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Causal pathways between impulsiveness, cocaine use consequences, and depression

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HIGHLIGHTS

- Examined impulsiveness, cocaine use consequences and depression among cocaine users
- Depression occurs as outcome of impulsiveness, which exerts effect on consequences.
- Cocaine use consequences function as pathway between impulsiveness and depression.
- Higher trait impulsiveness associated with earlier age of cocaine use onset
- Cocaine use did not moderate the relationship between consequences and depression.

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ABSTRACT

Aims: The present study examined whether lifetime cocaine use consequences mediate the relationship between trait impulsiveness and current depression symptoms among regular cocaine users.
Methods: Regular cocaine users ($N = 108$) were assessed using: Barratt Impulsiveness Scale subscales (non-planning, attentional, motor sub-scales) to measure trait impulsiveness; a standardized Drug History and Use Questionnaire to measure cocaine use and related consequences; and Beck Depression Inventory to measure current depression symptoms.
Results: All impulsiveness subscales were positively associated with an earlier age of first cocaine use, a higher degree of current depression symptoms and a greater number of lifetime cocaine use consequences. In three separate simple mediation tests, lifetime cocaine use consequences partially mediated the relationship between each of the impulsiveness subscales (non-planning: $R^2 = .42$; attentional: $R^2 = .40$; motor: $R^2 = .24$) and current depression symptoms. Separate moderated mediation analyses failed to demonstrate an interaction between lifetime cocaine use and cocaine-related consequences predicting depression symptoms for the mediation models.
Conclusions: Cocaine-related consequences function in a more nuanced manner than just an outcome of impulsiveness or cocaine use, but as a pathway between trait impulsiveness and current depression symptoms.

1. Introduction

Regular cocaine users report higher levels of trait impulsiveness than non-users (Coffey, Gudleski, Saladin, & Brady, 2003; Patkar et al., 2004; Poling, Kosten, & Sofuoglu, 2007; Vonmoos et al., 2013). More importantly from the standpoint of clinical prediction, high trait impulsiveness is associated with increased cocaine use quantity and long-term cocaine consumption (Moeller et al., 2001; Vonmoos et al., 2013), increased craving (Tziortis, Mahoney, Kalechstein, Newton, & De La Garza, 2011), fewer days of treatment attendance (Moeller et al., 2001; Patkar et al., 2004), greater withdrawal symptom severity (Moeller et al., 2001), and a greater number of depression symptoms (Vonmoos et al., 2013).

Regular cocaine users also report substantially higher rates of lifetime major depression (Falck, Wang, Siegal, & Carlson, 2004; Herrero, Domingo-Salvany, Torrens, & Brugal, 2008) and current major depression (Rounsaville et al., 1991) than non-users. Hasin et al. (2002) examined the time sequence of depression and cocaine and substance dependence; participants demonstrated nearly four times the likelihood of substance-induced or abstinence-induced major depression compared to prior-onset major depression. Comorbid depression

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among regular cocaine users has been associated with greater urges to use cocaine during treatment (Brown et al., 1998), increased subjective high when using cocaine and increased depressive symptoms during initial abstinence (Ulsaner, Kalechstein, Richter, Ling, & Newton, 1999), greater likelihood of relapse (Hasin et al., 2002; McKay et al., 2002), and poorer medication response aimed at reducing cocaine use (Gonzalez, Feingold, Oliveto, Gonsai, & Kosten, 2003).

Impulsiveness is a multi-dimensional construct tied to antecedents and consequences of cocaine and other drug dependence (de Wit, 2009; Perry & Carroll, 2008; Winstanley, Olausson, Taylor, & Jentsch, 2010), making it important to distinguish mechanisms of influence. There are several pathways through which impulsiveness might alter the expression (e.g., course, severity) of cocaine use, abuse, and dependence. For instance, recent data indicate that cocaine users with higher (vs. lower) trait impulsiveness have reduced frontal–cortical gray matter (Crunelle et al., 2014; Moreno-Lopez et al., 2012), which may perpetuate cocaine use and exacerbate its long-term adverse consequences via reduced executive control of behavior (Jentsch & Taylor, 1999) and/or emotion dysregulation (Fox, Axelrod, Paliwal, & Sinha, 2007). One pathway that may connect impulsiveness to depression is through chronic cocaine use-related adverse consequences. In a recent study, higher trait impulsiveness among recreational and dependent cocaine users was correlated with greater depression symptoms and long-term cocaine consumption (Vonmoos et al., 2013).

