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Increased self-reported impulsivity in methamphetamine users maintaining drug abstinence

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Abstract

Background—Impulsivity has been proposed as an important factor in the initiation and maintenance of addiction. Indirect evidence suggests that some methamphetamine users report less impulsivity when they are using methamphetamine compared to when abstinent, but this hypothesis has not been directly tested.

Objectives/Methods—In this study, self-reports of impulsivity were obtained from 32 methamphetamine-dependent (DSM-IV) research participants and 41 healthy control subjects, using the Barratt Impulsiveness Scale-11. The methamphetamine users were assessed during an active period of methamphetamine use, as determined through urinalysis, and again after approximately one week of confirmed abstinence. Control subjects likewise completed two assessments. A subset of participants also completed serial assessments of the Beck Depression Inventory (Methamphetamine Group, $N = 17$, Control Group, $N = 38$) and the Methamphetamine Withdrawal Questionnaire (Methamphetamine Group, $N = 12$).

Results—There was a significant interaction of group with time on impulsivity ($p = 0.044$), reflecting a significant increase from the first to the second assessment in the methamphetamine users ($p = 0.013$), but no change among healthy control subjects. In contrast, depressive and withdrawal symptoms significantly decreased between the first and second assessment in the methamphetamine users (p 's < 0.01). Change in impulsivity in methamphetamine users was not significantly correlated with change in withdrawal or depression (p 's > 0.05).

Conclusions—These findings suggest that methamphetamine users report more impulsivity when abstaining from drug use, an effect that is not significantly related to methamphetamine withdrawal. Attenuation of impulsivity may reinforce continued methamphetamine use in these individuals.

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Declaration of Interest

The investigators have no conflicts of interest or financial disclosures to report.

Keywords

Drug abuse; impulsivity; methamphetamine; withdrawal; self-medication; abstinence; stimulant

Introduction

Substantial evidence points to a link between substance abuse and impulsivity (1–3), with impulsivity theorized to be both a predisposing factor for substance use and a consequence of it (4–6). Indeed, in the DSM-5, substance use disorder is characterized by the failure to inhibit substance use despite recurrent negative consequences (7). In animals exposed to stimulants, impulsivity, inferred from performance on a delay-discounting task, predicts the degree of sensitivity to drug-induced reward (i.e., conditioned place preference) and proclivity for drug self-administration (8, 9). In human methamphetamine users, self-reported impulsivity predicts poor response to treatment (10).

When compared to healthy control subjects, methamphetamine users report higher levels of impulsivity. For example, using the Barratt Impulsiveness Scale-11 (BIS-11), briefly abstinent (i.e., clean for two days) methamphetamine-dependent subjects obtained significantly higher scores than age and gender-matched control subjects (3). Some evidence additionally suggests that treatment-seeking methamphetamine users have higher BIS-11 scores than treatment-seeking cocaine users (10), although cocaine users also have elevated scores relative to healthy comparison subjects (11).

Although impulsivity is typically regarded as a multi-factorial personality trait, research has indicated that impulsivity may vary over time as a function of state-dependent and contextual factors, including drug intoxication, recency of drug use and withdrawal (4). Studies have found, for example, that recent stimulant use reduces impulsivity on behavioral measures tapping various aspects of the impulsivity construct. Acute administration of either *d*-amphetamine or methamphetamine reduces the discounting of delayed rewards by human subjects who do not use drugs (12) and by rats (13). Administration of methylphenidate to cocaine users reduces their errors of commission on a color-identification task, suggestive of improved inhibitory control (14). Cocaine users also exhibit better performance on tests of attention and working memory, which require self-control, after recent cocaine administration relative to assessments taken during abstinence (15–17), although non-significant effects of recent cocaine use on cognition have also been noted (18).

While the above findings may suggest that methamphetamine users would also self-report lower levels of impulsivity when they were actively using methamphetamine compared to when abstinent, relatively little research has examined this issue. In a cross-sectional study of methamphetamine-dependent participants abstinent for various durations, subjects who were abstinent for 30 days reported non-significantly higher scores on the BIS-11 than those who were abstinent for 6 days, possibly suggesting a subtle reduction in impulsivity from recent use (19). On the other hand, a longitudinal study of cocaine users showed that those who decreased their cocaine use over one year tended to report decreased impulsivity on the BIS-11, while those who increased their use tended to report increased impulsivity (20).

These longitudinal results are contrary to the aforementioned literature, and may reflect differences in the acute versus chronic effects of stimulant use on impulsivity.

