Unrestricted access to methamphetamine or cocaine in the past is associated with increased current use

C. Culbertson, R. De La Garza II, M. Costello and T. F. Newton

1 David Geffen School of Medicine at the University of California Los Angeles, Department of Psychiatry and Biobehavioral Sciences, Los Angeles, CA, USA
2 Baylor College of Medicine, Department of Psychiatry and Behavioral Sciences, Houston, TX, USA

Abstract

Laboratory animals allowed to self-administer stimulants for extended periods of time escalate drug intake compared to animals that self-administer under temporally limited conditions. To our knowledge, this phenomenon has not been systematically investigated in humans. We interviewed 106 (77 male, 29 female) methamphetamine (Meth) and 96 (81 male, 15 female) cocaine (Coc) users to determine if they had experienced discrete period(s) of unrestricted access to unlimited quantities of Meth or Coc in the past. Fifty-eight Meth users and 53 Coc users reported having a discrete period of unrestricted access in the past, but not in the present. Meth-using participants with a prior history of unrestricted access reported significantly more current Meth use, compared to Meth users with no prior history of unrestricted access. Specifically, these participants reported more days used in the past 30 d, more days of use per week, greater use per day and greater total use per week ($p < 0.05$ for each). Coc-using participants with a prior history of unrestricted access also reported significantly more current Coc use, compared to Coc users with no prior history of unrestricted access. This was true across all measures of current use for these participants, including more days used in the past 30 d, more days of use per week, greater use per day, and higher total use per week ($p < 0.02$ for each). Taken together, these results suggest that a history of unrestricted access to stimulants is associated with long-lasting increases in stimulant use.

Key words: Cocaine, methamphetamine, unrestricted access.

Introduction

Stimulant abuse presents a significant health problem on an international scale. In the United States alone, approximately 5 million individuals reported past month use of a stimulant in 2006. Illicit substances including cocaine (Coc), crack-cocaine and methamphetamine (Meth) accounted for 75% of this recent use (SAMHSA, 2007). Regular use of these stimulants commonly leads to addiction, which is defined as a chronically relapsing disorder characterized by compulsive drug-taking behaviour with impairment in social and occupational functioning (Koob and Kreek, 2007). Numerous factors including genetics, environment and, as examined here, prior drug exposure contribute to the development of stimulant addiction (Compton et al., 2005; Ellenbroek et al., 2005; Haile et al., 2007).

Stimulants such as Meth and Coc exert changes on neurological systems responsible for cognition, reward, and conditioned learning (Everitt et al., 2001; Jentsch and Taylor, 1999; Koob and Le Moal, 1997; Robinson and Berridge, 1993; Vanderschuren and Everitt, 2004). Animal models of drug self-administration using 1-h (short access; ShA) and 6-h (long access; LgA) sessions have been developed to examine limited vs. extended stimulant use. The intention of this research is to gain a better understanding of the...
neurological and behavioural adaptations that accompany a transition from drug abuse (e.g. ShA) to drug dependence (e.g. LgA). Rodents allowed LgA to Coc and Meth demonstrate an escalation in stimulant intake when compared to ShA animals (Ahmed and Koob, 1998; Ben-Shahar et al., 2004; Kitamura et al., 2006) suggesting that extended access to stimulants perpetuates an increase in drug consumption. In addition, animals in the LgA Coc self-administration condition display a greater susceptibility to drug-induced reinstatement of drug seeking following extinction training when compared to ShA animals (Ahmed and Cador, 2006; Kippin et al., 2006; Mantsch et al., 2004). These findings imply that extended access to stimulants increases the incidence of relapse to drug-seeking and -taking following a period of abstinence. Increasing the unit dose of Coc available to LgA rodents further enhances drug intake and relapse susceptibility (Kitamura et al., 2006; Mantsch et al., 2003). Twenty-four-hour self-administration models utilizing discrete trials, which more closely model human drug-taking behaviour, have also demonstrated that increasing the availability of the drug (i.e. number of discrete trials per 24-h period and unit dose available) leads to an enhancement of drug intake over time (Morgan et al., 2002; Roberts et al., 2002). Although far less work concerning Meth has been conducted using this model, Kitamura and colleagues have shown a very similar escalation in Meth intake relative to the length of access and unit dose. Thus, differential access to stimulants (i.e. time and amount) produces distinct patterns of drug-taking behaviour in rodents.

