Farrell et al., 2002; Graf et al, 1977). Psychosis induced by psychostimulant drugs is typically a transient phenomenon that involves symptoms of delusions and hallucinations, and less commonly, disorganised speech and grossly disorganised behaviour (American Psychiatric Association, 2000). Delusions usually involve themes of persecution, while hallucinations most commonly may manifest in the auditory and visual senses, but can occur in any of the senses. These symptoms can be accompanied by repetitive stereotyped behaviour, social withdrawal and increased philosophical concern (Davis and Schlemmer, 1980; Harris and Batki, 2000).

Psychostimulant psychosis can also be accompanied by an emotionally brisk or labile state, agitation, and sometimes seemingly irrational hostile behaviour (Ellinwood, 1971). Symptoms of psychosis usually last hours to days, and in severe cases, can lead to hospitalization and require sedation and/or antipsychotic medication. In rare cases, the condition can last weeks to months, or can remit and recur over a longer period of time, contiguous with drug use and other life stressors (Karch, 2002; Sato et al*,* 1992).

Psychostimulant users are at high risk of experiencing psychotic symptoms if they suffer from pre-existing schizophrenia, mania or other psychotic disorders. Among such individuals, these drugs can

precipitate or exacerbate psychotic episodes (Curran et al, 2004). What needs to be borne in mind is that psychostimulant users, like all illicit drug using populations, have elevated rates of pre-existing schizophrenia and other psychotic disorders (Regier et al, 1990). Despite this, the majority of psychostimulant users who experience psychotic symptoms after taking these drugs have no known history of schizophrenia, mania or other chronic psychotic disorders (McKetin et al, 2006).

Although vulnerability to psychotic symptoms varies among psychostimulant users, these symptoms appear to be remarkably common among regular users of these drugs. McKetin et al (2006b) reported that amongst Australian methamphetamine users 23% had experienced a clinically significant psychotic symptom in the past year and 13% screened positive for a psychotic disorder (compared to 1.2% of the general population). Earlier Australian research had reported that half of methamphetamine users had experienced clinically significant feelings of persecution or hallucinations since using methamphetamine (Hall et al, 1996). Moreover, the prevalence of these symptoms had significantly increased since the onset of amphetamine use. Similarly high proportions of psychosis and psychotic symptoms have been reported internationally (Chen et al, 2003; Matsumoto et al, 2002; Sommers et al, 2006; Thirthali & Benegal, 2006; Zweben et al, 2004). Cocaine users demonstrate similarly high levels of psychotic symptoms (Bartlett et al, 1997; Curran et al, 2004; Kaye & Darke, 2004b; Satel et al, 1991; Thirthali & Benegal, 2006). As many as half of cocaine users seen in clinical settings experience paranoia and hallucinations (Bartlett et al, 1997; Satel et al, 1991; Thirthali & Benegal, 2006). High rates are also seen amongst non-clinical samples. In Australia, 38% of current cocaine users had current, clinically significant symptoms of paranoia, and 12% had recently experienced hallucinations (Darke & Kaye, 2004). Importantly, as with methamphetamine, the prevalence of these symptoms had increased dramatically since cocaine use commenced.

A number of factors have been associated with increased risk of developing psychotic symptoms. Symptoms of psychosis are most likely to occur among chronic, dependent users of the drug, rather than infrequent users (Kaye & Darke, 2004b; McKetin et al, 2006b; Thirthali & Benegal, 2006; Zweben et al, 2004). In the McKetin et al (2006b) study, 31% of dependent methamphetamine users had psychotic symptoms, compared to 13% of non-dependent users. Longer periods of psychostimulant use, and heavier use, also increase risk (Bartlett et al, 1997; Curran et al, 2004; et al, 2006; Zweben et al, 2004). The injection of psychostimulants has also been associated with increased

risk of psychotic symptoms (Brady et al, 1991; Hall et al, 1996; Kaye & Darke, 2004b; Matsumoto et al, 2002; Zweben et al, 2004). In Australia, paranoia was present in 46% of injecting cocaine users compared to 25% non-injectors (Darke & Kaye, 2004). Similarly, hallucinations were far more prevalent amongst injectors than non-injectors (17 v 3%). These findings, however, may reflect the higher levels of dependence seen amongst injectors than the effects of route of administration *per se*. Finally, as would be expected, a pre-existing history of psychotic symptoms increases the risk of psychosis, or psychotic symptoms, induced by psychostimulants (Chen et al, 2003; Hall et al, 1996; Kaye & Darke, 2004b; McKetin et al, 2006b).

