Published in final edited form as:

Am J Addict. 2009 ; 18(6): 481–487. doi:10.3109/10550490903205876.

Influence of Verbal Recall of a Recent Stress Experience on Anxiety and Desire for Cocaine in Non-Treatment Seeking, Cocaine-Addicted Volunteers

Richard De La Garza II, PhD, Liza H. Ashbrook, BA, Sarah E. Evans, PhD, Caitlin A. Jacobsen, BS, Ari D. Kalechstein, PhD, and Thomas F. Newton, MD

Baylor College of Medicine, Menninger Department of Psychiatry & Behavioral Sciences, Houston, Texas

Abstract

It has long been postulated that stress increases the risk of drug abuse and relapse. The principal goal of this project was to evaluate the effects of verbal recall of a recent stress experience (specifically meaningful to each individual) on physiological and subjective measures in cocaine-addicted participants. Subjects described a recent stressful non-drug-related experience and a neutral non-stressful experience, and then completed mood and drug effect questionnaires, while heart rate and blood pressure were recorded. Participants ($N = 25$) were predominantly African American and male. As a group, participants used cocaine for more than 15 years and ~18 of the last 30 days, and a majority reported use of nicotine and/or alcohol. All participants were evaluated during a time in which they tested positive for cocaine metabolite. On a scale of 1–10, participants reported their verbal recall of a recent stress event as highly stressful and their verbal recall of a recent neutral event as non-stressful ($p < 0.0001$). The self-reported vividness of this recall was high (>8 out of 10) for both the stress and neutral events. Heart rate and systolic and diastolic blood pressure did not differ after verbal recall of either stress or neutral events. Similarly, self-reported subjective effects (including ratings of anxiety and craving for cocaine) did not differ after verbal recall of either stress or neutral events. In summary, despite the fact that participants recounted highly stressful and vivid memories, this experience did not elicit significant changes in cardiovascular or subjective effects. These data suggest that simply recalling a stressful event may not be a sufficient enough stimulus to contribute to craving or relapse in cocaine-addicted individuals.

INTRODUCTION

The problem of cocaine dependence remains a major medical, social, and legal concern, yet some progress has been made since rates of cocaine dependence have declined since the 1980s and 1990s. According to the 2007 National Survey on Drug Use and Health, there were 906,000 persons aged 12 or older who had used cocaine for the first time within the past 12 months; this averages to ~2,500 initiates per day. Most (66%) of the 0.9 million recent cocaine initiates were 18 or older when they first used. The average age at first use among recent initiates aged 12 to 49 was 20.2 years. In 2007, an estimated 22.3 million persons aged 12 or older were classified with substance dependence or abuse in the past year

Copyright © American Academy of Addiction Psychiatry

Address correspondence to Dr. De La Garza, II, Baylor College of Medicine, DeBakey VAMC, Bldg 100 Room 5C-278, 2002 Holcombe Blvd., Houston TX 77030. rg12@bcm.edu.

Declaration of interest

The authors report no conflict of interest. The authors alone are responsible for the content and writing of the paper.

(9% of the population aged 12 or older). Of these, 1.6 million individuals met criteria for cocaine-dependence.

The reinforcing properties produced by cocaine are related to inhibition of transporters for dopamine (DA) and norepinephrine.¹ Increased firing and neurotransmitter release by DA neurons projecting from the ventral tegmental area (VTA) to the nucleus accumbens has been implicated as a mechanism contributing to reinforcement from food and other natural reinforcers, drugs of abuse, and electrical brain stimulation.²

