Published in final edited form as:
Drug Alcohol Depend. 2011 July 1; 116(1-3): 80–85. doi:10.1016/j.drugalcdep.2010.11.028.

Psychoticism and neuroticism predict cocaine dependence and future cocaine use via different mechanisms

James J. Prisciandaro, **Aimee L. McRae-Clark**, **Megan M. Moran-Santa Maria**, **Karen J. Hartwell**, and **Kathleen T. Brady**
Medical University of South Carolina; Department of Psychiatry and Behavioral Sciences; Clinical Neuroscience Division; 67 President Street, MSC861; Charleston, SC 29425

Abstract

Background—Personality characteristics have been associated with cocaine use. However, little is known about the mechanisms through which personality could impact drug use. The present study investigated the cross-sectional and prospective relationships between personality dimensions (i.e., impulsivity, neuroticism) and problematic cocaine use. Reactivity to a pharmacological stressor as a potential mediator of the relationship between neuroticism and future cocaine use was also examined.

Methods—Participants were 53 cocaine-dependent individuals and 47 non-dependent controls. Subjects completed the Eysenck Personality Questionnaire (EPQ) at baseline and were administered i.v. corticotrophin releasing hormone (CRH; 1 μg/kg). Cocaine use in the 30 days following CRH administration was measured.

Results—Cocaine-dependent individuals had higher scores on the psychoticism (i.e., impulsivity, aggression; $p = 0.02$) and neuroticism ($p < 0.01$) scales of the EPQ than non-dependent controls. Cocaine-dependent individuals also had a greater subjective stress response to CRH than controls ($p < 0.01$). Cocaine-dependent individuals with elevated psychoticism used significantly more cocaine over the follow-up period ($p < 0.05$), whereas individuals with elevated neuroticism trended towards using cocaine more frequently over the follow-up ($p = 0.07$). Finally, there was a trend for an indirect effect of neuroticism on frequency of cocaine use through subjective reactivity to CRH.

Conclusions—The findings extend past research on the association between personality and cocaine use, and suggest that motives for cocaine use may systematically vary across personality characteristics. Moreover, tailoring therapeutic interventions to individuals' personalities may be an area that warrants further investigation.

Keywords

psychoticism; neuroticism; personality; cocaine; corticotrophin releasing hormone; stress

Corresponding author: James J. Prisciandaro; Medical University of South Carolina; Department of Psychiatry and Behavioral Sciences; Clinical Neuroscience Division; 67 President Street, MSC861; Charleston, SC 29425; fax: (843) 792-0528; prisciandaro@musc.edu.

1. Introduction

Cocaine use is a major public health concern. The 2008 National Survey on Drug Use and Health (NSDUH) reported that approximately 1.9 million Americans were current cocaine users, and that 1.4 million had dependence on, or abuse of, cocaine between 2007 and 2008 (SAMHSA, 2009). These numbers are especially concerning because cocaine use is consistently associated with substantially increased mortality (SAMHSA, 2010), psychiatric illness (Conway et al., 2006), functional impairment (Lozano et al., 2008), and criminal behavior (ONDCP, 2009). Understanding factors that contribute to the etiology and maintenance of problematic cocaine use is vital to reducing the negative impact of cocaine on individuals and society.

Personality characteristics, including impulsivity (i.e., the tendency to respond without forethought; Robinson et al., 2009) and neuroticism (i.e., the tendency to experience negative emotional states; Matthews et al., 2003), have been shown to predict symptoms of substance dependence (Bottlender et al., 2005; Grekin et al., 2006; Sher et al., 2000). Research concerning personality characteristics and cocaine use has been less common, but has generally supported the findings obtained by the broader substance abuse literature. For example, cocaine users have been found to be elevated on measures of impulsivity (Lane et al., 2007; Moeler et al., 2002; Saiz et al., 2003), and neuroticism (Terracciano et al., 2008). Furthermore, rodent research has established impulsivity as a predictor of cocaine use escalation (Anker et al., 2009) and relapse (Economidou et al., 2009). Unfortunately, little research has examined the prospective relationship between personality characteristics and cocaine use in cocaine-dependent humans.