The goal of the current longitudinal study was to evaluate whether methamphetamine-dependent subjects' (N = 32) self-reported impulsivity changes between the period of recent methamphetamine use (i.e., demonstrated by urine toxicology) and a week of confirmed abstinence (6.78 ± 2.95 days). Based on the aforementioned literature, we hypothesized that impulsivity would increase with abstinence. Healthy control participants (N = 41) were also evaluated at similar timeframes to control for effects of repeated test exposure. Impulsivity was assessed with the BIS-11; although this measure is often used to measure trait impulsivity, recent evidence suggests that it is sensitive to changes in impulsivity induced by behavioral intervention (21). Finally, symptoms of methamphetamine withdrawal and depression were also longitudinally assessed to determine whether withdrawal symptoms were associated with changes in impulsivity. During early abstinence (e.g., the first two weeks), methamphetamine users commonly show elevated scores on measures of withdrawal and depression (i.e., Methamphetamine Withdrawal Questionnaire; Beck Depression Inventory; 22), so we sought to evaluate whether these changes were coincident with potential alterations in impulsivity.

Method

Participants and Procedure

Thirty-two methamphetamine-dependent subjects, who were not seeking treatment, and 41 healthy control subjects participated (Table 1). Participants were initially recruited for studies of brain structure and cognition (e.g., 23, 24). Nine subjects participated in a previous study of methamphetamine withdrawal symptoms (22). All participants were fluent in English, received a thorough description of study procedures, and provided written informed consent, consistent with UCLA Institutional Review Board guidelines. Twenty-two of the methamphetamine-dependent subjects completed the study as inpatients at the UCLA General Clinical Research Center (GCRC), and the other participants completed the study on a nonresidential basis after closure of the GCRC. All participants completed medical and psychiatric screening procedures, including the Structured Clinical Interview for DSM-IV (SCID-IV) for Axis I diagnoses, and were medically healthy, unmedicated and without major comorbid psychiatric conditions. For a more detailed description of exclusionary criteria see previous manuscripts (22, 23).

Participants in the Methamphetamine Group tested positive for methamphetamine at the first assessment, and tested negative for methamphetamine and other illicit substances (amphetamine, opiates, cocaine, benzodiazepines) at the second assessment (control participants tested negative at all time points). Given the long duration in which marijuana can be detected through urinalysis, brief abstinence from marijuana for nonresidential participants was verified through saliva testing (Oratect, Grapevine, TX), with all participants endorsing at least 4 days of abstinence at re-testing (however, rates of marijuana use for both groups were low; see Table 1). Abstinence for residential participants was supervised. Both residential and non-residential subjects were allowed to smoke cigarettes *ad libitum*.

Methamphetamine Group subjects reported a mean of 0.87 days since last methamphetamine use at first administration of BIS-11 ($SD = 1.01$; Range 0 to 3) and 6.78 days of abstinence from methamphetamine when re-tested ($SD = 2.95$; Range 3 to 16). A subset of participants were also twice administered the Beck Depression Inventory (BDI; 38 Control and 17 Methamphetamine) and the Methamphetamine Withdrawal Questionnaire (MAWQ; 12 Methamphetamine), reporting an average of 0.69 and 0.50 days since last methamphetamine use at the first administration ($SDs = 0.79$ and 0.67 ; respectively, Ranges 0 to 2), and an average of 8.01 and 5.00 days of abstinence at retesting, respectively ($SD = 1.57$; Range 6 to 12; $SD = 1.48$; Range 3 to 7, respectively).

Measures

Barratt Impulsiveness Scale-11 (25)—The Barratt Impulsiveness Scale-11 is a 30-item measure with a four-point Likert-type response style that is commonly used to assess impulsivity. Original research suggested that it was comprised of three primary subscales—attentional impulsiveness, motor impulsiveness and non-planning impulsiveness (25). However, more recent psychometric analysis has failed to support the dimensionality of the original subscales, both in community samples (26) and methamphetamine users (27). Based on factor analysis, a new bifactor model has been proposed with subscales reflecting “cognitive impulsivity” and “behavioral impulsivity” (see 26). We used as our primary dependent measure the total BIS-11 score, with subscales analyzed post-hoc using the bifactor model. Test-retest reliability of the BIS in our study was adequate ($r = 0.874$).

Beck Depression Inventory (28)—The BDI is a 21-item multiple-choice measure of recent depression-related symptoms that is widely used as a screener for depression.

Methamphetamine Withdrawal Questionnaire—The MAWQ is a 30-item measure with a four-point Likert-type response style that assesses methamphetamine withdrawal symptoms. The MAWQ is an adapted version of the Amphetamine Withdrawal Questionnaire (29), which includes additional symptoms that are common in methamphetamine withdrawal (e.g., anger, headache) (22).