The neurobiological circuits involved in stress appear to overlap with those involved in drug reward, and dysregulation of the hypothalamic pituitary adrenal (HPA) axis has been documented in drug-addicted individuals.³⁻⁴ A number of pre-clinical reports have demonstrated that the HPA axis plays a role in the reinforcing effects produced by cocaine.⁵⁻¹⁰ In humans, pharmacological (by administration of compounds like cortisol or the α 2-antagonist yohimbine) or psychological (by presentation of physical or emotional stressors) activation of the HPA axis is postulated to contribute to craving and may promote relapse. For example, acute cortisol administration triggered craving in individuals with cocaine dependence.^{11,12} In an outpatient clinical trial, dehydroepiandrosterone (a neurosteroid) treatment was associated with significantly higher levels of cortisol, increased probability of increased cocaine use, and decreased retention in treatment.¹³

Not all pre-clinical reports indicate a role for HPA axis activation in the effects produced by cocaine, however.¹⁴⁻¹⁷ In humans, the role for HPA axis activation in the effects produced by stimulants has also been questioned. Fischman and colleagues showed that neither cortisol nor dexamethasone altered the subjective effects of cocaine in cocaine abusers.^{18,19} In addition, treatment with metyrapone, an inhibitor of cortisol synthesis, suppressed baseline cortisol levels without significantly altering the subjective effects produced by cocaine.²⁰

Taken together, available data suggest that the subjective and reinforcing effects produced by cocaine are relatively independent of HPA axis activation. Recently, however, Sinha and colleagues have shown that stress imagery increased self-rated anxiety and cocaine craving.²¹⁻²⁷ While the specific mechanisms of stress imagery are unknown, laboratory studies using imagery of drug-related cues²⁸⁻³⁰ and internal cues^{22,24,31-33} have shown significant increases in drug craving and physiological reactivity. The data from Sinha and colleagues suggest that stress may induce relapse by increasing craving for cocaine. To expand on these efforts, the primary aim of this study was to evaluate the effects of verbal recall of a recent stress experience (specifically meaningful to each individual) on physiological and subjective measures in cocaine-addicted participants.

MATERIALS AND METHODS

Subjects

Twenty-five cocaine-dependent, non-treatment seeking volunteers were enrolled and met inclusion criteria using a randomized, within-subjects study design. Basic demographic and drug use information are presented in Table 1.

Volunteers were recruited through advertisements and were paid for their participation. All participants met DSM-IV-TR criteria for current cocaine dependence and were not seeking treatment at the time of the study. Diagnostic assessments were conducted by research staff who received formal training and certification. Participants were required to have recently used cocaine, documented by a positive urine test for benzoylecgonine, a longer lasting

metabolite of cocaine. One potential participant was excluded for not meeting this requirement.

Participants were required to comprehend all study procedures and to be able to describe a stressful situation not involving drugs. Five otherwise eligible participants were excluded for not meeting this criterion. Other exclusion criteria included a lifetime history of seizure disorder head trauma, dependence on other drugs (eg, alcohol) except for nicotine, or lifetime history or current Axis-I psychiatric disorder (eg, psychosis, depression, any anxiety disorder, bipolar disorder). Heart disease, asthma, Parkinson's disease, and other medical conditions were also exclusionary (one was excluded for this reason). Current use of psychotropic medications (eg, risperdone; two were excluded for this reason) or medications acting on the HPA axis were not allowed.

This study was conducted at The University of California Los Angeles (UCLA) and approved by the UCLA Medical Institutional Review Board and all subjects gave informed consent after being fully informed about potential risks of participation.

Study Design

Subjects came to UCLA medical center for one screening day and two study days. On the first day, after signing the informed consent form, potential subjects completed screening assessments. These included demographic and drug use information, the Addiction Severity Index-Lite, the Mini International Neuropsychiatric Interview (all modules), and the Substance Use Inventory. After determining that volunteers were eligible for the study, participants were invited to return for the study sessions.

We developed a novel paradigm to examine the effects of verbal recall of stress on craving in cocaine-dependent volunteers. Our experimental design differed considerably from that used by Sinha and colleagues since we did not include an extra session for acclimatization to the laboratory environment, relaxation training, and imagery training, and no manual was used. We feel that our simple paradigm of spontaneous, unrehearsed, first-person accounts more closely approximates what happens in the real world when an individual vividly recalls a stressful event.

