Risky Business: Sexual Behavior and Cocaine Use Disorder

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THESIS

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LIST OF ABBREVIATIONS

HIV	Human Immunodeficiency virus
STD	Sexually transmitted disease
ACT	Acceptance and Commitment Therapy
MBRP	Mindfulness Based Relapse Prevention
EFT	Episodic Future Thinking
SUDs	Substance use disorders
PTSD	Post-traumatic Stress Disorder
ADHD	Attention-deficit/hyperactivity disorder
MDD	Major depressive disorder
MSM	Men who have sex with men
SDT	Sexual Discounting Task
CUD	Cocaine use disorder
SMART	Sequential, multiple assignment, randomized trial
RAB	Risk Assessment Battery
ASI	Addiction Severity Index
AIS	Avoidance and Inflexibility Scale
DERS	Difficulties in Emotion Regulation
DTS	Distress Tolerance Scale
FFMQ	Five-Facet Mindfulness Questionnaire
AUClog	Area under the curve with a log-transformation
SCID-5	Structured Clinical Interview for DSM-5
CNRA	Center for Neurobehavioral Research on Addiction

SUMMARY

Individuals who use crack cocaine are at an increased risk for human immunodeficiency virus (HIV) transmission, primarily due to risky sexual behavior. Previous literature has suggested that both substance use and risky sexual behavior may be driven by similar processes; although, it is unclear which mechanism would be the optimal target in dual interventions for cocaine use disorder and sexual risk behavior. Two analyses examined five emotional and behavioral mechanisms that have been associated with drug use and risky sexual behavior. Results from the analyses suggested that emotion regulation, experiential avoidance, distress tolerance, mindfulness, and delay discounting were not significantly related to risky sexual behavior or cocaine use severity among individuals with cocaine use disorder.

I. INTRODUCTION

A. Background

Approximately 14-21 million individuals are estimated to use crack cocaine worldwide (Fischer et al., 2015). Crack cocaine use has gradually declined since peak years in the early to mid-1980s, yet there are still significant health care costs related to its use (Degenhardt et al., 2014; Johnston et al., 2018; Shiels, Freedman, Thomas, & De Gonzalez, 2018). One health concern related to crack cocaine use is human immunodeficiency virus (HIV). An estimated 0.8% of adults, aged 15 to 49, live with HIV worldwide (WHO, 2017). However, based on a review of previous studies, the United Nations Office on Drugs and Crime (2017) reported that the pooled prevalence of HIV among individuals with non-injecting use of cocaine and crack cocaine in the United States is 18%. Crack cocaine use may also advance the progression of HIV biologically, and individuals who use crack cocaine are over three times more likely to die of AIDS-related causes compared to those who do not use crack cocaine (Baum et al., 2009; Cook et al., 2008). Among individuals who use cocaine and heroin, unsafe injection use (e.g. sharing needles) is the primary concern related to HIV risk (Chaisson et al., 1989; Meacham et al., 2016). However, when examining HIV risk behavior among people who solely use crack cocaine, the literature has primarily found risks related to risky sexual behavior (Edlin et al., 1994). In fact, findings suggest that those who use crack cocaine are more likely to have more sexual partners, have sex with an intravenous drug user, pay for sex, trade sex for money or drugs, and have a sexually transmitted disease (STD) in their lifetime relative to people who do not use drugs (Word & Bowser, 1997; Booth, Watters, & Chitwood, 1993). Further, when compared to other drugs such as opiates, crack cocaine use has been linked to higher levels of sexual risk-taking (Bosma-Bleeker & Blaauw, 2018). This high rate of sexual risk-taking among people who use crack cocaine has also been associated with higher rates of HIV (Booth, Watters, & Chitwood, 1993). Thus, sexual HIV-risk behavior in individuals who use crack cocaine is an area of concern for public health.