Although personality characteristics appear to be important contributors to problematic cocaine use, they are, by definition, distal factors. Little research has examined the mechanisms through which personality characteristics might impact cocaine use. One well-established proximal predictor of cocaine use, dependence, and relapse is stress (Brady and Sinha, 2005; Kreek and Koob, 1998; Sinha, 2001). Corticotropin-releasing hormone (CRH), in particular, is thought to play a critical role in cocaine dependence and relapse through its effects on the hypothalamic pituitary adrenal (HPA) axis and extended amygdala (Koob and Kreek, 2007). Recent research (Brady et al., 2009; Back et al., 2010) has demonstrated that individuals with cocaine dependence subjectively experience more stress in response to CRH administration than non-dependent controls, and that this elevated stress response is associated with relapse to cocaine use. Interestingly, neuroticism has also been associated with HPA dysfunction. For example neuroticism has been correlated with an increased cortisol response to CRH (Zobel et al., 2004) and naloxone (Mangold et al., 2006) administration (cf., McCleery and Goodwin, 2001; Oswald et al., 2006). Given that neuroticism has been associated with elevated response to CRH, and the response to CRH has been shown to predict relapse in cocaine dependent individuals, it is possible that neuroticism may impact cocaine use via elevated reactivity to CRH. Thus, while some personality characteristics have been associated with cocaine use, the mechanisms through which personality factors impact cocaine use have not been systematically investigated.

The primary goals of the present study were: 1) to replicate past research that has demonstrated elevated impulsivity and neuroticism in cocaine-dependent individuals relative to controls, 2) to examine the ability of impulsivity and neuroticism to prospectively predict future cocaine use in cocaine-dependent individuals, and 3) to examine the magnitude of stress response to CRH as a potential mediator of the relationship between neuroticism and cocaine use.

2. Methods

2.1. Participants

Subjects were recruited through media advertisements in the local Charleston area: 53 participants were non-treatment seeking cocaine-dependent men and women; the remaining 47 participants were non-cocaine-dependent controls. Potential participants were screened by telephone, and eligible participants were asked to complete a clinical interview and physical examination. Cocaine dependent participants met DSM-IV criteria for Cocaine Dependence and indicated cocaine as their primary drug of choice. General exclusion criteria included: major medical (e.g., diabetes, HIV) and psychiatric conditions (e.g., affective disorders, posttraumatic stress disorder) that could affect the HPA axis, BMI ≥ 35, synthetic glucocorticoid or exogenous steroid therapy within 1 month of evaluation, pregnancy or nursing, DSM-IV criteria for substance dependence (except caffeine, nicotine, marijuana, or alcohol) within the past 60 days. A small portion of the sample (3 cocaine dependent and 4 control female participants) were taking contraceptive medications at the time of the study.

2.2. Measures

Axis I psychiatric disorders were assessed using the Structured Clinical Interview for DSM-IV (First et al., 1994). Cocaine use (dollar amount) during the month prior to and after the study was assessed using the time-line follow-back (TLFB; Sobell and Sobell, 1992). Personality was measured using the Eysenck Personality Questionnaire (EPQ; Eysenck & Eysenck, 1975). The EPQ provides assessment of 3 personality dimensions: Extraversion, neuroticism, and psychoticism (i.e., impulsivity). Factor analytic research has demonstrated that the neuroticism and psychoticism scales of the EPQ strongly and selectively correlate with other major neuroticism and impulsivity scales, respectively (e.g., Zuckerman et al., 1993). The relationship between neuroticism and negative emotion is robust, and moderated by situational stress (Matthews et al., 2003; Suls, 2001). Although associations between neuroticism and psychophysiological response have been difficult to replicate (Matthews et al., 2003), a recent meta-analysis of the relationship between personality and laboratory-induced stress found that Neuroticism is reliably associated with poor cardiovascular recovery after stress (Chida and Hamer, 2008). The EPQ psychoticism scale has been repeatedly associated with antisocial behavior (Blackburn, 1993) and behavioral measures of impulsivity (Edman et al., 1983; Rawlings, 1984).

2.3. Procedures

The present study was part of a larger study investigating gender differences in cue and stress reactivity. Cue and stress data have been presented in separate manuscripts (Brady et al., 2009; Waldrop et al., 2009; Moran-Santa Maria et al., 2009). IRB-approved written informed-consent was obtained prior to the commencement of any study procedures. Participants were informed about all study procedures, including the laboratory stress tasks. Participants completed diagnostic, cocaine use history, and personality assessments during a baseline screening visit. Eligible participants were scheduled for a two-night hospital stay at the General Clinical Research Center (GCRC) of the Medical University of South Carolina (MUSC). At least two days of abstinence from all substances except caffeine and nicotine were required prior to admission. Abstinence was confirmed by a breathalyzer test, (AlcoSensor III, Intoximeters Inc.) and urine drug screen (Roche Diagnostics). Participants were admitted to the GCRC at 20:00 h on the evening prior to testing to control for extraneous variables (e.g., sleep, nicotine and caffeine intake) that could affect CRH reactivity. Twenty-four hour nicotine replacement therapy was maintained throughout the hospital stay for cigarette smokers (≥ 20 cigarettes/day = 21mg patch; 10–19 cigarettes/day = 14mg patch; 5–9 cigarettes/day = 7mg patch).