Before the testing session, study participants completed the Beck Depression Inventory,³⁴ the Profile of Mood Status,³⁵ and the Brief Symptom Inventory.³⁶ On the study day, participants completed two sessions and the order was randomized among participants (Table 2). One session focused on a recent event identified as "most stressful" and the other session focused on a recent event identified as "non-stressful." One research assistant was in the room at the same time who sat behind the participant throughout the session. The assistant recorded vital sign measurements (using a Scout automatic monitoring system) and handed the participant questionnaires at specified time points as described in Table 2. A quiet atmosphere was maintained during the session and participants were instructed to not casually interact with the assistant, but to remain focused on the task and to not let external thoughts or noises distract them.

The assistant gave the participants specific examples of stressful events, including relationship breakups, or losing a job or housing. The participant was asked whether or not they had something in mind that would fit the criteria, and they invariably responded in the affirmative. The assistant then gave the participants specific examples of unacceptable events including being arrested for possession of illegal drugs or events that occurred while under the influence of drugs (as utilized by Sinha and colleagues²⁷).

Participants described the event, including specific details using verbal responses, and described feelings and sensory experiences. While the subject was given these basic instructions, the description of the event was basically open-ended, so each subject could have chosen a different descriptive style and content.

Perceived stress of the event must have been rated above an 8 on a scale from 1–10 to be included. As above, the assistant gave the participants specific examples of non-stressful events included going shopping, fixing a meal, or watching television. Again, the participant was asked whether or not they had something in mind that would fit the criteria, and they invariably responded in the affirmative. Perceived stress of these events must have been rated below a 2 on a scale from 1–10 to be included (as utilized by Sinha and colleagues²⁷).

During each session, participants were asked to close their eyes and visualize the experience as vividly as possible, as if it were really happening to them at that very moment. Recall and visualization of the event lasted five consecutive minutes. Before the session and at regular intervals for 60 min afterward, self-reported subjective effects and cardiovascular measures were assessed (described below). The descriptions provided by the participants during the laboratory sessions were not recorded by audio or video (in order to evaluate content later) since the IRB did not approve this aspect of the initial human subjects application. A written summary was made by the interviewer during the session, but these were qualitative in nature and therefore not included in the data analyses or discussion.

After the first session (and subsequent monitoring) was completed, subjects had a brief rest period and then the second recall session began (Table 2). If a participant described a stressful event during the first period, a non-stressful event was described during the second period, or vice-versa. The second recall period consisted of the same procedures as the first except that a different event was recounted and visualized. After sessions were completed, subjects were discharged.

Physiological and Subjective Measures

Physiological measures (heart rate, and systolic and diastolic blood pressure) were measured at baseline (–15 min) and at 5, 10, 15, 20, 30, 45 and 60 min after each recall session. This time course was selected on the basis of previous reports by Sinha and colleagues.²⁷

Subjective responses were assessed with the visual analog scale (VAS) and the Craving Questionnaire Now (CQ-Now). These were administered at baseline (–15 min) and 5, 15, 30 and 60 min after the recall session began.

For the VAS scale, subjects reported the degree to which they felt “any drug effect,” “high,” “good effects,” “bad effects,” “like cocaine,” “desire for cocaine,” “depressed,” “anxious,” “stimulated,” and “likely to use cocaine.” In response to each question, participants selected a multiple of 10 on a 0 to 100 scale.

For the CQ-Now, participants reported their craving on a 45-item questionnaire. Participants rated how much they agreed with each item on a 7-point Likert scale,³⁷ items included, for example, “I crave cocaine right now,” “I am thinking of ways to get cocaine” and “I am going to use cocaine as soon as possible.” The outcomes obtained using this instrument did not differ from those obtained using the VAS and were therefore not included in the final outputs shown in this manuscript.

