Australian Psychologist, June 2005; 40(2): 96 – 108

The Australian Psychological Society Ltd

Depression and other psychological health problems among methamphetamine dependent patients in treatment: Implications for assessment and treatment outcome

K. R. DYER & C. C. CRUICKSHANK

School of Medicine and Pharmacology, University of Western Australia, Crawley, Western Australia, Australia

Abstract

Amphetamines are second to cannabis as the most prevalent illicit drug used in Australia, and amphetamine abuse and dependence are associated with significant health and psychosocial harms. The current paper presents a series of studies investigating the prevalence of depression and other psychological problems among Western Australian patients receiving treatment for methamphetamine dependence. In the first study, a medical case-note audit explored the psychological profile among 218 consecutive admissions to an inpatient methamphetamine detoxification program. In the second study, the Beck Depression Inventory (BDI-II, Beck, Steer, & Brown, 1996) was administered to 367 patients receiving outpatient treatment for methamphetamine or heroin dependence (Phase 1), and the relationship between scores on the BDI-II and methamphetamine intoxication was explored (Phase 2). High rates of depression and other psychological problems were identified. Approximately 46% of methamphetamine-dependent individuals entering an inpatient treatment unit had been previously diagnosed for a psychological health problem, with approximately 30% requiring admission into a psychiatric hospital. In the second study, the mean total BDI-II score was approximately 22, which is in the moderate range of depression. Methamphetamine-dependent patients' total BDI-II score was similar to that of psychiatric outpatients with clinical depression, but significantly greater than college students and psychiatric outpatients with anxiety disorders (Beck et al., 1996). Methamphetamine use was associated with responses on the BDI-II corresponding with cognitive symptoms, whereas combined methamphetamine and heroin use was associated with responses indicating problems in the somatic domain. Finally, it was found that methamphetamine intoxication at the time of testing, as indicated by a positive saliva methamphetamine screen, affected responses to the BDI-II. These data demonstrate that methamphetamine-dependent individuals will present with significant psychological symptoms that may affect the response to treatment for drug dependence.

Amphetamines are a group of psychostimulant drugs that are structurally related to the parent compound amphetamine (phenylisopropylamine). The d-isomer, dexamphetamine, is used clinically to treat attention deficit disorders, but is also a popular illicit recreational drug (Fetherston & Lenton, 2004). Methamphetamine (methyl-β-phenylisopropylamine) is a lipophillic molecule with potent action on the sympathetic and central nervous systems. Methamphetamine is eliminated slowly and the half-life in humans ranges from 6 to 34 hr ($M = 12$ hr) (Davidson, Gow, Lee, & Ellinwood, 2001; Newton et al., 2003). Although very similar in chemical structure, methamphetamine is more potent than amphetamine, (Murray, 1998; Topp, Degenhardt, Kaye, & Darke, 2002). Methamphetamine is currently the most common congener used in Western Australia (Fetherston & Lenton).

Amphetamines are second to cannabis as the most prevalent illicit drug used in Australia. Approximately 9% of Australians report lifetime amphetamine use, and 5% of people aged between 20 and 29 years old report use in the previous month (Australian Institute of Health and Welfare, 2002). According to data collected in 2001, approximately 12% of West Australians aged above 14 years have used amphetamines illegally, and the prevalence is twice as great among the 18 – 34 age group (25%). An estimated 60% of Western Australian injecting drug users use methamphetamine (Fetherston & Lenton, 2004) and enquiries about methamphetamine account for the highest proportion of illicit drug

Correspondence: Dr K. R. Dyer, School of Medicine and Pharmacology, University of Western Australia, QEII Medical Centre MBDP M510, 35 Stirling Highway, Crawley, WA 6009, Australia. E-mail: kdyer@receptor.pharm.uwa.edu.au

ISSN 0005-0067 print/ISSN 1742-9544 online
Published by Taylor & Francis Ltd
DOI: 10.1080/00050060500094647

inquiries to the government drug and alcohol telephone information service in Western Australia (Drug and Alcohol Office, 2004).

Acute methamphetamine effects include hypophagia, hypertension, elevated respiration rate, pupil dilation, insomnia, decreased fatigue, and feelings of heightened confidence, well-being and contentment (Comer et al., 2001; Hart et al., 2001; Hawks, Mitcheson, Ogborne, & Edwards, 1969; Martin, Sloan, Sapira, & Jasinski, 1971). Methamphetamine is structurally related to the neurotransmitters dopamine (DA), noradrenaline (NA) and serotonin (5-HT) and acts as an indirect agonist of the catecholaminergic systems (Nordahl, Salo, & Leamon, 2003; Seiden, Sabol, & Ricaurte, 1993). Methamphetamine releases catecholamines from presynaptic endings, blocks catecholamine reuptake, and (at high doses) inhibits catecholamine metabolism by monoamine oxidase (Davidson et al., 2001; White & Kalivas, 1998). Acute administration increases extracellular DA levels through the reverse transport of DA and by displacement of DA from vesicular stores (Fleckenstein, Gibb, & Hanson, 2000). Methamphetamine also impacts upon 5-HT, NA and glutamatergic systems through interactions with 5-HT transporters, monoamine transporters and *N*-methyl-D-aspartate (NMDA) receptors (Murray, 1998). Chronic use of methamphetamines is associated with (a) depletion of presynaptic neurotransmitter stores; (b) down-regulation of neurotransmitter transporters and receptors; and (c) neurotoxicity, via reactive metabolites of dopamine and serotonin, which may produce necrosis, and subsequent apoptosis of neurons (Davidson et al., 2001). Repeated administration of the drug is associated with decreased striatal concentrations of DA and DA metabolites in several brain regions (Nordahl et al., 2003) possibly associated with loss of DA and 5-HT terminals and related pathways (Davidson et al.; Murray, 1998). Neurotoxicity may occur within days of drug exposure and may persist for months or years (Davidson et al.; Newton et al., 2003; Nordahl et al., 2003). Even if not indicative of neurotoxicity, decreased DA levels (approximately 50% of nondrug user levels) are consistent with motivational changes observed in methamphetamine patients in the early/intermediate treatment period (Davidson et al.).

Amphetamines are dependence-forming drugs, and dependence is associated with adverse effects on psychiatric, health and social functioning (Sekine et al., 2001; Yui, Goto, Ikemoto & Ishiguro, 2000). Once physical dependence has developed, a physical withdrawal syndrome will arise during periods of abstinence, or when circulating amphetamine levels are reduced. There are three primary symptom clusters within the amphetamine withdrawal syndrome: (a) hyperarousal symptoms, composed of drug craving, agitation, and vivid/unpleasant dreams; (b) reversed vegetative symptoms, consisting of decreased energy, increased appetite and craving for sleep; and (c) anxiety-related symptoms, comprising anxiety, slowing of movement, and loss of interest or pleasure (Srisurapanon, Jarusuraisin, & Jittiwutikan, 1999). Acute withdrawal appears to peak after 1 – 2 days of abstinence, and is largely resolved after 10 days (McGregor et al., 2003). However, symptoms such as mood lability, irritability, sleeping difficulties and cognitive deficits (Volkow, Chang, Wang, Fowler, Franceschi, et al., 2001; Volkow, Chang, Wang, Fowler, Leonido-Yee et al., 2001; Wyatt & Zidonis, 1998), may persist for several months (e.g., Oswald & Thompson, 1963; Volkow, Chang, Wang, Fowler, Franceschi, et al., 2001; Volkow, Chang, Wang, Fowler, Leonido-Yee et al., 2001; Watson, Hartmann, & Schildkraut, 1972). Sleep architecture is disturbed upon amphetamine abstinence, and may prolong depressed mood and related symptoms (Gossop, Bradley & Brewis, 1982; Oswald & Thompson; Watson et al.). Clinically, former and current methamphetamine-dependent patients may appear distractible and often have difficulty in sustaining attention and suppressing irrelevant task information (Nordahl et al., 2003; Ornstein et al., 2000; Salo et al., 2002), which may be associated with methamphetamine-induced damage to the DA and 5-HT systems (Nordahl et al.). There is currently a dearth of information to guide the evidence-based management of amphetamine withdrawal and rigorous clinical trials supporting effective pharmacotherapies or other treatment regimens have not been reported (Srisurapanont, Jarusuraisin & Kittirattanapaiboon, 2001).