During the two days of testing at the GCRC each participants completed the Trier Social Stress Task, CRH administration, and a cocaine cue exposure paradigm. Only data obtained from the CRH administration task were used in this investigation. Activities on the test day included breakfast (08:30 h), sedentary activities (e.g., reading), insertion of an indwelling intravenous catheter in the non-dominant forearm (11:50 h), lunch (12:00 h), acclimation, and Trier or cocaine cue exposure (counterbalanced between participants; 14:00 h). At 17:00 h, ovine CRH 1 μg/kg (Ferring Pharmaceuticals, St. Prex, Switzerland) was administered over 1 min via i.v. catheter to directly stimulate the HPA axis (Contoreggi et al., 2003). Subjective stress and blood samples were collected immediately prior to and immediately following CRH administration, as well as at multiple points post-CRH administration (5, 15, 30, 60 min). Subjective stress was assessed using a visual analog scale anchored with adjective modifiers (from 0 = "not at all" to 10 "extremely") that was derived from the Within Session Rating Scale (Childress et al., 1986). Participants used the scale to rate their responses to questions, such as, "How stressed out do you feel right now?"

2.4. Cortisol assays

Blood samples were collected in EDTA-prepared tubes and immediately iced. Samples were centrifuged under refrigeration and the serum was frozen at −70° C until assayed. Roche Diagnostics Elecys 2010 immunoassay analyzer and kits based on electrochemiluminescence competitive immunoassay with a functional sensitivity (lowest reportable concentration) of 8.0 nmol/l (.29 μg/dl) and intra-assay reproducibility (coefficient of variation, CV) of less than 2% were used.

2.5. Statistical methods

Although 100 individuals participated in the present study, 35 participants were missing at least one of the 16 variables of interest. Of the 35 participants with missing data, 83% were missing ≤ 3 data points; the remaining 17% were missing between 4 and 6 data points. The most common pattern of missingness involved participants who did not complete the EPQ (n = 16), but completed all other measures of interest. Other common patterns of missingness included participants that did not attend the follow-up visit (n = 7), participants that didn't answer particular demographic questions (n = 4), and participants that did not have available CRH response data (n = 8). In the present study, the data were not missing completely at random (Little's MCAR test: $\chi^2 = 160.62$, $p = 0.02$). Therefore, multiple imputation, with 5 imputed data sets derived using fully conditional Markov Chain Monte Carlo simulation methods, was implemented to produce unbiased estimates (Little and Rubin, 2002). In Markov Chain Monte Carlo multiple imputation, a small number of data sets are generated with missing values replaced by imputed values. These imputed values are generated through an iterative simulation procedure that models the distribution of missing values conditional on observed data as well as previously simulated missing data (Tanner and Wong, 1987). All generated data sets are subsequently analyzed separately, and the results from these separate analyses are statistically combined to reflect the uncertainty in parameter estimates caused by imputation. Since the statistical combination of parameter estimates is not presently possible for models with multiple dependent variables, the present study employed regression models with single dependent variables (Little and Rubin, 2002).

First, cocaine-dependent and non-dependent individuals were compared on demographic characteristics using t-tests (for continuous variables) and chi-square tests (for categorical variables). Second, multiple regression models were estimated to test whether cocaine-dependent and non-dependent individuals differed in terms of personality characteristics (i.e., extraversion, neuroticism, and pychoticism on the EPQ) or reactivity (i.e., peak change in cortisol and self-reported stress from baseline) to CRH. Demographic covariates were employed in the model. Group differences in reactivity to CRH in this sample have already

been documented (Brady et al., 2009), and were tested in the present investigation to replicate Brady and colleagues (2009) findings across different statistical methodologies. Third, multiple regression models were estimated to examine the relationships between: 1) personality characteristics and post-study cocaine use (i.e., % days and total amount in dollars used in the month following study participation), 2) personality and stress reactivity, and 3) stress reactivity and post-study cocaine use in cocaine-dependent individuals (n = 53). Because pre-study and post-study cocaine use are highly associated (Paliwal et al., 2008), the analogous measure of cocaine use for the month prior to study entry was covaried in each model involving post-study cocaine use. The association between stress reactivity and any post-study cocaine use (i.e., relapse) in this sample has been examined (Back et al., 2010), however the present study extended these analyses to additional cocaine use variables (e.g., percent days used). Finally, we used Preacher and Hayes' (2008) INDIRECT macro to test our mediation hypothesis regarding the proposed indirect effect of neuroticism on cocaine use via stress reactivity. Modern methods of testing statistical mediation focus on estimating the product of the regression coefficients involving a) the predictor (e.g., neuroticism) and the mediator (e.g., CRH reactivity), and b) the mediator and the outcome (e.g., cocaine use); the product of these coefficients is commonly referred to as "*ab*." To evaluate the statistical significance of the indirect effect, one must compare the ratio of *ab* to its estimated standard error to an appropriate sampling distribution. The estimated indirect effect cannot be tested for significance against a standard normal sampling distribution because the distribution of the product of two coefficients (e.g., *ab*) is skewed. As such, Preacher and Hayes' (2008) IDIRECT macro uses nonparametric resampling techniques to create an empirical approximation of the *ab* sampling distribution. In the present study, bias corrected and accelerated confidence intervals around the indirect effect were created using 5000 bootstrap resamples per model. These particular resampling parameters have been supported by the simulation work of MacKinnon and colleagues (2004). All statistical models were evaluated with and without gender statistically controlled. Because gender was not significantly related to any outcomes across models, results are presented without gender controlled. All analyses were conducted in SPSS 17.0.