Translating these preclinical findings to human models of addiction suggests that extended exposure to stimulants (i.e. LgA self-administration) might significantly increase future levels of drug consumption (i.e. escalation) and enhance susceptibility to relapse during periods of abstinence (i.e. higher rates of reinstatement). Humans may engage in extended stimulant use during a period of unrestricted access to Meth or Coc. Unrestricted access may occur under a variety of conditions including involvement in stimulant production, distribution, sales, or through personal relations with persons in the drug trade. Individuals with a history of unrestricted access provide an opportunity to investigate the effects of extended stimulant exposure in humans, compared to users that have no experience with unrestricted access. The purpose of the present study was to compare current drug-taking behaviour between Meth and Coc users with and without a prior history of unrestricted access.

Materials and methods

Participants

Participants were recruited through advertisements and paid for their participation. Potential participants were first screened over the phone to determine eligibility, then scheduled to attend an in-person screening session at the University of California Los Angeles (UCLA). All of the subjects self-reported regular Meth or Coc use (but not both) and were not seeking treatment at the time of the interview. Other inclusion criteria included age between 18 yr and 55 yr, and having screened positive for Meth or Coc. All participants also self-reported no current medical problems, no prescribed drug use or history of psychiatric diagnosis. Participants included in this study provided informed consent for a study approved by the Institutional Review Board at UCLA. Participants reporting unrestricted access in the last 30 d were excluded from analysis in order to remove any overlap between recent unrestricted access and current drug-use patterns.

Study design

Participants attended a 1-d outpatient-screening interview at UCLA. During this visit, participants completed a series of questionnaires concerning demographics, health, mood, and drug use. Trained research staff also interviewed each participant to obtain additional information regarding past drug use.

Measures

Demographic information, years of drug use, and recent drug use were gathered using self-report questionnaires. Additional drug use information was obtained during an interview session in which participants were presented with six glass test tubes, randomly labelled 1–6, containing varying amounts (0.2 g, 0.6 g, 0.8 g, 1.0 g, 1.4 g, 1.8 g) of substances visually similar to Meth or Coc. Blinded to the actual amount in each vial, participants were asked to identify the vial that best represented the amount of drug they use in a typical day and, on average, how many days they used per week. These two factors (i.e. amount used per day, and days of use per week on average) were combined to determine the average amount of drug used per week. To obtain a measure of cue-induced craving, participants were presented with a different set of six glass test tubes, randomly labelled A–F, containing a variety of powder substances intended to resemble Meth or Coc. Blinded to the actual substance in each vial, participants were
asked to identify the vial that most resembled their drug of choice. Once a vial was identified, participants were permitted to examine the vial for a short period (60 s), then asked to providing a craving rating from 0 (not at all) to 10 (the most possible). Depressive symptoms were assessed using the Beck Depression Inventory (BDI-II).

Next, participants were asked ‘Have you ever had a period in your life when you had unrestricted access to unlimited quantities of your drug of choice (i.e. Meth or Coc)?’ The investigator further explained this event as ‘a time when you were able to use as much Meth or Coc as you wanted with no restrictions or limits’. Those who accurately explained such an experience were prompted to describe the length of the unrestricted access period and how long ago the last episode occurred (i.e. the approximate date when the period began and ended). Only self-reported periods lasting $\geq$ 1 month were considered as a period of unrestricted access in order to distinguish between binge episodes and a period of long-term unrestricted access. Only participants whose period of unrestricted access ended $> 1$ month prior to the interview were included in the analyses since current unrestricted access would obviously influence all measures of current use.