Among methamphetamine-dependent individuals, it is difficult to differentiate primary psychological disorders from the mood disturbances associated with direct methamphetamine effects or the methamphetamine withdrawal syndrome. Nevertheless, it is generally agreed that methamphetamine-dependent individuals will display significant psychological symptoms. A South Australian survey of amphetamine users not in treatment found that two thirds of users self-reported symptoms of anxiety and depression, almost half of the sample reported mood swings and aggressive outbursts, while more than one third reported panic attacks and paranoia (Vincent, Shoobridge, Ask, Allsop, & Ali, 1998). Similarly, a survey of 200 amphetamine users in New South Wales found that anxiety (63%), depression (64%) and paranoia (47%), hallucinations (28%), panic attacks (21%), and suicidal thoughts (19%) were common psychological symptoms (Hando, Topp, & Hall, 1997). However, these studies did not use standardised tools to permit differential diagnoses. In general, there has been surprisingly little investiga-

tion regarding the valid assessment of psychological disorders among amphetamine users, and the relationship between psychological functioning and the response to treatment for amphetamine dependence.

A recent, rigorously designed US study has used standardised assessment tools to describe psychological symptoms among the largest treatment sample to date. The Methamphetamine Treatment Project (Zweben et al, 2004) examined psychiatric conditions among 1016 methamphetamine users participating in a trial of a manualised cognitive behavioural treatment. High levels of psychiatric symptoms were reported, particularly depression (60% of women and 50% of men at some stage in life; 34% of women and 24% of men at treatment entry) and attempted suicide (28% of women and 13% of men), anxiety and psychotic symptoms. There were also high levels of self-reported problems in controlling anger and violent behaviour. Approximately 26% of the sample reported symptoms severe enough to require admission into a psychiatric hospital at some point in their lives, while 32% had received prescribed psychiatric medications. Mean scores on the Beck Depression Inventory (BDI-II) were 15.5 ($SD = 9.9$, 0–52) among patients at treatment entry, which is in the mild range of depression (Beck, Steer & Brown, 1996). Higher BDI total scores were associated with more frequent use of methamphetamines within the past 30 days. The scope of study did not permit obtaining specific *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., *DSM-IV*) diagnoses in a consistent manner, while subjects were excluded if they met criteria for another Axis I substance dependence disorder. The study design also did not permit differentiation of methamphetamine intoxication symptoms or withdrawal-related symptoms from primary psychological symptoms. As such, the extent to which these results may be consistent with the profile of Australian drug treatment populations may be limited.

The recent increases in the prevalence of those who abuse methamphetamine and seek treatment, in conjunction with the preliminary evidence of methamphetamine effects upon behaviour and cognition, highlight the urgency of determining the interaction between methamphetamine-induced psychological harm and the successful resolution of methamphetamine dependence. The current paper presents three exploratory studies in which the prevalence of depression and other psychological problems were described among Western Australian patients receiving treatment for methamphetamine dependence. In the first study, the psychological profile among patients entering an inpatient methamphetamine detoxification program, and the relationship with treatment outcome, were documented. In the second study, the BDI-II (Beck et al., 1996) was administered to a representative sample of patients receiving outpatient treatment for methamphetamine dependence, and the relationship between scores on the BDI-II and methamphetamine intoxication was explored.

Methods

Subjects

Study 1 The sample consisted of 218 consecutive admissions to the Next Step detoxification unit between May 1995 and May 2003. Patients were selected for analysis if amphetamine or methamphetamine was identified as the primary drug problem requiring assisted detoxification. The sample was divided into two categories: (a) treatment completers (COMP) and (b) leavers (LAMA). The COMP group consisted of those patients who were retained in treatment until withdrawal severity was reduced sufficiently to allow safe discharge, as indicated by clinical assessment ($n = 138$). The LAMA group consisted of those patients who voluntarily initiated discharge against such medical advice ($n = 64$). Patients who were discharged for disciplinary reasons ($n = 14$) or who were transferred to other medical facilities ($n = 2$) were excluded from subsequent analyses; including one patient who was discharged to a psychiatric facility upon the emergence of severe psychotic symptoms.

The detoxification unit consisted of eight beds serving a patient population undergoing acute alcohol or other drug withdrawal. By day, the unit was attended by one medical officer and two nurses, and by night, a medical officer (on call) and two nurses. In the absence of an evidence-based clinical protocol, medication for amphetamine or methamphetamine detoxification was prescribed on an individual basis to treat emergent withdrawal symptoms (Cruickshank & Dyer, 2003). During admission to the unit, patients were also provided with opportunities to attend self-help and other group activities. No visitors were permitted during admission.

Study 2 Participants in this study were enrolled in the outpatient program at Next Step Specialist Drug and Alcohol Services (East Perth, Western Australia). In the first phase data were collected from 367 amphetamine- and heroin-dependent outpatients during 2002–2003, who were recruited for a larger study examining the psychometric properties of the BDI-II (Dyer, Marsh, & LaVincente, 2003; Newcombe & Dyer, 2003). Patients were classified according to whether they reported the use of methamphetamine, heroin, methamphetamine and heroin, or neither methamphetamine nor heroin in

the month prior to testing. Participants were recruited by being approached in the waiting area of the outpatient unit. Exclusion criteria were enrolment in the Next Step program for < 1 month, or receiving treatment for alcohol dependence. Participants were assured that all information provided was anonymous and confidential, and that the decision to participate would not affect their treatment program. All participants were volunteers and were given a lottery ticket with a prize of $AUD50.00 for participation. Data were collected in private rooms adjacent to the waiting area, and generally required approximately 15 min to complete.

In the second phase, 57 patients were drawn from a larger study conducted in 2003 examining the accuracy of an on-site saliva-based drug screen (Dyer , Taylor, Ilett, & Wilkinson, 2003). All participants were enrolled in the outpatient program at Next Step, and had indicated by self-report that they had used methamphetamines on at least one occasion in the prior month. Exclusion criteria were positive saliva drug screen results for drugs other than methamphetamine or benzodiazepines, or receiving treatment for alcohol or opioid dependence. Participants were assured that all information provided was anonymous and confidential, and that the decision to participate would not affect their treatment program. All participants were volunteers and were not paid for participation. Data were collected in private rooms adjacent to the waiting area, and generally required approximately 10 min to complete. Ethical approval to conduct these studies was provided by the University of Western Australia Human Research Ethics Committee.

Procedures and measures

Study 1 Data were extracted from the medical records of the patient sample. The sample was divided into two primary outcome categories: ''completed'' (completers, COMP) or ''left against medical advice'' (leavers, LAMA). Demographic data were obtained by clinicians during preadmission assessment using standardised assessment forms consisting of age, gender, marital status, employment status, ethnicity and residential status. Drug use data were obtained from preadmission assessment forms and included: most common route of administration; frequency of drug use (alcohol, amphetamines, benzodiazepines, cannabis, tobacco, opioids, hallucinogens and/or cocaine); duration of current episode of amphetamine use; age at first use of amphetamines; age first dependent upon amphetamines; quantity of amphetamines used per day; and drug treatment history.

Entire medical files, including assessment forms, clinician notes and appended hospital record extracts, were individually scanned for historical evidence of diagnoses or hospitalisation for an Axis I psychological disorder. Categorical data were collected for: (a) self-harm (no self-harm; suicidal ideation; self-harm; hospitalisation for self-harm); (b) prior psychiatric hospitalisation (*no*; *yes*); (c) psychotic symptomology (no history of psychotic symptoms; history of psychotic symptomology (consisting of paranoia, delusions or hallucinations); history of psychosis); (c) psychiatric diagnosis of depression disorders, attention-deficit disorders, or schizophreniform disorders (not diagnosed; formal diagnosis); and (d) previous antidepressant prescription (*no*; *yes*).