3. Results

3.1. Differences between cocaine dependent (n = 53) and non-dependent individuals (n = 47)

Demographic characteristics of the overall sample are presented in Table 1. Cocaine-dependent individuals had higher rates of cigarette smoking and lower levels of educational attainment than non-dependent individuals; no other significant demographic differences were observed. Results from regression models comparing cocaine-dependent and non-dependent individuals in terms of personality and stress reactivity are presented in Table 2. Controlling for demographic differences (i.e., education, smoking status), cocaine dependent individuals had higher scores on the psychoticism (β = 1.23, p = 0.02) and neuroticism (β = 4.74, $p < 0.01$) scales of the EPQ, and higher self-reported stress following CRH administration (β = 0.96, $p < 0.01$), than did non-dependent individuals. There were no differences between cocaine dependent and non-dependent individuals on EPQ extraversion (p = 0.68) or cortisol reactivity to CRH administration (p = 0.49).

3.2. Personality, stress reactivity and future cocaine use (n = 53)

The associations between personality, stress reactivity, and post-study cocaine-use are presented in Table 3. Neuroticism (marginally) predicted the percentage of days participants' used cocaine post-study (β = 0.01, p = 0.07). In contrast, psychoticism significantly predicted the total amount of cocaine participants used post-study (β = 1.45, $p < 0.05$). Neuroticism (marginally) predicted self-reported stress reactivity in response to

CRH administration (β = 0.11, $p = 0.08$). However, neurtoticism did not predict cortisol reactivity to CRH ($p = 0.22$). Self-reported stress, but not cortisol, reactivity to CRH significantly predicted post-study cocaine use. Further analyses conducted for the present investigation demonstrated that the association between self-reported stress and post-study cocaine use was significant for percent days (β = 0.04, $p = 0.04$), but not for total amount of cocaine, used ($p = 0.59$). Explicit tests of an indirect path between neuroticism and cocaine use through stress reactivity had received marginal support: mean β = 0.004, 90% bias corrected and accelerated confidence intervals did not overlap with "0" for 4 of the 5 imputed data sets.

4. Discussion

The present study investigated the relationship between personality characteristics and cocaine use. Consistent with previous research, cocaine-dependent individuals had elevated scores on the psychoticism (i.e., impulsivity, aggression) and neuroticism (i.e., negative affectivity) scales of the EPQ and self-reported stress reactivity to CRH administration relative to non-cocaine dependent individuals. Within the subsample of cocaine dependent individuals, psychoticism, neuroticism, and self-reported stress reactivity to CRH all predicted post-study cocaine use (controlling for pre-study cocaine use). Finally, as hypothesized, the relationship between neuroticism and post-study cocaine use was partially mediated by self-reported stress reactivity to CRH administration. In other words, individuals elevated on neuroticism had higher levels of stress-reactivity to CRH, and these higher levels of reactivity were associated with their post-study cocaine use.

It is noteworthy that the relationships between personality characteristics, stress reactivity, and cocaine use were fairly specific. Whereas psychoticism predicted the amount of post-study cocaine use, neuroticism and stress reactivity predicted frequency of post-study cocaine use. Most studies investigating the relationship between personality characteristics and cocaine use have not distinguished between amount and frequency of use, however consistent with our findings, recent research has found that impulsivity is associated with binge patterns of crack/cocaine use in both humans (Lejuez et al., 2007) and rodents (Anker et al., 2009). It is likely that prefrontal, executive dysfunction is partially responsible for the inability of an individual to restrict cocaine use once it has been initiated; this prefrontal dysfunction may both precede (Horn et al., 2003), and be potentiated by (Fein et al., 2002; Porrino and Lyons, 2000), chronic cocaine use. Given its role in both cocaine use disorders and impulsivity, executive dysfunction (e.g., deficits in response inhibition) should be investigated as a potential mediator of the relationship between impulsivity and cocaine use in future research.