B. Drug Risk and Sexual Risk Processes

The reason for these relationships between crack cocaine use and sexual HIV-risk behaviors are unknown; however, previous studies have suggested that risky sexual behavior and drug taking behaviors may be driven by similar processes (Khantzian, 1985; Khurana et al., 2015; Khurana, Romer, Betancourt, & Hurt, 2017; Williams & Latkin, 2005). Several of these processes are targeted by existing therapies that attempt to address substance use, risky sexual behavior, or both. This raises the possibility of dual interventions that could efficiently address both drug use and sexual risk within the same therapeutic framework. For instance, elements from approaches such as motivational interviewing and cognitive behavioral therapy have been implemented in interventions to reduce sexual risk behavior and substance use (Lundahl, Kunz, Brownell, Tollefson, & Burke, 2010; Mausbach, Semple, Strathdee, Zians, & Patterson, 2007; McHugh, Hearon, & Otto, 2010; Shoptaw et al., 2005). However, studies have shown that these motivational and cognitive approaches are not successful at decreasing sexual risk behaviors and substance use for all individuals.

Previous studies have further identified several emotional and behavioral mechanisms that may contribute to both substance use and risky sexual behavior. These mechanisms are targeted in existing therapies such as Acceptance and Commitment Therapy (ACT), Mindfulness Based Relapse Prevention (MBRP), and Episodic Future Thinking (EFT). However, the strength of the relationship between these potential therapy targets and sexual risk-taking behavior in populations who use crack cocaine is unknown, making it difficult to select the optimal targets for intervention. Therefore, it is important to continue investigating these possible mechanisms to select interventions that could be applied in an efficient dual intervention format for individuals who use crack cocaine.

With an analysis of different intervention targets, we can identify the emotional or behavioral mechanism that is most related to risky sexual behavior in individuals with cocaine use disorder. Understanding these mechanisms can inform us which existing therapy (ACT, MBRP, EFT) may be most effective when targeting sexual risk behaviors in people who use crack cocaine. The emotional processes evaluated in these analyses are emotion regulation, experiential avoidance, and distress tolerance. The behavioral processes examined in these analyses are mindfulness and delay discounting. Previous studies that have investigated how each of these targets relate to substance use and sexual behavior are described below.

C. <u>Emotional Processes</u>

1. Emotion Regulation

Emotion regulation refers to an individual's ability to effectively manage emotional experiences (Gross, 1998). Emotion regulation is targeted in therapies such as ACT. The literature suggests that emotion regulation difficulties are associated with maladaptive behaviors, such as substance use (Bonn-Miller, Vujanovic, & Zvolensky, 2008; Fox, Axelrod, Paliwal, Sleeper, & Sinha, 2007). In fact, treatment-seeking individuals who use cocaine report more difficulties with understanding and managing emotions relative to controls (Fox et al., 2007). Findings have further revealed that patients who are dependent on alcohol and in inpatient treatment show significant reductions in emotion regulation difficulties at termination, thus suggesting emotion regulation is an important target in substance use treatment (Fox, Hong, & Sinha, 2008).

Emotion regulation difficulties have also been associated with risky sexual behavior in patients with substance use disorders (SUDs) (Tull, Weiss, Adams, & Gratz, 2012). In particular, findings have demonstrated that emotion regulation difficulties are positively associated with the number of sexual partners and negatively associated with the likelihood of using condoms, while on drugs, in a sample of treatment-seeking individuals (Tull et al., 2012). Further, emotion dysregulation has also been identified as a possible mechanism underlying sexual risk-taking among college students (Messman-Moore, Walsh, & DiLillo, 2010).

These findings collectively support the idea that emotion regulation difficulties may drive substance use and risky sexual behavior, thus making it an critical mechanism to examine among samples who use crack cocaine.