High levels of trait impulsiveness among regular cocaine users seem to increase risk of greater cocaine-use consequences and comorbid depression symptoms (Moeller et al., 2001; Vonmoos et al., 2013). Although clinically relevant, it is not clear *how* trait impulsiveness exerts an influence on depression symptoms among chronic cocaine users. Thus, the aim of the present investigation was to examine the psychological mechanisms and outcomes associated with regular cocaine use. To accomplish this aim, we assessed trait impulsiveness, lifetime cocaine use and related consequences, and current depression symptoms among a sample of regular cocaine users. We specifically evaluated whether lifetime cocaine use consequences might mediate the relationship between trait impulsiveness and current depression symptoms. A variable can be considered a mediator, "to the extent that it accounts for the relation between predictor and criterion" (Baron & Kenny, 1986, p. 1176). Mediation analyses are advantageous because causality can be prioritized with the independent variable (i.e., trait impulsiveness) preceding the mediator (i.e., lifetime cocaine use consequences) in temporal sequence to predict the criterion (i.e., current depression symptoms; Baron & Kenny, 1986).

We theorized that depression symptoms would primarily function as an outcome of impulsive cocaine use-related consequences (see Hasin et al., 2002). To test this possibility, we hypothesized that the number of lifetime cocaine use negative consequences would mediate the relationship between trait impulsiveness and acute depression symptoms. Specifically, we predicted that regular cocaine users with a higher degree of trait impulsiveness would experience a greater number of lifetime cocaine use consequences and, as a result, experience a higher degree of current depression symptoms.

2. Material and methods

The local Institutional Review Board approved this study, which was conducted according to the Declaration of Helsinki. A Certificate of Confidentiality was obtained from the National Institutes of Health to provide further legal protection against forced disclosure of confidential study data.

2.1. Participants and procedure

Cocaine users ($N = 108$), ages 18–55 years who were not seeking treatment for their substance use were recruited via newspaper advertisements and word-of-mouth referral in the Detroit/metropolitan area for possible participation in one of two experimental laboratory-based cocaine self-administration studies, registered on www.clinicaltrials.gov as NCT00946660 (Greenwald, Ledgerwood, Lundahl, & Steinmiller, 2014) and NCT01392092.

Individuals who passed an initial telephone-screening interview were invited to undergo in-person comprehensive screening procedures. All participants were remunerated $25 for attending the screening session, during which they provided written informed consent for all screening assessments. In the event their screening session required additional time, participants were remunerated an additional $10 to complete the screening during a second session.

2.2. Measures

Alcohol-free breath samples (<.002%; Alco Sensor III breathalyzer) and no evidence of cognitive impairment based on estimated IQ score > 80 (Shipley Institute of Living Scale; Zachary, 1991) were required for informed consent. Volunteers provided a urine sample that was analyzed on-site for cocaine metabolites, benzodiazepines, opioids (positive cutoff ≥ 300 ng/ml), amphetamines (≥1000 ng/ml), barbiturates (≥200 ng/ml), and THC metabolites (≥50 ng/ml). However, urinalysis results did not determine inclusion in this analysis.

2.2.1. Cocaine use

Substance use screening included a locally developed, standardized, comprehensive Drug History and Use Questionnaire [DHUQ, routinely used in our laboratory studies, e.g., Greenwald, Steinmiller, Śliwerska, Lundahl, & Burmeister, 2013]. Cocaine use data obtained from the DHUQ included: Age of first cocaine use, age of first regular (three times a week or more) cocaine use, number of days using cocaine in the past month, number of days using cocaine in the past week, average number of cocaine uses/day during the past week, and the number of days using cocaine in the past week multiplied by the average number of cocaine uses/day during the past week. We also used DHUQ data to estimate the number of lifetime cocaine uses (ordinal response). For this analysis, we focused on the number of lifetime cocaine uses and cocaine-related consequences outlined in the questionnaire. Finally, the DHUQ lists 18 different types of potential consequences of lifetime cocaine use: overdose, seizure, shake/tremor, tolerance, impaired control, legal problem, accident/injury, health problem, intoxicated at work, missed work, lost job, intoxicated at school, missed school, fight, driving under the influence, family problem, financial problem, and emergency department visit. The participant checked whether s/he had ever experienced each event (scored present/absent); the total score reflects the number of different types of lifetime consequences endorsed.

2.2.2. Trait impulsiveness

The Barratt Impulsiveness Scale (BIS-11; Barratt & Patton, 1983; Patton, Stanford, & Barratt, 1995; Zaparniuk & Taylor, 1997) is a 30-item standardized self-report measure of trait impulsiveness; the scale includes 3 second-order subscales: attentional (impulsive decision making), motor (propensity to engage in spontaneous behavior) and non-planning (lack of concern for the consequences of one's future actions).

2.2.3. Current depression symptoms

Current depression symptoms were assessed using the second version of the Beck Depression Inventory (BDI-II; Beck, Steer, & Brown, 1996), a 21-item measure that assesses past 14-day neurovegetative depressive symptoms. Participants who scored in the range of moderate to severe depression were provided a referral for treatment. In the event suicidal thoughts were reported, a licensed clinical psychologist met with the participant to conduct a risk assessment and arrange for hospitalization if deemed necessary.