Both individuals with cocaine dependence and individuals elevated on neuroticism had higher levels of self-reported stress reactivity to CRH. Interestingly, individuals with high levels of neuroticism did not have higher levels of cortisol following CRH relative to individuals with low levels of neuroticism. As reported by Brady and colleagues (2009), cocaine dependent individuals also did not have higher levels of cortisol following CRH administration relative to non-cocaine dependent individuals. Although some prior studies have demonstrated a relationship between either cocaine dependence or neuroticism and elevated cortisol reactivity to CRH (e.g., Contoreggi et al.; Zobel et al., 2004), other studies have not (Mendelson et al., 1988; McCleery and Goodwin, 2001). Further research is needed to investigate these discrepancies.

The present study represents an important step in teasing apart the differential associations with cocaine use among individuals with diverse personality profiles. Although both psychoticism and neuroticism were associated with cocaine use in the present study, only

neuroticism was associated with use via stress reactivity to CRH. As noted earlier, executive dysfunction or response inhibition may explain why psychoticism is associated with cocaine use; this possibility should be explored in future research. If the present study's findings are replicated and extended by future research, the differentiation of reasons for cocaine use between individuals with different personality profiles may present valuable opportunities to improve the efficacy of therapeutic interventions by tailoring them to individuals' personalities. For example, psychotherapy approaches for cocaine dependent individuals with elevated psychoticism could focus on preventing binge use and inhibiting prepotent responses, whereas approaches for individuals with elevated neuroticism could focus on stress management and distress tolerance.

This discussion should be viewed in light of the present study's limitations. First, although our sample size was comparable to similar investigations, replication with larger sample sizes would increase confidence in the present study's findings. In particular, testing indirect effects requires relatively high sample sizes; the present study's indirect effect of neuroticism on cocaine use through stress reactivity would have likely been more reliably significant given a larger sample size (Fritz and MacKinnon, 2007). Second, only one dose of CRH was tested in the present study which may have limited our ability to detect group differences (Schluger et al., 2003). Third, because we did not employ a placebo control group for the CRH administration procedure, it is possible that some portion of the observed association between neuroticism and reactivity to CRH is attributable to individuals' non-specific distress to drug challenge. Although no existing studies that have investigated the association between neuroticism and CRH reactivity have employed a placebo control group, the broader literature suggests that, while there may be some relationship between placebo-related distress and neuroticism, this relationship is not substantial (Netter et al., 1998; Davis et al., 1995). Finally, we were not able to standardize menstrual cycle phase for women, and differences in cycle phase are associated with HPA axis functioning (Kajantie and Phillips, 2006). In addition, three cocaine dependent women and four non-dependent control women reported taking contraceptive medications which have also been shown to impact HPA hormonal responding to laboratory stressors (Burleson et al., 1998; Komesaroff et al., 1999). However, given the relatively small percentage of individuals taking contraceptive medications (5.6% in the cocaine dependent group and 8.5% in the non-dependent group), we do not expect that contraceptives had a significant impact on the present findings. Despite the above limitations, the present study adds to the extant literature by demonstrating relationships between cocaine dependence, cocaine use, and personality characteristics, and by providing marginal support for the indirect effect of neuroticism on cocaine use through reactivity to a biological stressor.

In summary, the present study demonstrated associations between personality (i.e., psychoticism, neuroticism) and cocaine dependence, and between personality and future cocaine use in cocaine-dependent individuals. Both psychoticism and neuroticism predicted future cocaine use, but only the relationship between neuroticism and use was mediated by reactivity to CRH. Further research is needed to replicate and extend the present study's findings. Moreover, these data support a growing literature demonstrating the importance of personality in predicting of drug seeking behavior and relapse.

References

Anker JJ, Perry JL, Gliddon LA, Carroll ME. Impulsivity predicts the escalation of cocaine self-administration in rats. Pharmacol Biochem Behav. 2009; 93:343–348. [PubMed: 19490925]

Back SE, Hartwell K, DeSantis SM, Saladin M, McRae-Clark AL, Price KL, Moran-Santa Maria MM, Baker NL, Spratt E, Kreek MJ, Brady KT. Reactivity to laboratory stress provocation predicts relapse to cocaine. Drug Alcohol Depend. 2010; 106:21–27. [PubMed: 19726138]

Blackburn, R. Theory, Research and Practice. Wiley; Chichester: 1993. The Psychology of Criminal Conduct.