Study 2 All participants provided general demographic details, information regarding their drug use and preexisting medical and psychological complaints, and details of their current treatment regimen. Participants were given via interview the BDI-II (Beck et al., 1996), which is a widely used 21-item self-report measure developed to assess depression using the criteria in the *DSM-IV* (American Psychiatric Association [APA], 2000). The validity of the BDI-II against other measures of depression, internal consistency, and test–retest reliability have been determined among college and psychiatric samples (Beck et al.). Previous studies suggest that it is an instrument of adequate reliability and validity for identifying the presence and severity of depressive symptoms within the samples studied to date (e.g. Beck et al.; Dozois, Dobson & Ahnberg, 1998; Osman et al., 1997). It has been recommended for use with drug treatment populations (Dawe & Mattick, 1997), but detailed psychometric evaluation among Australian drug-using populations have not been reported. Factor analyses conducted with the BDI-II have generally revealed subscales pertaining to somatic, cognitive and affective symptomatology. The particular items that load on to each scale vary depending upon the population in question and the version of the BDI; but the underlying nature of the subscales remains consistent (Beck et al.). For the present analyses, the following subscales were derived from a confirmatory factor analysis (Dyer, Marsh, et al., 2003): the cognitive scale consisted of sadness, pessimism, past failure, guilty feelings, punishment feelings, self-dislike, self-criticalness, suicidal thoughts and worthlessness. The affective scale consisted of loss of pleasure, crying, agitation, loss of interest, indecisiveness, irritability and loss of sexual interest. The somatic scale consisted of loss of energy, changes in sleep pattern, appetite changes, concentration difficulty and fatigue.

In the second phase, in addition to the aforementioned information, participants also provided a saliva sample for the qualitative assessment of recent illicit

drug use. Saliva has been shown to be an alternative biological matrix for the detection of drugs, with the advantage of being non-invasive, rapidly and easily collected and resistant to tampering (Cone, 1993; Rouen, Dolan, & Kimber, 2001). Because saliva is an essentially protein-free ultra-filtrate of plasma, saliva drug concentration represents the bioavailable proportion of the drug, reflects plasma drug concentration (Haeckel & Hanecke, 1996) and concentrations may be used to determine pharmacokinetic parameters (Cone; Jenkins, Oyler, & Cone, 1995). On-site testing of saliva for opioids, methadone, benzodiazepines, cannabis, cocaine, dexamphetamine, methamphetamine was conducted using the Cozart RapiScan (Cozart Bioscience Limited, Oxfordshire, UK). This system consisted of an oral fluid collection swab, a disposable cartridge (containing a lateral flow immunoassay employing colloidal gold-labelled antibodies to drugs of abuse) and a reflectance spectrophotometer, which displayed either a positive or negative result on the output screen. Quantitative saliva methamphetamine concentrations were determined by gas chromatography–mass spectrometry (GC-MS), using previously described methods (Dyer, Taylor et al., 2003).

Statistical analyses

In the first study, differences in continuous data were compared between completers and leavers using Student's *t* tests. Categorical data were compared using Fisher's exact test; and the Pearson correlation coefficient was determined to identify significant correlations among study parameters. In the second study (Phase 1) data were compared among patients who had used methamphetamine, heroin, methamphetamine and heroin, or neither methamphetamine nor heroin during the month prior to data collection. In the second phase, data were compared between methamphetamine users who provided a saliva sample that was positive for methamphetamine and those who did not. Analyses of variance were performed, with drug group as the between-subjects factor, and BDI-II test scores as the within-subjects factor, with group differences explored by Tukey honestly significant difference (HSD) post hoc analyses. One-sample *t* tests were used to compare BDI-II total scores of the patient groups with published scores provided by (a) 500 psychiatric outpatients with clinical depression, (b) 120 college students, (c) 264 psychiatric outpatients with mood disorders and (d) 88 psychiatric outpatients with anxiety disorders (Beck et al., 1996). All data were analysed via SPSS for Windows 10.1 (SPSS, Chicago, IL, USA). Unless otherwise specified, all continuous data are reported as mean $\pm$ SEM.

Results

Study 1: Psychological profile among an inpatient treatment sample

Demographic data for the sample are presented in Table 1. The average age of treatment entrants was 26.6 ± 0.4 years (range: 18–46 years). Male subjects were well-represented (60.4%), which is consistent with other studies of amphetamine user groups (Derlet, Rice, Horowitz, & Lord, 1989; Hando et al., 1997; White, 2000). Patients were predominantly single (75%), unemployed (65%), and in comparison with recent demographic data for Perth, Western Australia, there was an overrepresentation of both residential instability (13%) and Aboriginal/Torres-Straight Islander ethnicity (16%) (Australian Bureau Of Statistics, 2001). Demographic characteristics of the sample were consistent with a description of injecting drug users from the same locale; 92% of whom reported using methamphetamine in the preceding 6 months (Hargreaves & Lenton, 2002).

The mean age at first use of amphetamines was 18.8 ± 0.4 years (range 10–39 years). Mean age at the onset of dependence was 21.3 ± 0.41 years (range 12–39 years). Most patients used amphetamines most days of the week (94%) and by injection (91%). The typical mean daily amount used was 1.1 ± 0.1 g (range 0.01–5 g) and the mean duration of the current episode of use was 19.1 ± 2.0 months (range 0.25–168 months). The number of days between last amphetamine use (by self-report) and inpatient admission was 3.0 ± 0.3 days (range 0–35 days). Use of other substances in the last month was widespread (alcohol 67%, benzodiazepines 41%, cannabis 76%, tobacco 90%). In particular, cocaine (13%; COMP: 9%, LAMA: 23%, $\chi^2 = 4.48$; $p < .05$), hallucinogen (15%; COMP: 10%, LAMA: 24%, $\chi^2 = 4.62$; $p < .05$) and opioid (25%; COMP: 21%, LAMA: 35%, $\chi^2 = 4.23$; $p < .05$) use were more common among those who did not complete treatment. A large proportion of the patients had previously received treatment for problematic drug use (77%), while counselling (30%) and inpatient withdrawal (28%) were the most common among these.

Formal psychiatric diagnoses were common, occurring among 46% of the patients (Table 1). Depressive disorders were the most common diagnoses, occurring among 35% of cases. Psychiatric morbidity was evident for a substantial proportion of the sample, but did not differ significantly between the treatment groups (46%; COMP: 49%, LAMA: 39%, $\chi^2 = 1.84$, *ns*). The prevalence of diagnosed attention-deficit disorders was significantly higher among leavers than completers (COMP: 3%; LAMA: 13%; $\chi^2 = 6.98$; $p < .05$), but depression (COMP: 41%; LAMA: 22%; $\chi^2 = 6.98$; $p < .05$) was more common among completers (Table 1). A

history of psychotic features (psychotic symptoms or psychosis) was documented among 35% ($n = 70$) of the sample. Past experience of psychosis was documented among 14% of the sample ($n = 29$) and leavers were twice as likely to have experienced a prior psychotic episode as completers (COMP: 10%; LAMA: 23%; $\chi^2 = 6.28$; $p < .05$). Many patients in the sample had been previously admitted to an inpatient psychiatric facility (30%, $n = 61$). The proportion of methamphetamine patients presenting with a previous psychiatric admission increased 1.5-fold from 1996 (22%) to 2003 (Jan. – May, 33%) (Figure 1). Previous psychiatric hospitalisation was not related to outcome.

Many patients presented with a history of self-harm (47%), including a substantial proportion of the sample who were previously hospitalised for self-harm (20%). The majority of patients experienced suicidal ideation at some time prior to admission (61%). There were no significant differences between completers and leavers among these factors.