Data Analysis

Data were analyzed using StatView 5.0 (SAS Institute, Inc.). Descriptive statistics were compiled for demographic variables and analyzed using appropriate non-parametric tests.

For physiological measures and subjective effects, data were analyzed as change from baseline since the greatest effects were observed at the 5 min post-procedure time point. Specifically, the maximum change occurred between baseline ($T = -15$ min) and immediately after the recall session ($T = 5$ min). This data analysis approach is similar to that used by other groups.^{27,38} These data were then analyzed using a one-way analysis of variance (ANOVA) with the neutral versus stress sessions analyzed as a within-subjects variable. Statistical significance was set at $p < 0.05$.

RESULTS

Participants were mostly male and African American (Table 1). All participants met DSM criteria for cocaine dependence and their preferred route of cocaine use was smoking (100%). In addition to frequent cocaine use, a majority of participants were cigarette smokers and frequent users of alcohol, though none met dependence criteria for alcohol.

Ratings of “perceived stress” for stressful events were significantly higher than ratings of “perceived stress” for neutral events ($F_{1,48} = 3244$, $p < 0.0001$) (Figure 1). Ratings for “imagery vividness” did not differ during recall between stressful and neutral events and were above 8 on a scale from 1 to 10 ($F_{1,48} = 0.8$, $p = 0.39$).

The verbal recall of recent stress induced similar changes in heart rate and blood pressure as compared to recall of a neutral event (p 's $> .05$) (Table 3). The verbal recall of recent stress also induced similar changes in self-reported subjective effects as compared to the recall of a neutral event (p 's $> .05$) (Table 3).

DISCUSSION

In this study, participants recounted highly stressful events in the recent past which they rated as highly vivid, yet these did not elicit significant changes in blood pressure and heart rate, and did not elicit significant changes in positive or negative subjective effects.

Of interest, while some self-report subjective measures showed trends to increase in the stress versus neutral recall conditions (e.g., “anxious” and “stimulated”), the absolute changes from baseline were strikingly low (~5 out of 100 points on a VAS scale). Change in self-reported “desire for cocaine” reached only 6 out of 100 after the recall of a stress event, and this was not statistically different from the change after recall of the neutral event.

We created a novel paradigm loosely based on the stress imagery studies previously published by Sinha and colleagues.^{21–27} A very important question is why the current outcomes differ from those previously published by that group. Using the most parsimonious design we could construct, we asked participants to verbally recall a recent stress and a recent neutral event and then we recorded physiological and subjective effects immediately after. We did not include relaxation training or other factors that might contribute to the larger magnitude change observed in earlier studies. An important difference between our approach and that used previously is that Dr. Sinha's data focus on the role of stress in relapse among treatment-seeking patients, while our experimental approach provides information on the effects of verbal recall of a recent stress experience in producing craving in non-treatment-seeking volunteers. Related to this, Dr. Sinha's treatment-engaged patients were abstinent from cocaine for several days and sometimes weeks, whereas all participants included in the current study had recent self-reported use, which was confirmed by positive cocaine metabolite urine just prior to testing.

There are several limitations to this study. First, our sample consisted mostly of males, and others have shown gender differences in outcomes using the stress imagery protocol.²¹

Notwithstanding, in that study differences between genders were not observed following stress imagery, including anxiety and craving for cocaine. In a separate report, the same group used functional magnetic resonance imaging during the imagery tasks and showed greater left frontolimbic activation in females as compared to males.³⁹ Another shortcoming is the lack of lifetime stress assessment. We speculate that individuals who have chronic daily stressors (eg, homelessness) may exhibit blunted responses after visualizing a stressful experience, and this may confound data interpretation. Describing stressful events is aversive and there is a natural tendency to decrease aversiveness. Since we did not make a specific attempt to monitor participant's attempts to decrease aversiveness during recall this may have influenced outcomes.