3.2.2 Depression, suicide and anxiety

Psychostimulant psychosis is certainly the most conspicuous form of psychopathology associated with the use of such drugs. The fact that psychosis is so conspicuous, however, should not distract attention from other forms of psychopathology that are more common, more chronic, and potentially more debilitating. Depressive symptoms are particularly common among psychostimulant users, and may have fatal consequences (Copeland & Sorenson, 2001; Hando et al, 1997; Kaye & Darke, 2004b; Majewska, 1996; Nnadi et al, 2005; Platt, 1997; Sommers et al, 2006; Zweben et al, 2005). Amongst psychostimulant users, the majority report a lifetime prevalence of depression (e.g. 62%: Hall, et al, 1996; 60%: Zweben et al, 2004), whilst a third have clinically significant current depression (Kaye & Darke, 2004b). These figures are further emphasised by recent Australian research that indicated a third of methamphetamine users had been diagnosed with depression at some point in their lives (McKetin et al, 2005a).

As would be expected, given these high rates of depression, rates of suicidal ideation and attempted suicide are also high (Darke & Kaye, 2004; Garlow et al, 2003; Hall et al, 1996; Roy, 2001; Zweben et al, 2004). Studies indicate that approximately a quarter of psychostimulant users have a lifetime history of attempted suicide: 29% (cocaine, Roy 2001), 28% (cocaine, Darke & Kaye, 2004), 27% (methamphetamine, Zweben et al, 2004), 23% (methamphetamine, Hall et al, 1996). Darke & Kaye (2004) also reported that 7% of cocaine users had attempted suicide in the preceding 12 months. By comparison, 3.6% of the Australian population have a lifetime history of attempted suicide, with 0.4% having made an attempt in the preceding 12 months (Pirkis et al, 2000).

Consistent with the high levels of depression and global pathology, high levels of anxiety disorders have also been reported (Hall, et al, 1996; Kaye & Darke, 2004b; McKetin et al, 2005a; Sommers et al, 2006; Zweben et al, 2004). A half of Australian methamphetamine users in Hall et al (1996) reported symptoms of anxiety prior to initiation into methamphetamine use, and three quarters had experienced severe anxiety symptoms since methamphetamine use. Similarly, 38% of Australian cocaine users had current, clinically significant symptoms of anxiety (Kaye & Darke, 2004b). As with depression, these figures are emphasised by the fact that 11% of Australian methamphetamine users have received a diagnosis of an anxiety disorder at some stage in their lives (McKetin et al, 2005a).

As was the case with psychosis, higher levels of depression, suicide and anxiety have been associated with longer psychostimulant use careers, more frequent use, dependence and injecting (Darke & Kaye, 2004; Hall et al, 1996; Hando et al, 1997; Kaye & Darke, 2004b; Lexau et al, 1998; McKetin et al, 2006b; Sommers et al, 2006; Zweben et al, 2004). The latter finding could be a reflection of higher levels of psychostimulant dependence seen amongst injectors, rather than injecting *per se*.

3.2.3 Violent behaviours

There has been increasing attention in recent years to a perceived link between psychostimulant use and violent behaviours. According to McKetin et al., (2006c), such an association is plausible for three main reasons. First, there is experimental evidence that chronic use of the drug can increase aggressive behaviour (Sokolov et al, 2004, 2006). Second, acute intoxication may enhance or augment aggressive response in someone who is threatened or provoked (McEllistren, 2004). Finally, as discussed above, psychostimulant use is associated with a risk of psychosis, which can be accompanied by violent behaviours.