2. Experiential Avoidance

Experiential avoidance refers to the avoidance of unpleasant internal states (e.g., emotions, thoughts, bodily sensations) (Stotts et al., 2015). This mechanism is also targeted in therapies such as ACT. Experiential avoidance plays a role in the maintenance of substance use and predicts contingency management outcomes in treatment-seeking adults who are dependent on crack cocaine (Stotts et al., 2015). It is hypothesized that patients who do not respond to treatment may also experience behavioral inflexibility, such that they are unable to adapt and engage in nondrug use behaviors during negative states (Stotts et al., 2015). Studies have also proposed that individuals with high levels of experiential avoidance may engage in substance use as a form of positive reinforcement (i.e. enhancement) and negative reinforcement (i.e. coping) (Chawla & Ostafin, 2007). Findings further indicate that smokers may be prone to inflexibility; thus, tobacco use may serve as a way to avoid emotionally challenging states (Zvolensky, Farris, Schmidt, & Smits, 2014). Smoking cessation programs targeting avoidance and inflexibility of distressing thoughts, feelings, and sensations regarding patient's substance use have also led to better treatment outcomes relative to standard care (Zvolensky et al., 2014). These types of treatments place an emphasis on addressing thoughts, feelings, and sensations (e.g., negative mood, nicotine withdrawal) to improve psychological flexibility and decrease avoidance, in order to promote behavior that is aligned with individuals' goals and values (Bond et al., 2011).

The literature demonstrates that experiential avoidance may play a similar function in risky sexual behavior. Those with high levels of experiential avoidance may engage in risky sexual activity for immediate feelings of pleasure and in attempt to avoid aversive internal states (Brem, Shorey, Anderson, & Stuart, 2018). Studies further indicate that experiential avoidance including psychological inflexibility may, for example, serve as a mediator between post-traumatic stress disorder (PTSD) symptoms and compulsive sexual behavior among women in substance use treatment (Brem et al., 2018). Similar findings suggest that experiential avoidance also serves as a mediator between depressive/anxiety symptoms and compulsive sexual behavior among women in residential treatment for substance use disorders (Brem, Shorey, Anderson, & Stuart, 2017).

Overall, these findings suggest that it may be beneficial to target experiential avoidance and psychological inflexibility in therapy to decrease both substance use and risky sexual behavior among individuals with cocaine use disorder.

3. Distress Tolerance

Distress tolerance refers to an individual's ability to endure intense and negative psychological states (Simons & Gaher, 2005). Distress tolerance is targeted in therapies such as MBRP. Findings have indicated that distress tolerance is closely related to impulsive behaviors (Anestis et al., 2012). Non-treatment seekers with low distress tolerance may be more likely to participate in risky behaviors such as substance use (Buckner, Keough, & Schmidt, 2007; Gorka, Ali, & Daughters, 2012). Among non-treatment seekers with low distress tolerance, substance use may also aid in coping with negative affect (Kaiser, Milich, Lynam, & Charnigo, 2012).

However, the relationship between distress tolerance and sexual risk-taking has been less studied and results are more mixed. Difficulties with distress tolerance have been linked to increased sexual risk-taking among patients with SUDs and depressive symptoms and among non-treatment seeking individuals with attention-deficit/hyperactivity disorder (ADHD) symptoms (Tull & Gratz, 2013; Van Eck, Flory, & Willis, 2015). In the study on patients with SUDs, there was no main effect of distress tolerance on risky sexual behavior. However, the results revealed a significant interaction between major depressive disorder (MDD) and distress tolerance, such that individuals with MDD and low distress tolerance reported the highest number of casual sexual partners (Tull & Gratz, 2013). Similar results were found in a study examining non-treatment seeking individuals with ADHD symptoms. Here, there was also no main effect of distress tolerance on sexual behavior. However, the findings did show a significant interaction of ADHD symptoms and distress tolerance, such that individuals with high levels of ADHD symptoms and high distress intolerance on three subscales (i.e. regulation, appraisal, and tolerance) reported the highest number of sexual partners (Van Eck et al., 2015).

Overall, these findings indicate that distress tolerance is an important target for intervention to decrease risk for substance use. Although, the relationship between distress tolerance and risky sexual behavior is less understood. Due to the limited literature, distress tolerance should be further investigated as a targetable process related to risky sexual behavior in cocaine use disorder.