Study 2, Phase 1: Depression among outpatient methamphetamine users

A total of 367 outpatients participated in the first phase. Participants had a mean age of 33.7 ± 0.5 years (range 18 – 53 years) and 62% ($n = 227$) were

Table 1. Psychiatric characteristics of patients receiving inpatient amphetamine withdrawal management 1995 – May 2003

	Sample ($n = 202$)	Completers ($n = 138$)	Leavers ($n = 64$)
Age, years (SE)	24.9 (0.5)	26.8 (0.5)	26.4 (0.7)
Gender (% female)	39.6	39.9	39.1
No usual residence (%)	12.9	11.9	15.3
Indigenous (%)	16.1	15.5	17.2
Antidepressant prescription (%)	43.1	47.1	34.4
Formal psychiatric diagnosis (%)	46.0	49.3	39.1
Depression (%)	34.7	40.6	21.9**
Schizophrenia (%)	6.5	5.3	9.3
Attention-deficit disorders (%)	6.0	2.6	13.0*
Prior psychiatric hospitalisation (%)	30.2	34.1	21.9
Prior psychotic symptoms (%)$^{+}$	20.3	22.5	15.6
Prior documented psychosis (%)$^{++}$	14.4	10.1	23.4*
History of self-harm (%)	46.5	46.4	46.9
Hospitalised for self-harm (%)	20.3	20.3	20.3

Note. $^{+}$Prior psychotic symptoms refer to patient self-reports of experiencing psychotic-type symptoms without medical verification. $^{++}$Prior documented psychosis refers to verified previous episodes of psychosis.
*$p < .05$ for completers vs leavers (Fisher's exact test).
**$p < .01$ for completers versus leavers (Fisher's exact test).

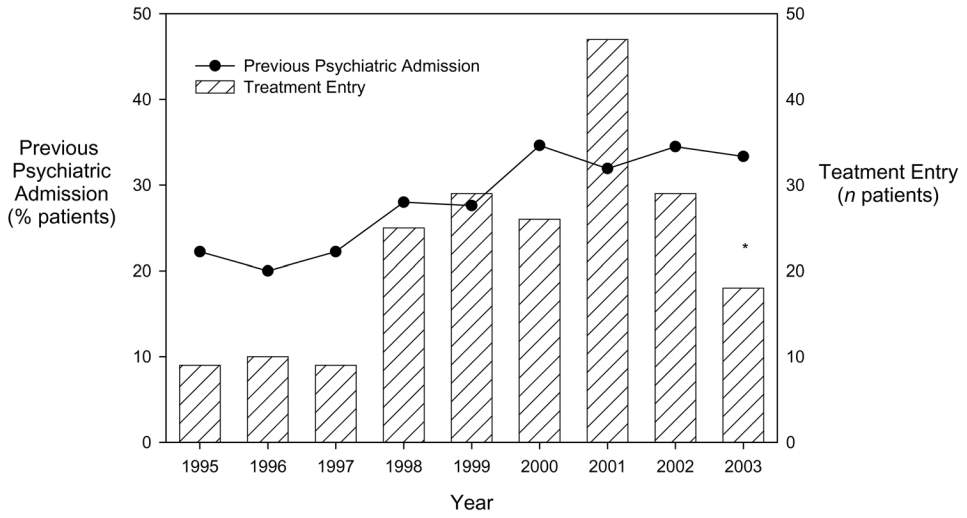

Figure 1. Treatment entry and prior psychiatric admission by date of treatment. Number of inpatient admissions for treatment of amphetamine withdrawal for each year (boxes) and the proportion of admissions presenting with at least one prior psychiatric admission. The date of treatment year refers to admission into Next Step for amphetamine withdrawal, and is not necessarily the same as the year of psychiatric admission. Note that data for 2003 were collected from admissions during the four months January – May 2003 only.

male. Approximately 77% ($n = 283$) of the sample had received high school education and 22% ($n = 81$) were tertiary educated. Approximately 24% ($n = 88$) of the sample were employed and 25% ($n = 92$) were either married or in a defacto relationship. Alcohol was consumed by 44% ($n = 161$) of participants in the previous month, while 57% ($n = 209$) used benzodiazepines, 5% ($n = 18$) used cocaine, 7% ($n = 26$) used MDMA and 62% ($n = 227$) used cannabis. Participants had been enrolled in treatment for 3.3 ± 0.3 years (range 30 days – 20 years).

Approximately 38% ($n = 140$) of the current sample reported using heroin in the previous month on a mean of 11.9 ± 1.0 days (range 1 – 30 days). These participants had first used heroin when 19.3 ± 0.3 years (range 11 – 38 years) of age, while regular heroin use began when participants were 22.1 ± 0.4 years (range 12 – 38 years) of age. The mean daily cost of heroin use was reported at $AUD59.2 ± 10.1 (range $AUD0 – $860). Approximately 37% ($n = 136$) of the current sample reported the use of methamphetamine in the previous month on a mean of 8.9 ± 0.8 days (range 1 – 30 days). The mean age of first methamphetamine use was 19.2 ± 0.5 years (range 10 – 45 years), and regular use began at a mean age of 20.8 ± 0.7 years (range 12 – 44 years). The mean daily cost of methamphetamine use was $AUD124.5 ± 22.6 (range $AUD20 – $800). The majority of the sample injected methamphetamines (88% inject, 12% oral or intranasal). There were no significant differences between heroin users and amphetamine users in the rates of other drug use, time in treatment or demographic variables.

The sample ($n = 367$) was divided into four groups: Those who reported using both amphetamines and heroin in the prior month (14%, $n = 51$), those who reported using only amphetamines (23%, $n = 85$) or heroin (24%, $n = 89$), and those who had used neither heroin nor amphetamine (53%, $n = 142$) in the month prior to testing. There was no significant difference in the number of days that amphetamines were used in the previous month between amphetamine users (7.9 ± 0.9 days, range 1 – 30 days) and those who used amphetamines and heroin (10.12 ± 1.5 days, range 1 – 30 days; $t(134) = -1.32$, *ns*). However, participants who used amphetamines and heroin in the previous month used heroin on more days than those who used only heroin (14.3 ± 1.6 days compared with 7.4 ± 1.1 days; $t(135) = -3.6$, $p < .0001$).

Figure 2 presents the mean scores on the BDI-II and related subscales among these participants. The mean total BDI score for the current sample (22.7 ± 0.7; range 0 – 58) was in the moderate range of depression (Beck et al., 1996) and was similar to

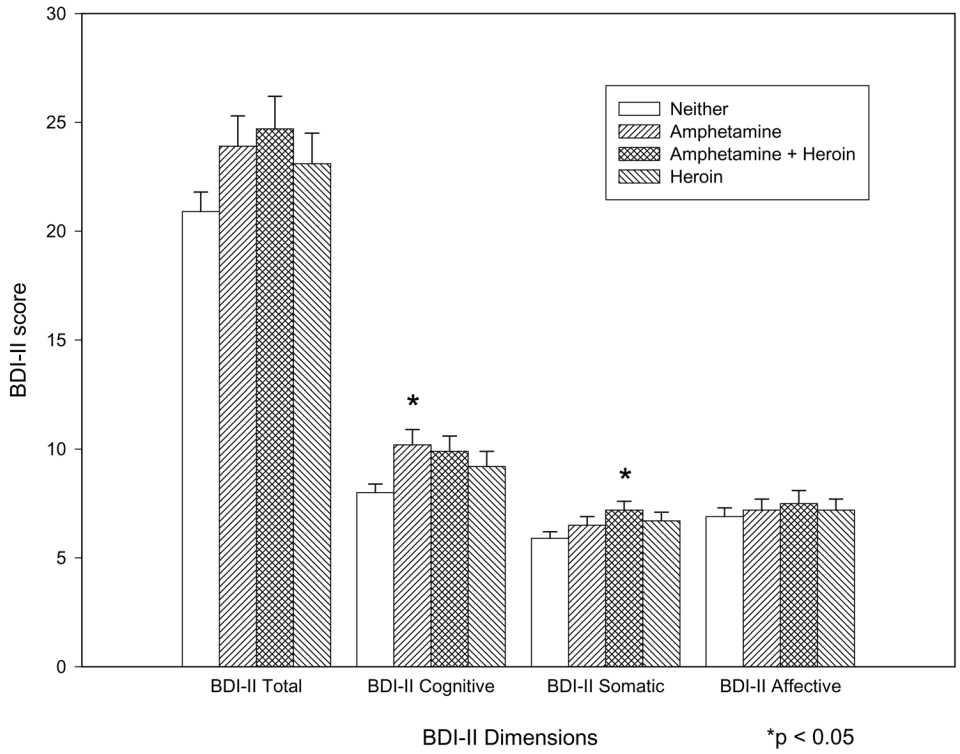

Figure 2. Beck Depression Inventory-II (BDI-II) total score and cognitive, somatic and affective BDI-II dimensions among patients who reported the use of methamphetamine ($n = 85$), heroin ($n = 89$), methamphetamine and heroin ($n = 51$) or neither methamphetamine nor heroin ($n = 142$) in the month prior to testing.

that of psychiatric outpatients with clinical depression (22.5 ± 12.8; $t(366) = 0.3$; *ns*) (Beck et al., 1996). It was significantly greater than college students (12.6 ± 9.9: $t(366) = 15.56$, $p < .0001$), and patients with anxiety disorders (19.38 ± 11.5: $t(366) = 5.06$, $p < .0001$) but significantly lower than psychiatric outpatients with mood disorders (26.57 ± 12.2: $t(366) = -6.01$, $p < .0001$) (Beck et al., 1996).