**Data analysis**

The primary outcome measures of this study were self-reported unrestricted access to Meth or Coc and current Meth/Coc use. Second, we measured the length of unrestricted access, time since unrestricted access, and other drug use (e.g. alternate stimulants, alcohol, nicotine and marijuana) in the past 30 d. ANOVA was used to assess differences between the two groups (unrestricted access and no unrestricted access) on all measures. Bivariate correlations were also conducted to uncover relationships between related variables (significance was set at $p < 0.05$). A general linear model multivariate analysis (ANCOVA) was used to account for any variable found to be associated with current use and any differences in subject characteristics across the two groups.

**Results**

**Meth participants’ characteristics**

This study sample consisted of 105 Meth-using (76 male, 29 female) participants. Detailed demographic data and drug use information are provided in Table 1. Participants were predominantly male (72%) and Caucasian (64%), aged $\sim 39$ yr with $\sim 12$ yr of education. On average, participants used Meth for $\sim 12$ yr. The majority of participants smoked cigarettes regularly (87%), drank alcohol (70%) and smoked marijuana (51%) in the past 30 d. Few Meth users reported any use of Coc (18%) in the past 30 d.

Fifty-four out of 105 (51%) Meth-using participants reported a history of unrestricted access. These individuals reported a mean duration of $142 \pm 186$ (mean $\pm$ s.d.) wk of unrestricted access, with a range of 4–728 wk. Participants reported on average $195 \pm 154$ wk since the last period of unrestricted access, with a range of 4–728 wk. No participant reported current unrestricted access.

**Coc participants’ characteristics**

This study sample consisted of 94 Coc-using (80 male, 14 female) participants. Detailed demographic data
and drug use information are provided in Table 2. These participants were almost entirely male (85%) and predominately African American (60%) aged 41 yr with 13 yr of education. On average, participants used Coc for 15 yr. The majority of participants smoked cigarettes regularly (76%), drank alcohol (69%) and smoked marijuana (34%) in the past 30 d. Very few Coc users reported any Meth use (8%) in the last 30 d.

Fifty out of 94 (53%) Coc-using participants reported a history of unrestricted access. These individuals reported a mean duration of 104 ± 124 wk of unrestricted access with a range of 4–520 wk. Participants reported on average 586 ± 490 wk since their last period of unrestricted access, with a range of 4–1820 wk. No participant reported current unrestricted access.

### Table 2. Participants’ characteristics: cocaine

<table>
<thead>
<tr>
<th>Prior unrestricted access</th>
<th>Yes</th>
<th>No</th>
</tr>
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<tbody>
<tr>
<td>Gender (%)</td>
<td></td>
<td></td>
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<tr>
<td>Male</td>
<td>76</td>
<td>95</td>
</tr>
<tr>
<td>Female</td>
<td>24</td>
<td>5</td>
</tr>
<tr>
<td>Ethnicity (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (not Hispanic)</td>
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<td>16</td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>8</td>
<td>27</td>
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<tr>
<td>African American</td>
<td>66</td>
<td>52</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>42.2±1.2</td>
<td>39.4±1.4</td>
</tr>
<tr>
<td>Education (yr)</td>
<td>12.6±0.3</td>
<td>12.7±0.4</td>
</tr>
<tr>
<td>Substance use</td>
<td></td>
<td></td>
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<tr>
<td>Cocaine (%)</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Years use</td>
<td>17.8±1.2**</td>
<td>11.8±1.4†</td>
</tr>
<tr>
<td>Nicotine (%)</td>
<td>77</td>
<td>76</td>
</tr>
<tr>
<td>Years use</td>
<td>22.6±2.2*</td>
<td>15.8±2.3†</td>
</tr>
<tr>
<td>Cigarettes per day</td>
<td>12.7±1.2</td>
<td>11.1±1.6</td>
</tr>
<tr>
<td>Methamphetamine (%)</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>Days in last 30 d</td>
<td>3.0±2.0</td>
<td>5.8±2.1</td>
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<tr>
<td>Alcohol (%)</td>
<td>57</td>
<td>83</td>
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<tr>
<td>Days in last 30 d</td>
<td>11.3±1.8</td>
<td>12.8±1.6</td>
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<tr>
<td>Cannabis (%)</td>
<td>28</td>
<td>50</td>
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<tr>
<td>Days in last 30 d</td>
<td>15.1±3.5</td>
<td>11.5±2.6</td>
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<tr>
<td>Other</td>
<td></td>
<td></td>
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<tr>
<td>BDI-II score</td>
<td>13.4±1.8</td>
<td>16.3±2.0</td>
</tr>
<tr>
<td>Cue-induced craving (1–10)</td>
<td>3.4±0.5</td>
<td>3.1±0.4</td>
</tr>
</tbody>
</table>