D. Behavioral Processes

1. Mindfulness

Mindfulness involves maintaining a non-judgmental awareness of current experiences that may be practiced through meditation (Roberts & Danoff-Burg, 2011). Mindfulness is targeted in therapies such as MBRP. Interventions targeting mindfulness have led to decreases in the frequency of drug use and reductions in relapse risk for patients in aftercare following substance use treatment and among incarcerated populations (Bowen et al., 2014, 2006). Mindfulness has further been associated with reductions in self-reported drug craving in treatment seeking samples (Witkiewitz, K., Bowen, S., Douglas, H., & Hsu, 2013).

However, research on mindfulness and sexual risk-taking is limited, and the literature provides mixed findings. A previous study among college students indicated that risky sexual behavior was not significantly related to mindfulness as a whole construct, and that it was only correlated with the awareness subscale (Roberts & Danoff-Burg, 2011). On the other hand, studies on the men who have sex with men (MSM) population, who were enrolled in a substance use and sexual risk reduction intervention, have attributed decreases in risky sexual behavior to mindfulness (Buttram & Kurtz, 2017). Mindfulness training to reduce sexual risk behavior has also become a focus of novel telephone-based interventions for individuals living with HIV (Salmoirago-Blotcher et al., 2017). These interventions have led to improvements in mindfulness and sexual risk reduction (Carey et al., 2020).

The literature indicates that targeting mindfulness in therapy may be beneficial to decrease substance use. However, due to the mixed findings on mindfulness and risky sexual behavior, additional research should further explore mindfulness as a potential mechanism to target sexual risk behavior in cocaine use disorder.

2. Delay Discounting

Delay discounting refers to the devaluing of long-term rewards in favor of immediate rewards (Odum, 2011). Delay discounting is targeted in therapies such as EFT. Studies have investigated delay discounting across several substance use disorders (G.J., W.K., & E.A., 1999; Heil, Johnson, Higgins, & Bickel, 2006). Higher rates of delay discounting have also been associated with increased substance use among college students (Kollins, 2003). Previous findings indicate that delay discounting is related to different aspects of substance use, including initiation, severity of use, drug use frequency and quantity, and substance use treatment response (Dougherty et al., 2014; MacKillop & Kahler, 2009; Strickland, Lile, & Stoops, 2017; Washio et al., 2011). Higher rates of delay discounting for hypothetical rewards and monetary outcomes have also been found among individuals with substance use disorders relative to controls (W. K. Bickel, Odum, & Madden, 1999; Warren K. Bickel & Marsch, 2001; Coffey, Gudleski, Saladin, & Brady, 2001; Heil et al., 2006). It has been argued that delay discounting is a trans-disease process that underlies several disorders and disease-related behaviors such as needle sharing, problem gambling, and poor health practices (Warren K. Bickel, Jarmolowicz, Mueller, Koffarnus, & Gatchalian, 2012).

Findings suggest that delay discounting may play a similar role in risky sexual behavior. Among adolescents, delay discounting for hypothetical monetary outcomes is positively associated with having sex before the age of 16 years and past or current pregnancy (Chesson et al., 2006). The Sexual Discounting Task (SDT) was also developed to assess delay discounting for sexual rewards to examine risky sexual behavior and has been used with non-treatment seeking samples who use cocaine (Johnson & Bruner, 2012, 2013). Sexual discounting has been associated with higher levels of sexual risk behavior among non-treatment seeking individuals who use cocaine and when compared to controls (Johnson & Bruner, 2012; Koffarnus et al., 2016).

These findings indicate it may be possible that delay discounting is the underlying mechanism that contributes to crack cocaine use and risky sexual behavior. Another potential explanation may be that crack cocaine use increases delay discounting, thus increasing risk for risky sexual behavior. Due to limitations in this secondary analysis, we are not able to disentangle these relationships to find a definitive answer. Nonetheless, it is worth analyzing the relationship between delay discounting and sexual risk behavior in cocaine use disorder to determine whether it is the best target for intervention.

E. <u>The Present Study</u>

The main research question this study explored was which targetable emotional or behavioral processes are most related to risky sexual behavior in treatment-seeking individuals with cocaine use disorder (CUD)? We had one overall hypothesis and five sub-hypotheses, corresponding to each of the targetable mechanisms investigated, i.e. experiential avoidance, emotion regulation, distress tolerance, mindfulness, and delay discounting.