Statistical Analyses

Demographic differences between methamphetamine and control subjects were tested using chi-square or t -tests, as appropriate. Changes in impulsivity over time by group were analyzed with mixed-design repeated-measure ANOVAs. Post-hoc paired t -tests were used to evaluate within group changes in impulsivity.

Results

Demographic Analyses

The Methamphetamine and Control Groups did not significantly differ in age, education, mother's education, ethnicity, gender, recent alcohol or marijuana use, all $ps > .05$ (Table 1). The Control Group had fewer cigarette smokers ($p < 0.001$) and a longer time interval between BIS-11 administrations ($p = 0.001$) than the Methamphetamine subjects (e.g., control subjects tended to reschedule their appointments). However, smoking status, cigarettes

smoked per day, and the time interval between BIS-11 assessments were not significantly related to change in BIS-11 scores over time, $p>0.05$. Days of methamphetamine use in the last 30 days, years of methamphetamine use, and grams of methamphetamine used in the week before the study were not associated with BIS-11 change scores, nor BIS-11 scores at either time point, $p>0.05$.

Impulsivity Analyses

A significant interaction was observed between group and time on BIS-11 scores ($F(1, 71)=4.19, p=0.044$), in addition to significant main effects of group ($F(1, 71)=26.10, p<.001$; Methamphetamine mean=68.97, $SE=1.85$; Control mean=56.35, $SE=1.64$), and time ($F(1, 71)=7.14, p=0.009$; Time 1 mean=61.67, $SE=1.25$; Time 2 mean=63.65, $SE=1.33$). Post hoc analysis of the interaction revealed that Methamphetamine Group subjects significantly increased in impulsivity from Time 1 (mean=67.22, $SD=11.21$) to Time 2 (mean=70.72, $SD=11.59$; $t(31)=-2.63, p=0.013$; Cohen's $d = 0.463$), while Control Group scores remained stable between Time 1 (mean=56.12, $SD=10.12$) and Time 2 (mean=56.59, $SD=10.97$; $t(40)= -0.58, p=0.566$; Cohen's $d=0.095$; see Figure 1A).

Post-hoc analysis of the revised BIS-11 subscales (26) revealed no statistically significant interactions between group and time on the "cognitive impulsivity" subscale ($F(1, 71)=0.87, p=0.355$) or the "behavioral impulsivity" subscale ($F(1, 71)=1.85, p=0.178$). On the original BIS-11 subscales, a significant group by time interaction was observed on the attentional impulsivity subscale ($F(1, 71)= 8.91, p=0.004$), while no significant interactions were observed on the motor or nonplanning subscales ($p>.40$). As before, the interaction on the attentional impulsivity subscale reflected the Methamphetamine Group subjects significantly increasing in impulsivity from Time 1 to Time 2 ($p=0.005$), while the Control Group remained stable over time ($p=0.904$).

Analyses of Depression and Withdrawal

A significant interaction was observed between group and time on BDI scores, ($F(1, 53)=49.73, p<0.001$). Main effects were also observed for group ($F(1, 53)=46.33, p<0.001$; Methamphetamine mean=8.35, $SE=0.82$; Control mean=1.53, $SE=0.54$) and time ($F(1, 53)=42.21, p<0.001$; Time 1 mean=6.94, $SE=0.59$; Time 2 mean=2.93, $SE=0.57$). Post hoc analysis revealed a significant decrease in BDI scores for Methamphetamine Group subjects from Time 1 (mean=12.53, $SD=6.76$) to Time 2 (mean=4.18, $SD=5.02$; $t(17)=5.44, p< 0.001$; Cohen's $d = 1.355$), while BDI scores for Control Group subjects remained unchanged from Time 1 (mean=1.39, $SD=2.05$) to Time 2 (mean=1.74, $SD=3.38$; $t(37)= -0.74, p=0.467$; Cohen's $d=0.133$; see Figure 1B).

In the Methamphetamine Group alone, methamphetamine withdrawal symptoms significantly decreased over time (MAWQ; Time 1 mean=9.58, $SD=5.13$; Time 2 mean=5.08, $SD=4.85$; $t(11)=3.13, p=0.010$; Cohen's $d = 0.902$; see Figure 1C). In the Methamphetamine Group, change in withdrawal and depression scores were not significantly correlated with change in BIS-11 scores ($p>0.05$).