The data reported clearly indicate that the procedure used did not induce any type of anxiety or mood change in the subjects. One explanation of this outcome is that the experimental procedures did not work to induce stress and that is the most likely explanation for the negative findings. The explanation we favor emphasizes that the goal of our experiment was not to induce a stress response or mood change, per se. Instead, our main goal was to model real-world experiences by evaluating whether recall of a recent stressful event would elicit physiological and subjective changes consonant with those described by other groups. We feel that acute recall of an event more closely approximates what "happens on the streets" and therefore more likely reflects how a person would respond (physiologically and behaviorally) after such an event. In our opinion, the negative findings do not mean that the experiment failed, but confirms that simply recalling a recent stressful event may not be sufficient to elicit physiological and behavioral changes that would contribute to craving or relapse in cocaine-addicted individuals.

In conclusion, the data in the current report coincide with previously published data in humans^{18–20,32} and non-human primates,^{14–17} and support the contention that the role of stress in cocaine use and relapse is not as straightforward as is often assumed. Thus, in future studies, we aim to identify the indirect links between exposure to stressful events and subsequent relapse. This study serves as an initial effort toward that goal.

Acknowledgments

This work was supported by grants DA 14593, DA 017182, DA 017754, and DA 17705 from the National Institutes of Health, Bethesda, Md (Dr. Newton).

The authors wish to thank Vicki Boss-Edwards, Cynthia Hurley, James J. Mahoney, III, and Matthew Costello for assistance with data collection.

References

1. Boghdadi MS, Henning RJ. Cocaine: pathophysiology and clinical toxicology. *Heart Lung*. 1997; 26:466–483. [PubMed: 9431493]
2. Bonci A, Bernardi G, Grillner P, Mercuri NB. The dopamine-containing neuron: maestro or simple musician in the orchestra of addiction? *Trends Pharmacol Sci*. 2003; 24:172–177. [PubMed: 12707003]
3. Goeders NE. The impact of stress on addiction. *Eur Neuropsychopharmacology*. 2003; 13:435–441.
4. Sinha R. The role of stress in addiction relapse. *Current Psychiatry Reports*. 2007; 9:388–395. [PubMed: 17915078]
5. Mantsch JR, Saphier D, Goeders NE. Corticosterone facilitates the acquisition of cocaine self-administration in rats: opposite effects of the type II glucocorticoid receptor agonist dexamethasone. *J Pharmacol Exp Ther*. 1998; 287:72–80. [PubMed: 9765324]