Bottlender M, Soyka M. Impact of different personality dimensions (NEO Five-Factor Inventory) on the outcome of alcohol dependent patients 6 and 12 months after treatment. Psychiatry Res. 2005; 136:61–67. [PubMed: 16023734]

Brady KT, Sinha R. Co-occurring mental and substance use disorders: the neurobiological effects of chronic stress. Am J Psychiatry. 2005; 162:1483–1493. [PubMed: 16055769]

Brady KT, McRae AL, Moran-Santa Maria MM, DeSantis SM, Simpson AN, Waldrop AE, Back SE, Kreek MJ. Response to CRH infusion in cocaine-dependent individuals. Arch Gen Psychiatry. 2009; 66:422–430. [PubMed: 19349312]

Burleson MH, Malarkey WB, Cacioppo JT, Poehlmann KM, Kiecolt-Glaser JK, Berntson GG, Glaser R. Postmenopausal hormone replacement: effects on autonomic, neuroendocrine, and immune reactivity to brief psychological stressors. Psychosom Med. 1998; 60:17–25. [PubMed: 9492234]

Childress AR, McLellan AT, O'Brien CP. Conditioned responses in a methadone population. A comparison of laboratory, clinic, and natural settings. J Subst Abuse Treat. 1986; 3:173–179. [PubMed: 3806730]

Contoreggi C, Herning RI, Na P, Gold PW, Chrousos G, Negro PJ, Better W, Cadet JL. Stress hormone responses to corticotropin-releasing hormone in substance abusers without severe comorbid psychiatric disease. Biol Psychiatry. 2003; 54:873–878. [PubMed: 14573313]

Conway KP, Compton W, Stinson FS, Grant BF. Lifetime comorbidity of DSM-IV mood and anxiety disorders and specific drug use disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry. 2006; 67:247–257. [PubMed: 16566620]

Davis C, Ralevski E, Sidney K, Neitzert C. The role of personality factors in the reporting of side effect complaints to moclobemide and placebo: A study of healthy male and female volunteers. J Clin Psychopharm. 15:347–352.

Economidou D, Pelloux Y, Robbins TW, Dalley JW, Everitt BJ. High impulsivity predicts relapse to cocaine-seeking after punishment-induced abstinence. Biol Psychiatry. 65:851–856. [PubMed: 19181308]

Edman G, Schalling D, Levander SE. Impulsivity and speed and errors in a reaction time task: A contribution to the construct validity of the concept of impulsivity. Acta Psycho. 1983; 53:1–8.

Eysenck, HJ.; Eysenck, SBG. Manual of the Eysenck Personality Questionnaire. London: Hodder and Stoughton; 1975.

Fein G, Di Sclafani V, Meyerhoff DJ. Prefrontal cortical volume reduction associated with frontal cortex function deficit in 6-week abstinent crack-cocaine dependent men. Drug Alcohol Depend. 2002; 68:87–93. [PubMed: 12167554]

First, MB.; Spitzer, R.; Gibbon, M.; Williams, J. Structured clinical interview for Axis I DSM-IV disorders. 1994. Patient Edition (SCID-I/P, vs 2.0)

Fritz MS, MacKinnon DP. Required sample size to detect the mediated effect. Psychol Sci. 2007; 18:233–239. [PubMed: 17444920]

Grekin ER, Sher KJ, Wood PK. Personality and substance dependence symptoms: Modeling substance-specific traits. Psychol Addict Behav. 2006; 20:415–424. [PubMed: 17176176]

Horn NR, Dolan M, Elliott R, Deakin JF, Woodruff PW. Response inhibition and impulsivity: an fMRI study. Neuropsychologia. 2003; 41:1959–1966. [PubMed: 14572528]

Kajantie E, Phillips DI. The effects of sex and hormonal status on the physiological response to acute psychological stress. Psychoneuroendocrinology. 2006; 31:151–178. [PubMed: 16139959]

Kreek MJ, Koob GF. Drug dependence: stress and dysregulation of brain reward pathways. Drug Alcohol Depend. 1998; 51:23–47. [PubMed: 9716928]

Koob GF, Kreek MJ. Stress, dysregulation of drug reward pathways, and the transition to drug dependence. Am J Psychiatry. 2007; 164:1149–1159. [PubMed: 17671276]

Komesaroff PA, Sudhir K, Esler MD. Effects of estrogen on stress responses in women. J Clin Endocrinol Metab. 1999; 84:4292–4293. [PubMed: 10566690]

Lane SD, Moeller FG, Steinberg JL, Buzby M, Kosten TR. Performance of cocaine dependent individuals and controls on a response inhibition task with varying levels of difficulty. Am J Drug Alcohol Abuse. 2007; 33:717–726. [PubMed: 17891664]

Lejuez CW, Bornovalova MA, Reynolds ER, Daughters SB, Curtin JJ. Risk factors in the relationship between gender and crack/cocaine. Exp Clin Psychopharmacol. 2007; 15:165–175. [PubMed: 17469940]

Little, RJA.; Rubin, DB. Statistical Analysis with Missing Data. 2. John Wiley; New York: 2002.

Lozano OM, Domingo-Salvany A, Martinez-Alonso M, Brugal MT, Alonso J, de la Fuente L. ITINERE Investigators. Health-related quality of life in young cocaine users and associated factors. Qual Life Res. 2008; 17:977–985. [PubMed: 18679826]

Mangold DL, Wand GS. Cortisol and adrenocorticotropic hormone responses to naloxone in subjects with high and low neuroticism. Biol Psychiatry. 2006; 60:850–855. [PubMed: 16950229]

Matthews, G.; Deary, IJ.; Whiteman, MC. Personality Traits. 2. Cambridge University Press; Cambridge: 2003.