Discussion

Compared to an assessment taken after recent use of methamphetamine (verified by positive urine toxicology), impulsivity self-reported by methamphetamine-dependent subjects was significantly higher following approximately a week of abstinence from drugs. In contrast, impulsivity among control subjects remained stable over time. In approximately the same testing timeframe, methamphetamine subjects also reported significant *decreases* in depression and methamphetamine withdrawal during early abstinence, suggesting that the increase in impulsivity observed during early abstinence was not due to the acute emotional or physical effects of methamphetamine withdrawal.

These findings provide tentative support for the hypothesis that, in dependent individuals, recent stimulant use may reduce impulsivity, acting as a negative reinforcer to maintain drug use. This view is consistent with reports that recent stimulant use may attenuate pre-existing cognitive deficits (14–17), while nonetheless contributing to increased cognitive dysfunction with chronic use (5, 30, 31). Similarly, given that chronic stimulant use appears to exacerbate impulsivity (20), reductions in impulsivity associated with recent use are likely to be temporary and counterproductive in the long-term. Since BIS-11 scores predict poor treatment response in methamphetamine users (10), the current findings suggest that increases in impulsivity in early abstinence may also contribute to treatment non-response.

If recent methamphetamine use increases positive affect, it is possible that reductions in positive affect associated with abstinence increase methamphetamine users' proclivity toward rash action, including drug relapse. Although not specifically targeted by the BIS-11, more recent conceptualizations of the impulsivity construct include the measurement of "urgency", or impulsive behavior elicited to alleviate negative emotion (e.g., see the Urgency, Premeditation, Perseverance, and Sensation Seeking (UPPS) Impulsive Behavior Scale, 32). Recent evidence, for example, suggests that negative urgency moderates the relationship between negative emotion and symptoms of alcohol dependence (33). Although speculative, it is possible that negative urgency increases in the early stages of abstinence. Trends have been identified, for example, between urgency and the tendency to relapse in polysubstance users undergoing inpatient detoxification (34). In the current study, although depressive symptoms and withdrawal did not increase over the assessment period, it is possible that some other, unidentified form of negative affect was increased at the second assessment and facilitated the rise in impulsivity.

Recent psychometric evaluation of the original BIS-11 subscales has not supported their dimensionality (25, 26), and a new bifactor model of the BIS-11 has been proposed with "cognitive impulsivity" and "behavioral impulsivity" subscales (25). These subscales are comprised of 6 and 7 items, respectively, and exclude some of the 30 BIS items to eliminate redundancy and heterogeneity within the subscales (25). The present analysis, however, did not show significant group by time interactions for either of these subscales (p 's > 0.10). A significant group by time interaction was observed on the original attentional impulsivity subscale (24) ($p = 0.004$), but not the motor or nonplanning impulsivity subscales (p 's > 0.40). Because the attentional subscale is likely not unidimensional (25), it is unclear precisely what aspects of impulsivity are driving the current findings. Additional research is

needed to clarify how the factorial structure of the BIS-11 is related to real-world impulsive behavior.

Limitations of this study should be noted. Given that the current results were obtained using relatively small sample sizes, replication is recommended for confirmation of the findings, potentially using multiple measures for enhanced assessment of the multi-dimensional impulsivity construct. Further, it should be noted that the period of active methamphetamine use evaluated in this study is not synonymous with methamphetamine intoxication, as a positive urinalysis at baseline has a detection window of 72–120 hours (Alpha Scientific Designs, Poway, CA), with some subjects reporting using hours before the testing and others up to 3 days prior. As such, the potential reduction in impulsivity observed at baseline may not reflect an acute drug effect. In addition, because the methamphetamine users studied here were only abstinent for approximately one week at retesting, it will be important to determine if impulsivity remains elevated with longer periods of abstinence. Further, depressive symptoms and withdrawal were not always assessed on the same day as impulsivity (although usually within one or two days); therefore, it cannot be conclusively stated that these symptoms were unrelated to the increases in impulsiveness, although clear divergent trends were noted. Similarly, the duration of abstinence reported by outpatients ($N = 10$) was not directly observed, although it was generally consistent with the duration between their first assessment (when positive for methamphetamine on urinalysis) and their re-test date (when negative on urinalysis). Finally, because methamphetamine use was not experimentally manipulated, a causal link to reduction in impulsivity cannot be assumed, although this appears to be a plausible explanation.