Values represent mean ± S.E.M.  
* vs. † (p < 0.05), ** vs. †† (p < 0.01).

### Figure 1. Self-reported methamphetamine (Meth) or cocaine (Coc) use in participants with a history of unrestricted access (URA) vs. participants with no history of unrestricted access (no URA) (number of days used in the past 30 d and average number of days of use per week) (*p < 0.05, **p < 0.01).

### Figure 2. Self-reported methamphetamine (Meth) or cocaine (Coc) use in participants with a history of unrestricted access (URA) vs. participants with no history of unrestricted access (no URA) (amount used per day in grams and average amount used per week in grams) (*p < 0.05, **p < 0.01).

**Meth: unrestricted access and drug use**

Meth users with a history of unrestricted access reported significantly more days of use in the past 30 d ($F_{1,102} = 6.2$ $p = 0.014$), more days of use per week ($F_{1,100} = 21.1$ $p = 0.0001$) (Figure 1), greater use per day ($F_{1,101} = 5.2$ $p = 0.025$), and greater total use per week ($F_{1,100} = 12.3$ $p = 0.001$) (Figure 2), compared to Meth users with no history of unrestricted access. No significant difference in years of use was observed between these two groups. When controlling for years of
use, participants with a history of unrestricted access continued to report significantly more current use of Meth across all measures, compared to participants without a history of unrestricted access \( (p < 0.05 \text{ for each}) \). Participants with a history of unrestricted access had higher scores on the BDI-II than participants with no history of unrestricted access \( (F_{1,34} = 5.4, p = 0.027) \). However, no significant correlation was observed between BDI scores and current measures of Meth use. No significant difference was seen between participants with a history of unrestricted access and those without regarding cigarette, alcohol, marijuana and Coc use in the past 30 d or demographic measures including gender, education, and age. Additionally, no significant differences were observed in cue-induced craving between these groups.

**Coc: unrestricted access and drug use**

Coc users with a history of unrestricted access reported significantly more days of use in the past 30 d \( (F_{1,96} = 8.5, p = 0.004) \), more days of use per week \( (F_{1,96} = 7.4, p = 0.008) \) (Figure 1), greater use per day \( (F_{1,92} = 6.1, p = 0.015) \), more total use per week \( (F_{1,96} = 8.9, p = 0.004) \) (Figure 2) and more years of use \( (F_{1,90} = 10.7, p = 0.002) \), compared to Coc users with no history of unrestricted access. When controlling for years of use, participants with a history of unrestricted access continued to report significantly more current use of Coc across all measures, compared to participants without a history of unrestricted access \( (p < 0.05 \text{ for each}) \). Coc using participants with no history of unrestricted access reported significantly more alcohol use than participants with a history of unrestricted access \( (F_{1,82} = 4.3, p = 0.041) \). No significant difference was seen between participants with a history of unrestricted access and those without regarding cigarette, marijuana use and Meth use in the past 30 d or demographic measures including education, and age. Additionally, no difference was observed in BDI-II scores or cue-induced craving between these groups.