There was no significant difference for the total BDI score between the drug-using groups. Mean scores on the subscales were affective 7.2 ± 0.25 (range 1–19); cognitive 9.1 ± 0.3 (range 1–27); and somatic 6.4 ± 0.2 (range 1–14). There were significant between-group differences for the cognitive ($F(3,363) = 3.06$, $p < .01$) and somatic BDI subscales ($F(3, 363) = 2.46$; $p < .05$). Post hoc analyses revealed that patients classed as users of amphetamine only had significantly greater BDI cognitive scores than patients who did not use heroin or amphetamines ($p < .01$). Patients who used both amphetamines and heroin scored significantly higher on the BDI Somatic subscale than patients who did not use these drugs ($p < .05$).

Study 2, Phase 2: Relationship between methamphetamine intoxication and depression

Phase 2 examined scores on the BDI-II among 57 patients who reported the use of methamphetamines in the month prior to testing. Comparisons were made between patients who provided a positive saliva test for methamphetamine at the time of testing ($n = 41$) and those who were not intoxicated by methamphetamines at the time of testing ($n = 16$). All saliva drug screens were confirmed and the mean saliva methamphetamine concentration was 680 ± 187 ng/ml (range 5–4599 ng/ml). To exclude the effects of other drugs of abuse, these participants provided negative saliva drug screens for all drugs except benzodiazepines, which was the primary drug prescribed to patients as part of their treatment regimen. Approximately 44% ($n = 25$) of the sample provided a positive saliva test for benzodiazepines, but there was no significant difference in benzodiazepine use between the groups ($\chi^2(1) = 0.34$, *ns*).

Participants had a mean age of 33.4 ± 1.2 years (range 17–53 years) and 61% were male. Approximately 28% ($n = 16$) employed and 11% ($n = 6$) were students. Approximately 33% ($n = 19$) lived alone, 6% ($n = 4$) in temporary accommodation and 33% ($n = 19$) with friends, partners or family. Approximately 47% ($n = 27$) used alcohol, 57% ($n = 33$) used benzodiazepines, 5% ($n = 3$) used cocaine, 14% ($n = 8$) used MDMA and 90% ($n = 51$) smoked cigarettes during the previous month. Approximately 64% ($n = 36$) had used cannabis on a mean of 15 ± 1.9 days (range 1–30 days) in the previous month. With regard to the use of prescribed medications, 42% ($n = 24$) had received medications for anxiety (diazepam), 26% ($n = 15$) received medications for depression, 16% for insomnia (temazepam) and 12% ($n = 7$) had received antipsychotic medication. There were no significant differences between the groups for these variables.

Methamphetamines were reported to be used on a mean of 7.8 ± 1.3 days (range 1–30 days) in the previous month. The mean daily cost of methamphetamine use was reported to be \$AUD109.40 $\pm$ 14.40 (range \$AUD20–\$400) and 87% of the sample injected methamphetamine. Participants had been receiving treatment for a mean of 4.9 ± 1.1 years (range 30 days–10 years). There was no significant difference between the groups for these variables.

Methamphetamine users who provided a positive saliva test for methamphetamine had a lower total BDI score (20.9 ± 1.8, range 0–45) than those who were not under the influence of methamphetamine (26.8 ± 3.2, range 1–45), although this difference did not reach significance ($t(55) = 1.69$, $p = .08$). However, there were significant differences between the groups in relation to their scores on the various BDI-II subscales. Participants who were intoxicated by methamphetamine at the time of testing, as indicated by a positive methamphetamine saliva screen, scored significantly lower on the cognitive (8.6 ± 0.8 compared with 11.5 ± 1.8: $t(55) = 1.77$, $p < .05$) and the somatic (5.9 ± 0.5 compared with 7.5 ± 0.7, $t(55) = 1.94$, $p < .05$) subscales than methamphetamine users who provided a negative methamphetamine saliva screen (Figure 3).

The mean BDI-II total score for methamphetamines users who provided a positive saliva test for methamphetamine (20.9 ± 1.8, range 0–45) was significantly greater than that of college students (12.6 ± 9.9: $t(40) = 4.72$, $p < .0001$), and significantly lower than patients with mood disorders (26.57 ± 12.2: $t(40) = -3.18$, $p < .001$). There were no significant differences from patients with anxiety disorders (1.38 ± 11.5: $t(40) = 0.40$, *ns*) or psychiatric outpatients (22.5 ± 12.8; $t(40) = 0.4$, *ns*), In contrast, the mean BDI-II total score for methamphetamine users who were not intoxicated by methamphetamine at the time of testing, as indicated by a negative methamphetamine saliva screen, were not significantly different from psychiatric outpatients with clinical depression ($t(15) = 0.2$, *ns*), mood disorders ($t(15) = .94$, *ns*), but were significantly greater than college students ($t(15) = 4.41$, $p < .001$) and outpatients with anxiety disorders ($t(15) = 2.30$, $p < .05$).

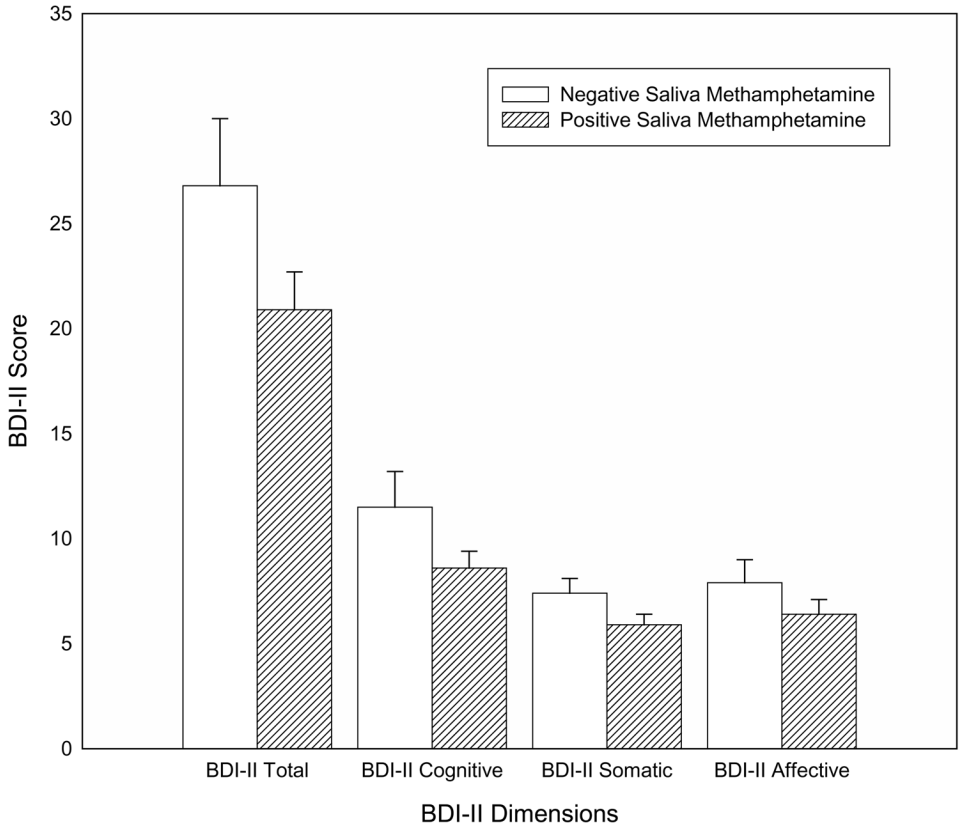

Figure 3. Beck Depression Inventory-II (BDI-II) total score and cognitive, somatic and affective BDI-II dimensions among patients who reported the use of methamphetamine in the previous month and provided a positive saliva drug screen for methamphetamine ($n = 41$) and those who did not ($n = 16$).