McCleery JM, Goodwin GM. High and low neuroticism predict different cortisol responses to the combined dexamethasone-CRH test. Biol Psychiatry. 2001; 49:410–415. [PubMed: 11274652]

MacKinnon DP, Lockwood CM, Williams J. Confidence limits for the indirect effect: Distribution of the product and resampling methods. Multivar Behav Res. 2004; 39:99–128.

Mendelson JH, Teoh SK, Lange U, Mello NK, Weiss R, Skupny A, Ellingboe J. Anterior pituitary, adrenal, and gonadal hormones during cocaine withdrawal. Am J Psychiatry. 1988; 145:1094–1098. [PubMed: 3414852]

Moeller FG, Dougherty DM, Barratt ES, Oderinde V, Mathias CW, Harper A, Swann AC. Increased impulsivity in cocaine dependent subjects independent of antisocial personality disorder and aggression. Drug Alcohol Depend. 2002; 68:105–111. [PubMed: 12167556]

Moran-Santa Maria MM, McRae-Clark AL, Back SE, DeSantis SM, Baker N, Spratt EG, Simpson AN, Brady KT. Influence of cocaine-dependence and early life stress on pituitary-adrenal axis responses to CRH and the Trier social stressor. Psychoneuroendocrinology. 35:1492–1500. in press. [PubMed: 20570051]

Netter P, Hennig J, Huwe S, Olbrich R. Personality related effects of nicotine, mode of application, and expectancies on performance, emotional states, and desire for smoking. Psychopharmacology. 1998; 1998:52–62. [PubMed: 9489934]

ONDCP. ADAM II 2008 Annual Report: Arrestee Drug Abuse Monitoring Program II (NCJ 226971). Office of National Drug Control Policy; Washington, DC: 2009.

Paliwal P, Hyman SM, Sinha R. Craving predicts time to cocaine relapse: further validation of the now and brief versions of the cocaine craving questionnaire. Drug Alcohol Depend. 2008; 93:252–259. [PubMed: 18063320]

Porrino LJ, Lyons D. Orbital and medial pr efrontal cortex and psychostimulant abuse: studies in animal models. Cereb Cortex. 2000; 10:326–333. [PubMed: 10731227]

Preacher KJ, Hayes AF. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. Behav Res Meth. 2008; 40:879–891.

Rawlings D. The correlation of EPQ psychoticism with two behavioural measures of impulsivity. Pers Indiv Differ. 1984; 5:591–594.

Robinson ESJ, Eagle DM, Economidou D, Theobald DEH, Mar AC, Murphy ER, Robbins TW, Dalley JW. Behavioural characterisation of high impulsivity on the 5-choice serial reaction time task: Specific deficits in “waiting” versus “stopping.” Behav. Brain Res. 2009; 196:310–316.

SAMHSA. Results from the 2008 National Survey on Drug Use and Health: National Findings (Office of Applied Studies, NSDUH Series H-36, HHS Publication No. SMA 09-4434). Substance Abuse and Mental Health Services Administration; Rockville, MD: 2009.

SAMHSA. Drug Abuse Warning Network, 2008: Area Profiles of Drug-Related Mortality. Substance Abuse and Mental Health Services Administration; Rockville, MD: 2010.

Sáiz PA, Portilla G-MP, Paredes B, Delgado J, Martínez Bascarán MT, Bobes J. Use of cocaine by secondary school students in northern Spain. Eur Addict Res. 2003; 9:138–143. [PubMed: 12837992]

Schluger JH, Bart G, Green M, Ho A, Kreek MJ. Corticotropin-releasing factor testing reveals a dose-dependent difference in methadone maintained vs control subjects. Neuropsychopharmacology. 2003; 28:985–994. [PubMed: 12700714]

Sher KJ, Bartholow BD, Wood MD. Personality and substance use disorders: A prospective study. J Consult Clin Psych. 2000; 68:818–829.

Sinha R. How does stress increase risk of drug abuse and relapse? Psychopharmacology. 2001; 158:343–359. [PubMed: 11797055]

Sobell, LC.; Sobell, MB. Timeline follow-back: a technique for assessing self-reported ethanol consumption. In: Allen, J.; Litten, RZ., editors. Measuring Alcohol Consumption: Psychological and Biological Methods. Humana Press; Totowa, NJ: 1992. p. 41-72.

Suls, J. Affect, stress, and personality. In: Forgas, JP., editor. Handbook of affect and social cognition. Mahwah, NJ: Erlbaum; 2001. p. 392-409.

Tanner MA, Wong WH. The calculation of posterior distributions by data augmentation. J Amer Statistical Assoc. 82:528–550.