**Length of unrestricted access and time since unrestricted access**

No relationship was observed in Meth users with a history of unrestricted access between the length of unrestricted access and days used in the past 30 d \( (r = 0.09, p = 0.57) \), days use per week \( (r = -0.02, p = 0.92) \), use per day \( (r = 0.09, p = 0.25) \) or amount of Meth use per week \( (r = 0.23, p = 0.14) \). No relationship was observed between time since unrestricted access and days used in the past 30 d \( (r = 0.01, p = 0.94) \), days use per week \( (r = -0.14, p = 0.35) \), use per day \( (r = -0.05, p = 0.76) \) and total use per week \( (r = -0.09, p = 0.55) \). Similarly, no relationship was observed in Coc users between the length of unrestricted access and days used in the past 30 d \( (r = -0.13, p = 0.40) \), days use per week \( (r = 0.06, p = 0.72) \), use per day \( (r = 0.09, p = 0.58) \), and total use per week \( (r = 0.05, p = 0.76) \), or time since unrestricted access and days used in the past 30 d \( (r = 0.23, p = 0.17) \), use per day \( (r = 0.10, p = 0.56) \), and total use per week \( (r = 0.24, p = 0.15) \). However, a significant positive correlation was observed between time since unrestricted access and days use per week \( (r = 0.38, p = 0.02) \) in Coc users.

**Years of use and current use**

A significant positive correlation was observed in all Meth users (i.e. unrestricted access and no unrestricted access) between years of use and days used in the past 30 d \( (F = 0.29, p = 0.003) \) and days use per week \( (r = 0.27, p = 0.007) \). Coc users also demonstrated a significant correlation between years of use and days used in the past 30 d \( (r = 0.24, p = 0.020) \) and days use per week \( (r = 0.25, p = 0.016) \).

**Measures of current use**

Meth users demonstrated a significant positive correlation between days used in the past 30 d and days use per week \( (r = 0.77, p = 0.000) \) and total use per week \( (r = 0.40, p = 0.000) \). Similarly, Coc users displayed a significant correlation between days used in the past 30 d and days use per week \( (r = 0.86, p = 0.000) \), use per day \( (r = 0.25, p = 0.017) \), and total use per week \( (r = 0.53, p = 0.000) \).

**Discussion**

Coc- and Meth-using participants with a history of unrestricted access reported significantly greater current Coc or Meth use, respectively, compared to participants with no history of unrestricted access. Meth-using participants with a history of unrestricted access reported increases in Meth consumption across all measures of current use when compared to Meth users with no history of unrestricted access. Similarly, Coc-using participants with a history of unrestricted access reported consuming more Coc on all measures and reported using for a greater number of years, compared to Coc users with no unrestricted access. Both Meth and Coc users showed a positive relationship between the years of use and current stimulant use. These results demonstrate that a self-reported period of unrestricted access (i.e. extended exposure to Meth...
and Coc) is associated with greater Meth or Coc use in the future.

The findings reported here parallel the extensive animal literature on LgA vs. ShA stimulant self-administration, which provides theoretical constructs to help explain the possible causes for the link between extended access and an escalation in consumption. Robinson and Berridge (1993) proposed that extended exposure to high doses of stimulants sensitizes mechanisms involved in the attribution of incentive salience, thus transforming drug wanting into intense craving, which then drives drug-taking behaviour in the absence of positive or negative reinforcement. Cue-induced craving was assessed in the present study to determine the effect of unrestricted access on craving for Meth or Coc. No differences were observed in Meth or Coc participants with and without a history of unrestricted access. These results are difficult to interpret due uncontrolled, individual specific variables including time of abstinence (i.e. withdrawal) (Newton et al., 2004) and availability of Meth or Coc (Yamamoto et al., 2007). More sophisticated methods of inducing cue reactivity in a controlled setting (Newton et al., 2006) would better elicit the role unrestricted access plays in altering subsequent craving for stimulants.