6. Deroche-Gamonet V, Sillaber I, Aouizerate B, et al. The glucocorticoid receptor as a potential target to reduce cocaine abuse. *J Neurosci*. 2003; 23:4785–4790. [PubMed: 12805318]
7. Ahmed SH, Koob GF. Cocaine- but not food-seeking behavior is reinstated by stress after extinction. *Psychopharmacology*. 1997; 132:289–295. [PubMed: 9292629]
8. Erb S, Shaham Y, Stewart J. Stress reinstates cocaine-seeking behavior after prolonged extinction and a drug-free period. *Psychopharmacology*. 1996; 128:408–412. [PubMed: 8986011]
9. Erb S, Shaham Y, Stewart J. The role of corticotropin-releasing factor and corticosterone in stress- and cocaine-induced relapse to cocaine seeking in rats. *J Neurosci*. 1998; 18:5529–5536. [PubMed: 9651233]
10. Leri F, Flores J, Rodaros D, Stewart J. Blockade of stress-induced but not cocaine-induced reinstatement by infusion of noradrenergic antagonists into the bed nucleus of the stria terminalis or the central nucleus of the amygdala. *J Neurosci*. 2002; 22:5713–5718. [PubMed: 12097523]
11. Elman I, Lukas SE. Effects of cortisol and cocaine on plasma prolactin and growth hormone levels in cocaine-dependent volunteers. *Addict Behav*. 2005; 30:859–864. [PubMed: 15833589]
12. Elman I, Lukas SE, Karlsgodt KH, Gasic GP, Breiter HC. Acute cortisol administration triggers craving in individuals with cocaine dependence. *Psychopharmacol Bull*. 2003; 37:84–89. [PubMed: 14608241]
13. Shoptaw S, Majewska MD, Wilkins J, Twitchell G, Yang X, Ling W. Participants receiving dehydroepiandrosterone during treatment for cocaine dependence show high rates of cocaine use in a placebo-controlled pilot study. *Exp Clin Psychopharmacol*. 2004; 12:126–135. [PubMed: 15122957]
14. Broadbear JH, Winger G, Cicero TJ, Woods JH. Effects of self-administered cocaine on plasma adrenocorticotrophic hormone and cortisol in male rhesus monkeys. *J Pharmacol Exp Ther*. 1999a; 289:1641–1647. [PubMed: 10336563]
15. Broadbear JH, Winger G, Woods JH. Cocaine-reinforced responding in rhesus monkeys: pharmacological attenuation of the hypothalamic-pituitary-adrenal axis response. *J Pharmacol Exp Ther*. 1999b; 290:1347–1355. [PubMed: 10454513]
16. Broadbear JH, Winger G, Woods JH. Self-administration of fentanyl, cocaine and ketamine: effects on the pituitary-adrenal axis in rhesus monkeys. *Psychopharmacology*. 2004; 176:398–406. [PubMed: 15114434]
17. Lee B, Tiefenbacher S, Platt DM, Spealman RD. Role of the hypothalamic-pituitary-adrenal axis in reinstatement of cocaine-seeking behavior in squirrel monkeys. *Psychopharmacology*. 2003; 168:177–183. [PubMed: 12652344]
18. Ward AS, Collins ED, Haney M, Foltin RW, Fischman MW. Ketoconazole attenuates the cortisol response but not the subjective effects of smoked cocaine in humans. *Behavioural Pharmacology*. 1998; 9:577–586. [PubMed: 9862083]
19. Ward AS, Collins ED, Haney M, Foltin RW, Fischman MW. Blockade of cocaine-induced increases in adrenocorticotrophic hormone and cortisol does not attenuate the subjective effects of smoked cocaine in humans. *Behav Pharmacol*. 1999; 10:523–529. [PubMed: 10780258]
20. Winhusen T, Somoza E, Harrer JM, et al. Metyrapone and cocaine: a double-blind, placebo-controlled drug interaction study. *Pharmacol Biochem Behav*. 2005; 80:631–638. [PubMed: 15820533]
21. Fox HC, Garcia M Jr, Kemp K, Milivojevic V, Kreek MJ, Sinha R. Gender differences in cardiovascular and corticoadrenal response to stress and drug cues in cocaine dependent individuals. *Psychopharmacology*. 2006; 185:348–357. [PubMed: 16514523]
22. Sinha R, Catapano D, O'Malley S. Stress-induced craving and stress response in cocaine dependent individuals. *Psychopharmacology*. 1999; 142:343–351. [PubMed: 10229058]
23. Sinha R, Fox H, Hong KI, Sofuoglu M, Morgan PT, Bergquist KT. Sex steroid hormones, stress response, and drug craving in cocaine-dependent women: implications for relapse susceptibility. *Exp Clin Psychopharmacol*. 2007; 15:445–452. [PubMed: 17924778]
24. Sinha R, Fuse T, Aubin LR, O'Malley SS. Psychological stress, drug-related cues and cocaine craving. *Psychopharmacology*. 2000; 152:140–148. [PubMed: 11057517]