Discussion

These studies have documented high rates of depression and other psychological problems among individuals receiving treatment for methamphetamine dependence. In Study 1, 46% of methamphetamine-dependent individuals entering an inpatient treatment unit had been previously diagnosed with an Axis I disorder. In the second study, the mean total BDI-II score was approximately 22, which is in the moderate range of depression. Methamphetamine dependent patients' total BDI-II score was similar to that of psychiatric outpatients with clinical depression, but significantly greater than college students and psychiatric outpatients with anxiety disorders (Beck et al., 1996). Methamphetamine use was associated with responses on the BDI-II corresponding with cognitive symptoms, whereas combined amphetamine and heroin use was associated with responses indicating problems in the somatic domain. Finally it was found that methamphetamine intoxication at the time of testing, as indicated by a positive saliva methamphetamine screen, affected responses to the BDI-II. Scores on the BDI-II Cognitive and Somatic subscales were reduced among methamphetamine-intoxicated subjects.

In Study 1, psychological problems were highly prevalent across the sample, a finding that is consistent with psychiatric comorbidity reported previously among amphetamine and methamphetamine users (Hawke, Jainchill, & De Leon, 2000; Kalechstein et al., 2000; Zweben et al., 2004). Approximately 46% of the sample had been diagnosed with a psychological disorder, with depression diagnosed in 35% of the patients. While the findings suggest that psychopathology is quite common and often severe among dependent methamphetamine users, this case-note study documents only the prevalence of nominal indicators of mental health, and the accuracy and comprehensiveness of previous diagnoses cannot be determined. The items explored in the present study reflect clinical recording based upon patient presentation and self-report. Nevertheless, the value of this study lies in its potential to inform the direction of more focused and systematic research into the mental health consequences of amphetamine use.

A previous diagnosis of depression was significantly more common among inpatients who completed treatment, but the reason for this finding is not clear. It is possible that depression may have been underreported among patients with a tendency

to leave treatment, or there may have been unreported differences in the treatment received by patients displaying depressive symptoms. Further research is warranted to examine the relationship between depression and treatment outcome. In contrast, diagnosed attention-deficit disorders were more common among leavers. Patients exhibiting characteristics of attention-deficit disorders appear to experience particular difficulty completing detoxification. Previous studies have demonstrated that long-term methamphetamine use is associated with cognitive deficits (reviewed in Nordahl et al., 2003), that are not dissimilar to the presentation of attention-deficit disorders (APA, 2000). Clinically, former and current methamphetamine-dependent patients may appear distractible and often have difficulty in sustaining attention and suppressing irrelevant task information (Nordahl et al.; Ornstein et al., 2000; Salo et al., 2002), which may be associated with methamphetamine-induced neurotoxicity (Nordahl et al.). Regardless of aetiology, adequate cognitive function is necessary to facilitate effective treatment outcomes. In a recent study of cocaine-dependent patients' response to cognitive behavioural therapy (CBT), it was found that completers of a 12-week program had demonstrated significantly better cognitive performance at baseline than patients who dropped out of treatment (Aharonovich, Nunes, & Hasin, 2003). A fundamental component of CBT is the use of cognitive processing as a mediator of behavioural change. To complete a CBT program, patients need to be able to focus, hold and sustain attention. Adequate cognitive functioning is required; lack of comprehension may cause frustration leading to premature termination (Aharonovich et al.). The extent to which these findings may be extrapolated to other treatment regimens has not been systematically examined. However, the results from the present study provide preliminary support for a relationship between attention difficulties and treatment retention. The principal author of the present paper (University of Western Australia) has recently established a clinic at Next Step to assess cognitive functioning among methamphetamine-dependent patients. The effectiveness of the clinic in developing effective individualised treatment programs, and promoting retention in treatment, is the focus of current research.

Previous studies have established that psychotic symptomology is a common consequence of chronic amphetamine use (Anggard, Jonsson, Hogmark, & Gunne, 1973; Bell, 1973; Ellinwood 1967; Griffith, Cavanaugh, Held, & Oates, 1970). We identified more than one third of cases where psychotic symptoms had been reported, and almost 15% where previous psychosis was documented. Previous experience of psychosis was reported among 20% of those who left the detoxification unit against advice, which was twice as prevalent as among those who completed treatment. As such, patients with a history of psychosis presenting for medically assisted methamphetamine withdrawal may require additional support. However, further research is urgently required to identify effective support interventions for those methamphetamine users who present with a history of psychosis.

Importantly, almost half of the inpatient sample had reported a history of self-harm. A more objective item, hospital admission associated with self-harm, was documented among 20% of the sample. Overall, 61% of cases revealed a history of suicidal ideation. The incidence of acute mental health problems among amphetamine users appears to be increasing over recent years. We noted a 1.5-fold increase from 1996 to 2003 in the proportion of patients who had previously been admitted to a psychiatric unit. During the final year of the study period, one third of the patients admitted to manage amphetamine withdrawal had previously experienced an acute psychiatric episode resulting in admittance to a psychiatric facility. These findings suggest that the mental health costs of methamphetamine dependence have increased in recent years. The increasing frequency of serious mental health issues may be associated with the emergence of potent forms of methamphetamine as the major forms of amphetamines in local illicit drug markets (Fetherston & Lenton, 2004). This distinction is important because methamphetamine is thought to be responsible for the protracted vulnerability to psychosis observed among some users, as opposed to amphetamine psychosis, which rarely persists beyond withdrawal (Iwanami et al., 1994).

Study 2 involved the administration of the BDI-II to a sample of patients receiving outpatient treatment for methamphetamine or heroin dependence. Many of the items within the BDI-II are similar to symptoms observed in opioid and methamphetamine withdrawal. As such, screening instruments such as the BDI-II will tend to overestimate the number of people who are depressed in drug-dependent populations (Arean, McQuaid, & Munoz, 1997). As such, population-specific norms are of paramount importance if the BDI-II is used to guide clinical decision making. The mean total BDI-II score among methamphetamine users in the present study was approximately 23, which is in the moderate range of depression (Beck et al., 1996). Methamphetamine users scored significantly greater on the BDI-II cognitive dimension than nonusers, while patients who used both methamphetamine and heroin scored significantly greater on the somatic dimension than nonusers. The total BDI-II score of the sample is greater than that reported among methampheta-

mine-dependent patients entering CBT (Zweben et al., 2004). This difference may be explained by the rigorous exclusion criteria utilised in the US study, where patients with coexisting substance dependence disorders and severe psychological impairments were not sampled. The sample in the present study were representative of the Next Step treatment population (Newcombe & Dyer, 2003) with regards to gender, age, treatment regimen and illicit drug use, and as such, are indicative of Western Australian drug-dependence treatment populations. Further, the BDI-II total scores of the present study are consistent with the BDI-II scores ($M = 22$) reported among male subjects entering a detoxification treatment program for opioid dependence (Buckely, Parker, & Heggie, 2001).

It is generally held that depression among opioid-dependent patients will reduce as a function of the drug-free period (e.g. Nunes, Donovan, Brady, & Quitkin, 1994), probably representing reduced opioid withdrawal severity, and resolution of the personal crises that often surround the decision to enter treatment. This implies an important strategy for distinguishing true depressive disorders from dependence sequelae, and persistence over time in treatment. However, this approach may not be effective for methamphetamine dependence because the methamphetamine withdrawal syndrome and associated dysphoria may persist for many months (Volkow, Chang, Wang, Fowler, Franceschi, et al., 2001; Volkow, Chang, Wang, Fowler, Leonido-Yee et al., 2001; Wyatt & Zidonis, 1998), and may be associated with methamphetamine-induced neurotoxicity (Nordahl et al., 2003; Sekine et al., 2001; Volkow, Chang, Wang, Fowler, Franceschi, et al., 2001; Volkow, Chang, Wang, Fowler, Leonido-Yee et al., 2001).