Markou and colleagues (1993) further defined drug craving as a manifestation of incentive motivation to consume psychoactive substances following repeated use. Although craving may not be directly measured in rodents, progressive ratio self-administration paradigms have been designed to measure the reinforcing efficacy and the underlying motivation to self-administer drugs of abuse (Markou et al., 1993). For example, LgA rodents displayed higher breaking points under a progressive ratio schedule for cocaine self-administration and an upward shift in the dose–response function when compared to ShA rodents (Paterson and Markou, 2003). Morgan et al. (2002) demonstrated similar changes in the reinforcing efficacy of cocaine using a progressive ratio schedule following exposure to self-administration with varying drug-exposure schedules (i.e. fixed ratio vs. discrete trials). These results demonstrate an increase in the reinforcing efficacy of cocaine following extended-access self-administration paradigms. Furthermore, this supports the incentive motivation hypothesis by demonstrating that ‘unrestricted’ rodents possess a greater motivation to obtain cocaine (i.e. will produce greater behavioural output for reward) compared to rodents with more restrictive access. Current use patterns measured in the present study may serve as a measure of the reinforcing efficacy of Meth or Coc and an indirect measure of motivation to obtain the drug. In this case, the results presented here suggest that a history of unrestricted access to Meth or Coc increases the reinforcing value of Meth or Coc in the future and may also reflect an enhanced motivation to seek, obtain and use the drug. However, these findings fail to extend to other substances of abuse, which also target neurobiological substrates within mesocorticolimbic regions known to mediate reward (Wise, 1996). In particular, participants with a history of unrestricted access reported similar levels of nicotine, alcohol, cannabis, and alternate stimulant use in the past 30 d when compared to participants with no unrestricted access. Interestingly, only a small portion of Meth-using participants reported Coc use in the past 30 d. Additionally, those reporting Coc use only reported a few days of use per month on average. An identical trend was seen in Coc-using participants regarding Meth use. This finding suggests that any increase in the reinforcement efficacy or sensitization to the motivational system produced during extensive stimulant exposure in humans is specific to the stimulant of choice (i.e. Meth or Coc) and not simply a sensitization of the general reward system.

An alternate theory, based on preclinical models of operand conditioning, suggests that a habitual stimulus–response behaviour develops with repeated exposure to stimulants causing drug taking to become compulsive (Everitt et al., 2001). LgA rodents demonstrated resistance to an aversive stimuli (e.g. foot shock) when paired with Coc self-administration while ShA animals displayed conditioned suppression of drug-seeking behaviour (i.e. no self-administration). No difference in the rewarding value of Coc, fear conditioning, or response capability was observed between the two groups suggesting that the LgA rodents develop inflexible and habitual drug-seeking behaviour (Vanderschuren and Everitt, 2004). According to this line of thought, a longer period of unrestricted access in humans would enhance habit learning and coincide with the development of compulsive drug-taking behaviour. However, we found no relationship between the length of unrestricted access and current drug use in Meth or Coc users with a history of unrestricted access. Habit learning may occur rapidly to intrinsically powerful reinforcements causing stimulus–response learning to develop even in participants with relatively limited drug exposure, which would cause a ceiling effect and explain the lack correlation observed in the present study.

Tolerance may play a significant role in enhancing current stimulant use in participants with a history of unrestricted access. Preclinical research has shown
that prolonged behavioural (Ben-Shahar et al., 2004, 2005), neurological (Ben-Shahar et al., 2006, 2007) and hormonal (Mantsch et al., 2003, 2004) tolerance to Coc develops in LgA animals while ShA animals typically display a sensitized response. Using discrete trials procedures, Roberts and colleagues demonstrated that sustained exposure to high levels of cocaine produced a rightward shift in the dose curve, suggesting that extended exposure leads to the development of enhanced tolerance. We observed no consistent relationship between the time since unrestricted access and current use. Therefore, tolerance developed during unrestricted access may be maintained over an extended period of time and prolonged by the continued use of stimulants after the period of unrestricted access has ended.