Violent behaviours appear common among psychostimulant users, particularly among people who inject these drugs (Hall et al, 1996; Kaye & Darke, 2004b; McKetin et al, 2006c; Sommers et al, 2006; Zweben et al, 2004). Hall et al (1996) reported that half of methamphetamine users exhibited violent behaviours since they began using methamphetamine. Importantly, violence was more common after initiation into methamphetamine use, and amongst injectors. More recent Australian data indicated that 12% of methamphetamine users had committed a violent crime in the preceding year (McKetin et al, 2005a). Amongst Australian cocaine users, 21% had committed a violent crime in the preceding year, this being far more common amongst cocaine injectors than non-injectors (29

v 6%) (Kaye & Darke, 2004b). Internationally, the picture appears remarkably similar. Zweben et al (2004) recently reported that 43% of methamphetamine users had problems controlling aggressive behaviour (Zweben et al*,* 2004), with symptoms more common amongst injectors and more frequent users. Similarly, Sommers et al (2006) recently reported that more than a third of methamphetamine users had assaulted someone whilst intoxicated with methamphetamine (Sommers et al, 2006).

At the epidemiological level, research in the United States demonstrated that the homicide rate in New York city covaried with the rate of cocaine positive homicide cases, an indicator of cocaine involvement in such violence. There was also a strong association between firearm deaths and cocaine, much of which was attributed to crack-related gang violence (Galea et al, 2002; Tardiff et al, 2005).

3.2.4 Summary of psychopathology and psychostimulant use

Unlike opioids, psychostimulant drugs can induce psychosis. Consistent with this profile, psychostimulant users have higher levels of psychosis than users of opioids and sedative drugs. In recent Australian research, 13% of methamphetamine users screened positive for psychosis, and 23% had experienced psychotic symptoms. Similarly, amongst Australian cocaine users 38% had paranoid symptoms, and 12% had recently experienced hallucinations. Psychotic symptoms are associated with longer term use, heavier use, dependence, injecting and a pre-existing history of psychotic symptoms.

Depression and suicide attempts are common. A third of methamphetamine users have received a diagnosis of depression at some point in their lives, and 11% have been diagnosed with an anxiety disorder. A quarter of psychostimulants users have a history of attempted suicide compared to 3.6% of the general population. Higher levels of depression, suicide and anxiety are associated with longer psychostimulant use careers, more frequent use, dependence and injecting.

Violent behaviours appear to be common among psychostimulant users, particularly among people who inject these drugs. Recent Australian data indicated that 12% of methamphetamine users and 21% of cocaine users had committed a violent crime in the preceding year.

Table 3
Summary of psychopathology and psychostimulant use

Key Points

- Unlike opioids, psychostimulant drugs can induce psychosis.
- Psychostimulant users have higher levels of psychosis than users of opioids, benzodiazepines and barbiturates.
- 13% of a sample of Australian methamphetamine users screened positive for psychosis, and 23% had experienced psychotic symptoms.
- 38% of a sample of Australian cocaine users had paranoid symptoms, and 12% had recently experienced hallucinations.
- Psychotic symptoms are associated with longer term use, heavier use, dependence, injecting and a pre-existing history of psychotic symptoms.
- A third of methamphetamine users have received a diagnosis of depression at some point in their lives, and 11% have been diagnosed with an anxiety disorder.
- A quarter of psychostimulants users have a history of attempted suicide compared to 3.6% of the general population.
- Higher levels of depression, suicide and anxiety are associated with longer psychostimulant use careers, more frequent use, dependence and injecting.
- Violent behaviours appear common among psychostimulant users, particularly among people who inject these drugs.
- Recent Australian data indicated that 12% of methamphetamine users and 21% of cocaine users had committed a violent crime in the preceding year.

4.0 SUMMARY

The current review aimed to examine in detail the epidemiology and major harms of psychostimulant use, and of cocaine and methamphetamine in particular. We will now briefly review the major findings.

4.1 Epidemiology

Psychostimulants are a class of drugs used by large numbers of people throughout the world. While the use of methamphetamine and cocaine are common, there appear to be about twice as many methamphetamine users as cocaine users. As with all illicit drug use, we saw that the use of psychostimulants is far more common amongst males.