In the present study it was found that current methamphetamine intoxication (as indicated by a positive saliva drug screen) lowered scores on the BDI-II. In particular, scores on the cognitive and somatic dimensions of the BDI-II were significantly lowered, consistent with methamphetamine direct effects (Comer et al., 2001). As such, accurate assessment of intoxication must occur before using the scale to guide clinical decision-making among this population. The ability to observe patients under conditions of prolonged abstinence generally facilitates determination of psychological diagnoses (Scott, Gilvarry, & Farrell, 1998). Nevertheless, there are potential problems in basing diagnostic decisions on a single interview. It would be ideal to use a structured interview, longitudinal behavioural observations and incorporate collateral information whenever possible (Carey & Correia, 1998).

In some clinical settings dually diagnosed patients are seen as a patient group with similar characteristics (Scott et al., 1998). However, coexistence of one or more drug use disorders with one or more mental health disorders creates significant complexity. In general, there is no substitute for individualised behavioural, psychometric and psychosocial assessment. Although such assessment is labour intensive, it would provide the detailed information needed to develop individualised and tailored treatment programs (Milby, Schumacher, & Stainback, 1997; Scott et al., 1998). Further, although clinicians may not be able to determine the primacy of a psychological disorder among methamphetamine users, nor rule out pharmacological sequalae, we believe that it remains important to attempt to stabilise the psychological condition of these individuals as a matter of priority over the determination of cause and effect. Such an approach may facilitate the retention of individuals within methamphetamine treatment programs.

Acknowledgements

The authors would like to thank Kim Newcombe, Melanie Robson and Catherine Wilkinson for assistance with these studies. The saliva drug screens were provided by BioMediq DPC. The confirmation of methamphetamine-positive saliva screens was conducted by Hayley Taylor, with the assistance of Assoc. Professor Ken Ilett (University of Western Australia) and PathCentre WA. The administration and analyses of the BDI-II were conducted in collaboration with Dr Ali Marsh (Curtin University of Technology, WA) and Ms Sophie LaVincente (University of Adelaide, SA). We would like to thank the patients and staff of Next Step Drug and Alcohol Services (WA) for their assistance with these projects.

References

Aharonovich, E., Nunes, E., & Hasin, D. (2003) Cognitive impairment, retention and abstinence among cocaine abusers in cognitive-behavioural treatment. *Drug and Alcohol Dependence, 71*, 207–211.

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text revision). Washington, DC: The Author.

Anggard, E., Jonsson, L. E., Hogmark, A. L., & Gunne, L. M. (1973). Amphetamine metabolism in amphetamine psychosis. *Clinical Pharmacology and Therapeutics, 14*, 870–880.

Arean, P., McQuaid, J., Munoz, R. (1997) Mood disorders: Depressive disorders. In S. Turner, & M. Hersen(Eds.), *Adult psychopathology and diagnosis* (3rd ed., pp. 230–255). New York: John Wiley & Sons.

Australian Bureau of Statistics (2001). 2001 Census Basic Community Profile and Snapshot. Retrieved 21 November 2003, from Australian Bureau of Statistics http://www.abs.gov.au/ausstats

Beck, A., Steer, R., & Brown, G. (1996) *BDI-II manual*. San Antonio: The Psychological Corporation.

Bell, D. S. (1973). The experimental reproduction of amphetamine psychosis. *Archives of General Psychiatry, 29*, 35 – 40.

Buckley, T., Parker, J., Heggie, J. (2001) A psychometric evaluation of the BDI-II in treatment seeking substance abusers. *Journal of Substance Abuse Treatment*, *20,* 197 – 204.

Carey, K., & Correia, C. (1998) Severe mental illness and addictions: assessment considerations. *Addictive Behaviors*, *23*, 735 – 748.

Comer, S. D., Hart, C. L., Ward, A. S., Haney, M., Foltin, R. W., & Fischman, M. W. (2001). Effects of repeated oral methamphetamine administration in humans. *Psychopharmacology*, *155* (4):397 – 404.

Cone E. J. (1993) Saliva testing for drugs of abuse. *Annals of the New York Academy of Science*, *694*, 91 – 127

Cruickshank, C. C. & Dyer, K. R. (2003) *In-patient symptom-triggered management of amphetamine withdrawal: clinical practice and treatment outcome*. Perth: Next Step Specialist Drug and Alcohol Services.

Davidson, C., Gow, A. J., Lee, T. H., & Ellinwood, E. H. (2001). Methamphetamine neurotoxicity: Necrotic and apoptotic mechanisms and relevance to human abuse and treatment. *Brain Research: Brain Research Review, 36*, 1 – 22.

Dawe, S., & Mattick, R. (1997) Review of diagnostic screening instruments for alcohol and other drug use and other psychiatric disorders. Canberra: Australian Government Publishing Service.

Derlet, R. W., Rice, P., Horowitz, B. Z., & Lord, R. V. (1989). Amphetamine toxicity: experience with 127 cases. *Journal of Emergency Medicine, 7*, 157 – 161.

Dozois, D., Dobson, K., Ahnberg, J. (1998) A psychometric evaluation of the BDI-II. *Psychological Assessment*, *10*, 83 – 89.

Drug and Alcohol Office (2003). *2001 National drug strategy household survey: First results for Western Australia: Data tables.* Retrieved 6 May 2004, from Drug and Alcohol Office http://www.dao.health.wa.gov.au/index.cfm?section = pubs

Drug and Alcohol Office (2004). *Alcohol and Drug Information Service Parent Drug Information Service. Bulletin 6.* Drug and Alcohol Office. Retrieved 6 May 2004, from Drug and Alcohol Office http://www.dao.health.wa.gov.au/index.cfm?section = - pubs

Dyer, K. R., Marsh, A., & LaVincente, S. (2003) *A psychometric evaluation of the Beck Depression Inventory-II among drug dependent patients.* Paper presented at the combined Australian Professional Society on Alcohol and Other Drugs (APSAD) and National Methadone Conference, Brisbane, November 16 – 19, 2003

Dyer, K. R., Taylor, H., Ilett, K., & Wilkinson, C. (2003) *Saliva, a novel matrix for identifying methamphetamine and cannabis use among dependent patients.* Paper presented at the combined Australian Professional Society on Alcohol & Other Drugs (APSAD) and National Methadone Conference, Brisbane, November 16 – 19, 2003.

Ellinwood, E. H. (1967). Amphetamine psychosis: I. Description of the individuals and the process. *Journal of Nervous and Mental Disease*, *144*, 273 – 283.

Fetherston, J., & Lenton, S. (2004). *WA drug trends 2003: Findings from the Illicit Drug Reporting System (IDRS)* (NDARC Technical Report No. 179). Perth WA, Australia: National Drug Research Institute, Curtin University.

Fleckenstein, A. E., Gibb, J. W., & Hanson, G. R. (2000). Differential effects of stimulants on monoaminergic transporters: Pharmacological consequences and implications for neurotoxicity. *European Journal of Pharmacolology, 406*, 1 – 13.

Gossop, M. R., Bradley, B. P., & Brewis, R. K. (1982). Amphetamine withdrawal and sleep disturbance. *Drug and Alcohol Dependence, 10*, 177 – 183.

Griffith, J. D., Cavanaugh, J. H., Held, J., & Oates, J. A. (1970). Experimental psychosis induced by the administration of d-amphetamine. In E. Costa, & S. Garattini, (Eds.), *Amphetamines and related compounds; Proceedings of the Mario Negri Institute for Pharmacological Research*, *Milan, Italy* (pp 897 – 904). New York: Raven Press.

Haeckel, R., & Hanecke, P. (1996). Application of saliva for drug monitoring. An in vivo model for transmembrane transport. *European Journal of Clinical Chemistry and Clinical Biochemistry*, *34*, 171 – 91.

Hando, J., Topp, L., & Hall, W. (1997). Amphetamine-related harms and treatment preferences of regular amphetamine users in Sydney, Australia. *Drug and Alcohol Dependence, 46*, 105 – 113.