Terracciano A, Löckenhoff CE, Crum RM, Bienvenu OJ, Costa PT Jr. Five-factor model personality profiles of drug users. BMC Psychiatry. 2008; 8:22. [PubMed: 18405382]

Waldrop AE, Price KL, DeSantis SM, Simpson AN, Back SE, McRae AL, Kreek MJ, Brady KT. Community-dwelling cocaine-dependent men and women respond differently to social stressors versus cocaine cues. Psychoneuroendocrinology. 2010; 35:798–806. [PubMed: 20004523]

Zobel A, Barkow K, Schulze-Rauschenbach S, von Widdern O, Metten M, Pfeiffer U, Schnell S, Wagner M, Maier W. High neuroticism and depressive temperament are associated with dysfunctional regulation of the hypothalamic-pituitary-adrenocortical system in healthy volunteers. Acta Psychiatr Scand. 2004; 109:392–399. [PubMed: 15049775]

Zuckerman M, Kuhlman DM, Joireman J, Teta P, Kraft M. A comparison of three structural models for personality: The big three, the big five, and the alternative five. J Pers Soc Psychol. 1993; 65:757–768.

Table 1

Demographic characteristics by Cocaine Dependence status (n = 100)

	Overall (n = 100)	**CD + (n = 53)**	**CD − (n = 47)**	***p***
Age, *M* (SD)	37.24 (11.17)	38.47 (10.74)	35.85 (11.58)	0.24
Gender, % male	51.00	52.83	48.94	0.70
Race, % Caucasian	56.57	50.00	63.83	0.17
Marital status, % married	15.31	9.62	21.74	0.10
Education, % ≥ some college	69.07	53.85	86.67	< 0.01
Smoking status, % smokers	69.00	79.25	57.45	0.02

Note. CD + = positive for Cocaine Dependence; CD− = negative for Cocaine Dependence.

Table 2

Multiple regression models predicting personality characteristics and stress reactivity (n = 100)

Outcome	R^2	Predictors	β	p
EPQ: Psychoticism	0.15	Cocaine Dependence	1.23	0.02*
		Education	−1.04	0.18
		Smoking status	0.30	0.60
EPQ: Extraversion	0.02	Cocaine Dependence	0.56	0.68
		Education	1.77	0.27
		Smoking status	0.07	0.96
EPQ: Neuroticism	0.16	Cocaine Dependence	4.74	< 0.01*
		Education	−0.53	0.77
		Smoking status	−1.44	0.29
CRH: Δ self-report stress	0.09	Cocaine Dependence	0.96	< 0.01*
		Education	−0.16	0.67
		Smoking status	−0.36	0.35
CRH: Δ cortisol	0.03	Cocaine Dependence	−24.83	0.49
		Education	−38.47	0.28
		Smoking status	−28.21	0.43

Note. Parameters were pooled across 5 imputed data sets. EPQ = Eysenck Personality Questionnaire; CRH = Corticotropin-releasing hormone.

* $p < 0.05$

Table 3

Multiple regression models predicting cocaine use and stress reactivity in CD+ (n = 53)

Outcome	R^2	Predictors	β	p
I. EPQ predicting cocaine use				
% days used	0.35	EPQ: Psychoticism	0.02	0.34
		EPQ: Extraversion	−0.01	0.53
		EPQ: Neuroticism	0.01	0.07†
		Baseline % days used	0.19	0.16
Total amount used	0.25	EPQ: Psychoticism	1.45	0.05*
		EPQ: Extraversion	−0.27	0.38
		EPQ: Neuroticism	0.19	0.58
		Baseline total amount used	0.12	0.04*
II. EPQ predicting stress reactivity				
CRH: Δ self-report stress	0.18	EPQ: Psychoticism	−0.05	0.69
		EPQ: Extraversion	0.85	0.11
		EPQ: Neuroticism	0.11	0.08†
CRH: Δ cortisol	0.16	EPQ: Psychoticism	−5.73	0.58
		EPQ: Extraversion	−7.32	0.23
		EPQ: Neuroticism	−5.28	0.22
III. Stress reactivity predicting cocaine use				
% days used	0.21	CRH: Δ self-report stress	0.04	0.04*
		CRH: Δ cortisol	< 0.01	0.82
		Baseline % days used	0.26	0.06†
Total amount used	0.11	CRH: Δ self-report stress	0.48	0.59
		CRH: Δ cortisol	−0.01	0.46
		Baseline total amount used	0.12	0.06†

Note. Parameters were pooled across 5 imputed data sets. Cocaine use variables were derived from the timeline followback. CD+ = Cocaine dependent; EPQ = Eysenck Personality Questionnaire; CRH = Corticotropin-releasing hormone.

*$p < 0.05$

†$p < 0.10$