The average increase in BIS-11 scores exhibited by methamphetamine users in the current study was approximately 3 points between the first and second assessments, although some individual subjects increased by 15 to 20 points. This average increase corresponds to a medium-range effect size (Cohen's $d = 0.463$, adjusted for dependent samples, 35). For reference, the difference in BIS-11 scores between methamphetamine users and control subjects at the first assessment was approximately 11 points (67.2 ± 11.2 ; 56.1 ± 10.1 , respectively). Given these data, the increase in impulsivity shown in the current study is, on average, likely to be of modest clinical significance, although a subset of users probably does exhibit meaningful alterations in impulsivity in abstinence. More data is needed regarding the correspondence between raw score differences on the BIS-11 and functional outcomes.

If the current data are replicated, it may be useful to target impulsivity in treatment not only in individual stages, but particularly as abstinence persists. Novel behavioral strategies are beginning to be explored for impulsivity reduction. For example, mindfulness meditation has shown some success in treating the disinhibition characteristic of adulthood attention-deficit hyperactivity disorder (ADHD, 36). Controlled breathing techniques and yoga-based strategies have been shown to reduce BIS-11 scores in adolescents (21). Goal management training, a type of cognitive rehabilitation which targets executive functions, has been shown to improve decision-making and response inhibition in patients with frontal lobe damage (37), but also in polysubstance users (38). Further exploring these strategies as adjuncts to treatment for methamphetamine use may prove fruitful.

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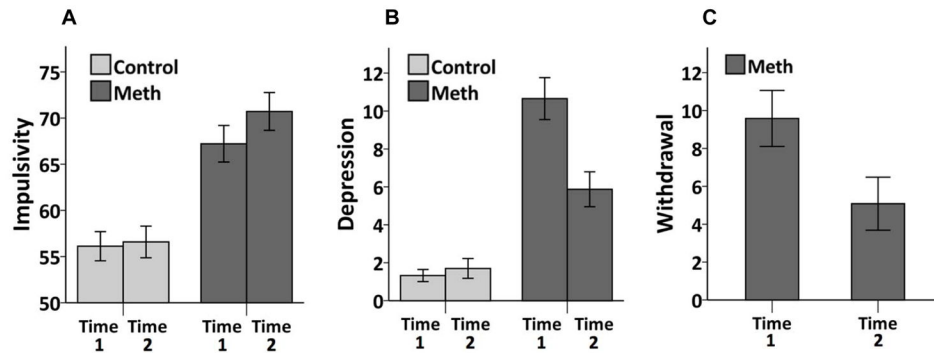


Figure 1. Changes in impulsivity, depression and withdrawal over time in methamphetamine users and control subjects

A. Methamphetamine users (Meth) ($N = 32$) show increased impulsivity over time ($p = 0.013$), while control subjects ($N = 41$) remain unchanged ($p = 0.566$). **B.** Methamphetamine users ($N = 17$) show decrease in depressive symptoms over time ($p < 0.001$), while control subjects ($N = 38$) show no change ($p = 0.467$). **C.** Methamphetamine users ($N = 12$) exhibit decrease in withdrawal symptoms over time ($p = 0.010$). Error bars represent ± 1 SEM.

Table 1

Characteristics of Research Participants

	Healthy Control	Methamphetamine-Dependent
Sample size	41	32
Age	34.2 ± 8.7	34.6 ± 10.8
Education (yr.)	13.0 ± 1.6	12.4 ± 1.3
Mother's Education (yr.)	12.6 ± 2.9	12.3 ± 3.2
Ethnicity		
Caucasian	15	16
African Am.	6	1
Hispanic	14	10
Other	6	5
Gender		
Male	23	17
Female	18	15
Cigarette Smokers (yes/no)	8/41	30/32***
Cigarettes/day (smokers only)	9.7 ± 7.3	12.5 ± 12.7
Days Alcohol/Past 30	1.9 ± 3.3	3.8 ± 6.6
Days Marijuana/Past 30	1.6 ± 5.2	3.3 ± 7.7
Days Methamphetamine/Past 30	--	20.7 ± 8.4
Duration of Methamphetamine abuse (yr.)	--	7.6 ± 6.0
Grams Methamphetamine/week	--	2.8 ± 3.0
Days between BIS Administrations	16.2 ± 7.2	10.5 ± 6.5** [†]
BIS 1 Total Score	56.1 ± 10.1	67.2 ± 11.2***
BIS 2 Total Score	56.6 ± 11.0	70.7 ± 11.9***

Note. Values are means ± *SDs*, where appropriate. The symbols, ** and ***, indicate significant differences from the respective control group at $p < 0.01$ and $p < 0.001$, respectively.

[†]For outpatient methamphetamine users, the days between BIS administrations were not always equivalent to the days of abstinence at retesting.