It is an error to think of psychostimulant users as users solely of their drug of choice, or of these types of drugs more generally. The evidence clearly showed that polydrug use is the norm amongst these populations, a finding that has clinical implications for increased risk of mortality and morbidity. As would be expected, the use of multiple psychostimulants appears to increase demands upon the cardiovascular system. There is, however, a tendency to think of psychostimulant and depressive drug combinations as being safe, as they effectively cancel each other out. This is not the case. In fact, such use patterns increase risk. In particular, the concomitant use of alcohol increases the toxicity of psychostimulants and places far greater demands upon the cardiovascular system. In the case of cocaine, the concomitant use of alcohol actually results in the metabolic production of a third psychoactive drug, cocaethylene. Similarly, the use of psychostimulants and heroin together may increase risk due to increased myocardial oxygen demand from the effects of the psychostimulant being coupled with the reduced respiration associated with opioids.

In recent years there has been a great deal of information given to user and drug agencies on the risks of using heroin with other drugs (McGregor et al, 2001). It is clear that education of users and drug agency staff on the harms associated with the use of psychostimulants with other drugs is a priority.

4.2 Major health effects

Perhaps the most important public health message to emerge from this review is the fact that both cocaine and methamphetamine are cardiotoxic. Both cocaine and methamphetamine place heavy

demands upon the cardiovascular system that can cause myocardial ischaemia and infarction. Importantly, toxic reactions can occur irrespective of dose, frequency of use, or route of administration. The effects of these drugs upon the cardiovascular system are insidious. While there is the risk of acute reactions to these drugs, they are also associated with the premature and accelerated development of coronary artery atherosclerosis. There is also a greatly increased risk of cerebrovascular accident ("stroke"). It is unlikely that these effects and risks are appreciated by users of these drugs.

Dependence upon these drugs is also a major deleterious health effect. Despite their image as being safer drugs than drugs such as the opioids, psychostimulant dependence is a substantial risk. The fact that half of methamphetamine and cocaine users in Australian samples were categorised as dependent on these drugs demonstrates the level of risk. This risk is particularly true of those who inject or smoke these drugs, or use more potent forms such as ice or crack. The widespread availability of ice clearly increases the risk of dependent use amongst psychostimulant users. Dependent psychostimulant users, like dependent users of any drug, will be at far greater risk of the negative health effects of these drugs.

Finally, it is important to recognise the increased risks of blood borne virus transmission associated with these drugs compared to drugs such as heroin. Cocaine, in particular, greatly increases the levels of risky behaviours and risk of blood borne virus infection. The younger age profile and the libidinal effects of psychostimulants also enhances the risk of sexual disease transmission. From the perspective of reducing viral transmission, psychostimulant users are a priority target group.

4.3. Major psychological effects

As we have seen, there are severe health effects associated with psychostimulants. There are also serious psychiatric syndromes associated with these drugs. Clearly, the most severe of these is psychostimulant induced psychosis. One of the major differences between psychostimulants and other widely used illicit drugs of dependence, such as heroin, is that psychostimulants can induce psychosis. As we have seen, this is particularly true of longer term, dependent users, and those with a pre-existing history of psychotic symptoms.

While much media and public attention focuses upon psychosis, there are extremely high rates of depression, suicide and anxiety disorders amongst these groups. These are more common than frank

psychosis, and may have fatal results. This is clearly illustrated by the rates of suicide seen amongst these populations, which are many orders of magnitudes in excess of those seen amongst the general population.

Overall, the psychological health of psychostimulant users is extremely poor, and rates of self-harm are high. This is a group at great risk. Psychiatric screening of psychostimulant users entering treatment appears necessary, as the consequences of these levels of pathology are severe.

Finally, and in all probability related to the psychopathology discussed in this review, violent behaviours appear common among psychostimulant users. This appears to be particularly true of those who inject these drugs. While there are plausible reasons to associate psychostimulant use with increased levels of violence, whether these rates are higher than those seen amongst dependent users of other drugs (e.g. heroin) is currently moot.

4.4 Conclusions

To summarise, the use of psychostimulants is associated with a number of extremely serious negative health effects. While high profile consequences such as psychosis are given prominence in the public debate, the sequelae extend far beyond this. These are a class of drugs that cause serious heart disease, have serious dependence liability and high rates of suicidal behaviours. The current public image of these drugs does not adequately portray the extensive, and in many cases insidious, harm that they cause.

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