25. Sinha R, Garcia M, Paliwal P, Kreek MJ, Rounsaville BJ. Stress-induced cocaine craving and hypothalamic-pituitary-adrenal responses are predictive of cocaine relapse outcomes. *Arch Gen Psychiatry*. 2006; 63:324–331. [PubMed: 16520439]
26. Sinha R, Lacadie C, Skudlarski P, et al. Neural activity associated with stress-induced cocaine craving: a functional magnetic resonance imaging study. *Psychopharmacology*. 2005; 183:171–180. [PubMed: 16163517]
27. Sinha R, Talih M, Malison R, Cooney N, Anderson GM, Kreek MJ. Hypothalamic-pituitary-adrenal axis and sympatho-adreno-medullary responses during stress-induced and drug cue-induced cocaine craving states. *Psychopharmacology*. 2003; 170:62–72. [PubMed: 12845411]
28. Robbins ST, Ehrman RN, Childress AR, O'Brien CP. Using cue reactivity to screen medications for cocaine abuse: a test of amantadine hydrochloride. *Addict Behav*. 1992; 17:491–499. [PubMed: 1332435]
29. Drobos DJ, Tiffany ST. Induction of smoking urge through imaginal and in vivo procedures: physiological and self-report manifestations. *J Abnorm Psychol*. 1997; 106:15–25. [PubMed: 9103714]
30. Carter BL, Tiffany ST. Meta-analysis of cue reactivity in addiction research. *Addiction*. 1999; 94:327–340. [PubMed: 10605857]
31. Litt MD, Cooney NL, Kadden RM, Gaupp L. Reactivity to alcohol cues and induced moods in alcoholics. *Addict Behav*. 1990; 15:137–146. [PubMed: 2343787]
32. Childress AR, Ehrman RN, McLellan AT, MacRae J, Natale M, O'Brien CP. Can induced moods trigger drug-related responses in opiate abuse patients? *J Subst Abuse Treat*. 1994; 11:17–23. [PubMed: 8201629]
33. Cooney NL, Litt MD, Morse PA, Bauer LO, Gaupp L. Alcohol cue reactivity, negative mood reactivity, and relapse in treated alcoholic men. *J Abnorm Psychol*. 1997; 106:243–250. [PubMed: 9131844]
34. Beck AT, Steer RA, Ball R, Ranieri W. Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. *J Pers Assess*. 1996; 67:588–597. [PubMed: 8991972]
35. McNair, DM.; Lorr, M.; Droppleman, LF. EDITS manual for the profile of mood states. Educational and Industrial Testing Service, Educational and Industrial Testing Service; 1971.
36. Derogatis LR, Melisaratos N. The Brief Symptom Inventory: an introductory report. *Psychological Med*. 1983; 13:595–605.
37. Tiffany ST, Singleton E, Haertzen CA, Henningfield JE. The development of a cocaine craving questionnaire. *Drug Alcohol Depend*. 1993; 34:19–28. [PubMed: 8174499]
38. Harris DS, Reus VI, Wolkowitz OM, Mendelson JE, Jones RT. Repeated psychological stress testing in stimulant-dependent patients. *Prog Neuropsychopharmacol Biol Psychiatry*. 2005; 29:669–677. [PubMed: 15913869]
39. Li CS, Kemp K, Milivojevic V, Sinha R. Neuroimaging study of sex differences in the neuropathology of cocaine abuse. *Gend Med*. 2005; 2:174–182. [PubMed: 16290890]

FIGURE 1.

Mean ratings of perceived stress and imagery vividness subsequent to the stress and neutral recall conditions. Data reflect mean $\pm$ s.e.m. ***reflects $p < 0.0001$.