The model of allostasis proposed by Koob and colleagues indicates that chronic stimulant use dysregulates the brain’s natural reward circuitry (as stated above), which lowers the hedonic set point through opponent processes (Koob, 1996; Koob and Le Moal, 1997). During Coc abstinence, rodents previously exposed to LgA Coc self-administration sessions displayed greater reductions in brain reward function, determined by a 30% increase in intracranial self-stimulation threshold, while ShA animals remained stable (Ahmed et al., 2002; Ahmed and Koob, 1998). Theoretically, LgA animals experience a decreased basal hedonic state after extended exposure to Coc and require more stimulation in order to achieve the same reward state that ShA animals experience with less stimulation. The results presented here support this hypothesis in a human population by demonstrating that unrestricted access is associated with greater future drug consumption.

Along these same lines, Meth-using participants with a history of unrestricted access had significantly higher depressive symptom scores than participants with no unrestricted access. This suggests that unrestricted access to Meth is associated with a decrease in basal mood levels, which may play a role in enhancing stimulant use. However, no such effect was observed in Coc users. A number of uncontrolled variables including time since last use, withdrawal and social stressors may have influenced the acute level of depressive symptoms reported by participants (Newton et al., 2004). As a secondary measure of basal hedonic state we examined current use of other substances of abuse. Individuals experiencing a lowered hedonic state may abuse or self-medicate with alcohol, nicotine cannabis or alternate stimulants in an attempt to balance the natural reward system in the absence of the stimulant of choice. However, these results were not observed in either of our populations. As such, no definitive conclusions can be made with regard to unrestricted access and long-term alterations to mood.

There are several limitations that should be noted regarding this study. The data reported here are based primarily on self-report. Thus memory, particularly in individuals that regularly abuse Meth or Coc, may be problematic for events that occurred many years prior to interview (Jovanovski et al., 2005; Scott et al., 2007). For this reason, we did not include self-report of Meth or Coc use during unrestricted access. Self-reported length of unrestricted access and time since unrestricted access cannot be validated, but still possess face validity. Over long periods of time it may be difficult for participants to recall the exact dates of unrestricted access, but they vividly recall experiencing a time of unrestricted access and recount significant life events that occurred during this period. No standardized categorization of unrestricted access exists, and therefore the method used in the present study is somewhat arbitrary by necessity. However, the consistency observed across a large and diverse population of Meth and Coc users with respect to a history of unrestricted access and current stimulant use implies the construct validity of this measure. Additionally, strong correlations were observed between all measures of current use in Meth and Coc users, demonstrating the ability of these individuals to accurately describe their current patterns of drug use. Future studies concerning unrestricted access should include recreational Meth and Coc users as well to gain an even broader understanding of the transitory states of stimulant addiction. The findings reported here generally coincide with the extensive preclinical literature regarding extended vs. controlled stimulant self-administration despite the obvious and inescapable differences in experimental design. Rodent self-administration paradigms including a more diverse spectrum of exposure lengths would more closely model the human population examined in the current study. Collecting longitudinal data on stimulant users that spanned from before to after unrestricted access would greatly contribute to understanding how such an event affects future drug use patterns. Additionally, assessing Meth and Coc users with and without a history of unrestricted access in a controlled laboratory setting would allow for a much closer examination into the structural, neurocognitive, and behavioural consequences of extended access to stimulants. None of these limitations, however, would have artificially produced the main finding of this study – that Meth or Coc users reporting a discrete period of unrestricted access in the past report...
significantly more current use of Meth or Coc, respectively. The results presented here demonstrated that prior unrestricted access to Meth or Coc is associated with an increase in current Meth or Coc consumption. Future studies need to examine neurological and behavioural differences between stimulant users with and without a history of unrestricted access to further decipher the consequences of unrestricted access. Such findings may provide insight into factors that lead from experimental stimulants use to addiction and guide novel preventative treatments for stimulant addiction.

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Statement of Interest

None.

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