Hargreaves, K., & Lenton, S. (2002). *Findings from illicit drug reporting system (IDRS)* (NDARC Technical Report No.134). Perth WA, Australia: National Drug Research Institute, Curtin University.

Hart, C. L., Ward, A. S., Haney, M., Foltin, R. W., & Fischman, M. W. (2001). Methamphetamine self-administration by humans. *Psychopharmacology*, *157*, 75 – 81.

Hawke, J. M., Jainchill, N., & De Leon, G. (2000). Adolescent amphetamine users in treatment: Client profiles and treatment outcomes. *Journal of Psychoactive Drugs*, *32*, 95 – 105.

Hawks, D., Mitcheson, M., Ogborne, A., & Edwards, G. (1969). Abuse of methylamphetamine. *British Medical Journal, 1* (659), 715 – 721.

Iwanami, A., Sugiyama, A., Kuroki, N., Toda, S., Kato, N., Nakatani, Y., et al. (1994). Patients with methamphetamine psychosis admitted to a psychiatric hospital in Japan. A preliminary report. *Acta Psychiatrica Scandinavia*, *89*, 428 – 432.

Jenkins, A., Oyler, J., & Cone, E. (1995) Comparison of heroin and cocaine concentrations in saliva with concentrations in blood and plasma. *Journal of Analytic Toxicology*, *25*, 670 – 679.

Kalechstein, A. D., Newton, T. F., Longshore, D., Anglin, M .D., van Gorp, W. G., & Gawin, F. H. (2000). Psychiatric comorbidity of methamphetamine dependence in a forensic sample. *Journal of Neuropsychiatry and Clinical Neuroscience, 12*, 480 – 484.

Martin, W. R., Sloan, J. W., Sapira, J. D., & Jasinski, D. R. (1971). Physiologic, subjective, and behavioral effects of amphetamine, methamphetamine, ephedrine, phenmetrazine, and methylphenidate in man. *Clinical Pharmacology and Therapeutics, 12*, 245 – 258.

McGregor, C., Srisurapanont, M., Jittiwutikan, J., Laobhripatr, S., Wonttan, T., & White, J. M. (2003). *Mapping the nature, time-course and severity of methamphetamine withdrawal.* Poster presented at College on Problems of Drug Dependence, 2003 Annual Meeting. Retrieved 20 November 2003, from http://biopsych.com:81/cpdd03_web/FMPro

Milby, J., Schumacher, J., & Stainback, R. (1997). Psychoactive substance use disorders: Drugs. In S. Turner, & M. Hersen (Eds.), *Adult psychopathology and diagnosis* (3rd ed., pp. 159 – 202). New York: John Wiley & Sons.

Murray, J. B. (1998). Psychophysiological aspects of amphetamine – methamphetamine abuse. *Journal of Psychology 132*, 227 – 237.

Newcombe, K., & Dyer, K. (2003) *2003 Next Step Consumer Survey*. Perth: Next Step Specialist Drug and Alcohol Services.

Newton, T., Cook, I., Kalechstein, A., Duran, S., Monroy, F., Ling, W., et al. (2003). Quantitative EEG abnormalities in recently abstinent methamphetamine dependent individuals. *Clinical Neurophysiology, 114*, 410 – 415.

Nordahl, T. E., Salo, R., & Leamon, M. (2003). Neuropsychological effects of chronic methamphetamine use on neurotransmitters and cognition: A review. *Journal of Neuropsychiatry and Clinical Neuroscience*, *15*: 317 – 325.

Nunes, E., Donovan, S., Brady, R., & Quitkin, F. (1994). Evaluation and treatment of mood and anxiety disorders in opioid dependent patients. *Journal of Psychoactive Drugs*, *26*, 147–153.

Ornstein, T., Iddon, J., Baldacchino, A., Sahakian, B., London, M., Everitt, B., et al. (2000) Profiles of cognitive dysfunction in chronic amphetamine and heroin abusers. *Neuropsychopharmacology*, *23*, 113–126.

Osman, A., Downs, W., Barrios, W., Kopper, B., Guttierez, P., & Chiros, C. (1997) Factor structure and psychometric characteristics of the BDI-II. *Journal of Psychopathology and Behavioral Assessment*, *19*, 359–376.

Oswald, I., & Thompson, M. (1963). Amphetamine and phenmetrazine addiction. *British Medical Journal 5354,* 427–431.

Rouen, D., Dolan, K., & Kimber, J. (2001) *A review of drug detection testing and an examination of urine, hair, saliva and sweat* (Technical Report No. 120). Sydney: National Drug & Alcohol Research Centre, University of NSW.

Salo, R., Nordahl, T. E., Possin, K., Leamon, M., Gibson, D. R., Galloway, G. P., et al. (2002). Preliminary evidence of reduced cognitive inhibition in methamphetamine-dependent individuals. *Psychiatry Research, 111*, 65–74.

Scott, J., Gilvarry, E., & Farrell, M. (1998). Managing anxiety and depression in alcohol and drug dependence. *Addictive Behaviors, 23*, 919–931.

Seiden, L. S., Sabol, K. E., & Ricaurte, G. A. (1993). Amphetamine: effects on catecholamine systems and behavior. *Annual Review of Pharmacology and Toxicology*, *33*, 639–677.

Sekine, Y., Iyo, M. , Ouchi, Y., Matsunaga, T., Tsukada, H., Okada, H., et al. (2001). Methamphetamine-related psychiatric symptoms and reduced brain dopamine transporters studied with PET. *American Journal of Psychiatry, 158*, 1206–1214.

Srisurapanont, M., Jarusuraisin, N., & Jittiwutikan, J. (1999). Amphetamine withdrawal: I. Reliability, validity and factor structure of a measure. *Australian and New Zealand Journal of Psychiatry*, *33*, 89–93.

Srisurapanont, M., Jarusuraisin, N., & Kittirattanapaiboon, P. (2001). Treatment for amphetamine withdrawal. *Cochrane Database of Systematic Reviews*, *4*, Retrieved 20 April 2002, from http://www.cochrane.org/

Topp, L., Degenhardt, L., Kaye, S., & Darke, S. (2002). The emergence of potent forms of methamphetamine in Sydney, Australia: A case study of the IDRS as a strategic early warning system. *Drug and Alcohol Review, 21*, 341–348.

Vincent, N., Shoobridge, J., Ask, A., Allsop, S., & Ali, R. (1998). Physical and mental health problems in amphetamine users from metropolitan Adelaide, Australia. *Drug and Alcohol Review, 17*, 187–195.

Volkow, N. D., Chang, L., Wang, G. J., Fowler, J. S., Franceschi, D., Sedler, M., et al. (2001). Loss of dopamine transporters in methamphetamine abusers recovers with protracted abstinence. *Journal of Neuroscience, 21*, 9414–9418.

Volkow, N. D., Chang, L., Wang, G. J., Fowler, J. S., Leonido-Yee, M., Franceschi, D., et al. (2001). Association of dopamine transporter reduction with psychomotor impairment in methamphetamine abusers. *American Journal of Psychiatry, 158*, 377–382.

Watson, R., Hartmann, E., & Schildkraut, J. J. (1972). Amphetamine withdrawal: Affective state, sleep patterns, and MHPG excretion. *American Journal of Psychiatry, 129*, 263–269.

White, R. (2000). Dexamphetamine substitution in the treatment of amphetamine abuse: An initial investigation. *Addiction, 95*, 229–238.

Wyatt, S. A., & Zidonis, D. (1998). Psychological and psychiatric consequences of amphetamines. In R. E. Tarter, R. T. Ammerman, & P. J. Ott (Eds.), *Handbook of substance abuse: Neurobehavioural pharmacology* (pp. 529–544). New York: Plenum Press.

Yui, K., Goto, K., Ikemoto, S., & Ishiguro, T. (2000). Stress induced spontaneous recurrence of methamphetamine psychosis: The relation between stressful experiences and sensitivity to stress. *Drug and Alcohol Dependence, 58*, 67–75.

Zweben, J. E., Cohen, J. B., Christian, D., Galloway, G. P., Salinardi, M., Parent, D., et al. (2004) Psychiatric symptoms in methamphetamine users. *American Journal on Addictions*, *13*, 181–190.