TABLE 1

Demographics and drug use

	(N = 25)
Gender	
Male	23
Female	2
Ethnicity	
White (not Hispanic)	2
Hispanic or Latino	3
African American	20
Age (years)	43.9 ± 1.3
Education (years)	13.1 ± 0.3
Cocaine Use	
Years of use	15.7 ± 2.0
Days of use in last 30 days	17.6 ± 2.0
Money (\$) spent/day	64.5 ± 10.3
*Frequency	4.6 ± 0.3
Nicotine Use	
# of all participants	17/25
Years of use	24.9 ± 2.0
Days of use in last 30 days	26.6 ± 1.9
Frequency	5.9 ± 2.0
Other Drug Use	
Methamphetamine	
# of all participants	2/25
Frequency	2.0 ± 0
Alcohol	
# of all participants	17/25
Frequency	3.2 ± 0.4
Marijuana	
# of all participants	5/25
Frequency	2.8 ± 0.9

* All frequency scores based on mean days of use during the last 6 weeks, classified as: 0 = did not use, 1 = once a month, 2 = 2–3 times per month, 3 = weekly, 4 = a few times per week, 5 = once a day, 6 = several times a day. All other data reflect mean ± s.e.m.

TABLE 2

Study design

Time (time point)	Activity
Arrival (~9:00 AM)	
9:30	Informed consent, Demographics, Urine Toxicology
10:00	ASI-Lite, MINI, BDI, BSI, POMS
Part I	
-15 min	BP, HR, VAS, CQ-Now
Time = 0 (~11:00 AM)	Begin Imagery Session (neutral or stress) <i>Description and visualization continue for 5 min</i>
T = 0, 10, 20, 45 min	BP, HR
T = 5, 15, 30, 60 min	BP, HR, VAS, CQ-Now
~12:00–12:15 PM	Complete Part I – participant is resting
Part II	
-15 min	BP, HR, VAS, CQ-Now
Time = 0 (~12:30 PM)	Begin Imagery Session (neutral or stress- <i>opposite of 11 AM</i>) <i>Description and visualization continue for 5 min</i>
T = 0, 10, 20, 45 min	BP, HR
T = 5, 15, 30, 60 min	BP, HR, VAS, CQ-Now
~1:30–1:45 PM	Complete Part II — participant is resting
2:00 PM	Discharge if stable

Abbreviations: ASI-Addiction Severity Index, BDI-Beck Depression Inventory, BP-blood pressure, BSI-Brief Symptom Inventory, HR-heart rate, CQ-Now-Craving Questionnaire Now, MINI-Mini International Neuropsychiatric Interview, POMS-Profile of Mood States, VAS-visual analog scale.

TABLE 3

Physiological and subjective effects outcomes

	Script type		Stats
	Neutral	Stress	
Physiological measures			
Heart Rate (bpm)	-1.2 ± 0.7	-1.6 ± 1.2	F _{1,48} = 0.06, p = 0.82
Systolic BP (mm Hg)	1.2 ± 2.7	3.2 ± 2.5	F _{1,48} = 0.30, p = 0.59
Diastolic BP (mm Hg)	1.9 ± 1.6	2.2 ± 1.4	F _{1,48} = 0.02, p = 0.90
Subjective effects (on a scale of 0–100)			
Any Drug Effect	0 ± 0	4.0 ± 3.6	F _{1,48} = 1.2, p = 0.27
High	0 ± 0	4.0 ± 4.0	F _{1,48} = 1.0, p = 0.32
Good	4.4 ± 2.3	2.0 ± 1.4	F _{1,48} = 0.8, p = 0.38
Like	2.8 ± 2.0	0 ± 0	F _{1,48} = 1.9, p = 0.17
Desire Cocaine	3.2 ± 1.6	6.0 ± 2.8	F _{1,48} = 0.8, p = 0.38
Depressed	1.6 ± 0.9	3.6 ± 2.2	F _{1,48} = 0.7, p = 0.40
Anxious	1.2 ± 0.7	6.8 ± 3.2	F _{1,48} = 2.9, p = 0.09
Stimulated	3.2 ± 1.3	9.6 ± 3.7	F _{1,48} = 2.7, p = 0.11
Access	3.2 ± 2.1	5.6 ± 2.7	F _{1,48} = 0.5, p = 0.48

All data reflect change from baseline (T = 5 min minus T = -15 min) and are represented as mean ± s.e.m.