Our overall hypothesis was that these potential mechanisms would significantly predict risky sexual behavior in our sample of treatment-seeking individuals with cocaine use disorder. Regarding the individual predictors, for experiential avoidance, we hypothesized that higher levels of experiential avoidance would be associated with higher levels of risky sexual behavior. For emotion regulation, we hypothesized that greater difficulties with emotion regulation would be associated with higher levels of risky sexual behavior. For distress tolerance, we hypothesized that lower levels of distress tolerance would be associated with higher levels of risky sexual behavior. For mindfulness, we hypothesized that lower levels of mindfulness would be associated with higher levels of risky sexual behavior. For delay discounting, we hypothesized that greater delay discounting would be associated with higher levels of risky sexual behavior. Regarding which predictor would account for the most variability in sexual risk, our hypothesis was open as these predictors have not previously been compared head-to-head.

In addition, a second analysis examined how these emotional and behavioral processes relate to cocaine use severity in individuals with cocaine use disorder, consistent with our desire to identify processes that drive both drug use and sexual risk taking. Our hypothesis, based on the previous literature, was that these potential mechanisms would significantly predict cocaine use severity in our sample of treatment-seeking individuals with cocaine use disorder. Regarding the individual mechanisms, we predict similar directional hypotheses as the ones listed for risky sexual behavior.

II. METHODS

A. Overall Design

A secondary analysis was conducted on data collected from an ongoing two-stage sequential, multiple assignment, randomized trial (SMART) aimed at developing adaptive interventions for cocaine cessation and relapse prevention (ClinicalTrials.gov Identifier: NCT02896712). This clinical trial is examining whether the use of Acceptance and Commitment Therapy (ACT) increases initial treatment response rates compared to standard counseling, and testing whether adding on a dopamine-targeted pharmacotherapy, modafinil, can help individuals who do not respond to initial treatment. The data used for this secondary analysis was based on the clinical trial's screening and baseline sessions only.

B. Participants

In the cocaine use severity analysis (N = 90), the majority of participants identified as Black/African American (80%), followed by White (15%), with the remainder (5%) identifying as either Asian, more than one race, or unknown. The average age was 49.85 years old (SD = 7.62), and the average education was 12.83 years (SD = 1.52). 3 participants were missing for the risky sexual behavior analysis (N = 87) due to exclusion of influential observations, and the demographics of the RAB sub-sample were highly comparable to the full sample.

Participants met criteria of at least moderate severity for cocaine use disorder based on the *Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition* (American Psychiatric Association, 2013). Additional eligibility criteria included being 18-60 years of age, providing a positive urine toxicology screen for cocaine metabolite during the intake process, and being in acceptable health on basis of interview, medical history, and physical exam. Exclusionary criteria included moderate or severe substance use dependence for substances besides cocaine, marijuana, alcohol or nicotine, alcohol dependence requiring detoxification, the presence of unstable psychiatric disorders (e.g. psychosis, dementia, or other axis I disorders), neurological conditions, severe medical conditions or contraindications to the study medication, impending incarceration, and pregnancy.

C. <u>Measures</u>

1. Sexual risk behaviors

The Risk Assessment Battery (RAB; Navaline et al., 1994) is a self-administered assessment of HIV risk behavior that asks questions regarding alcohol and drug use, needle use, sexual practices (e.g. number of sexual partners, frequency of sex for drugs), and concerns regarding HIV and testing. Higher scores on the RAB indicate higher levels of risky behavior.

The RAB's sexual risk subscale score was used as our primary dependent variable for our main analysis. Scores on the RAB sex risk index range from 0 to 1.0, with higher scores reflecting greater sexual risk. The sexual risk subscale score was used rather than the total score since the drug risk subscale focuses on injection use, which is uncommon in individuals who solely use crack cocaine (Meacham et al., 2016). Individuals who use both cocaine and heroin are not strongly represented in our sample, as individuals with more than mild opioid use disorder are excluded from participation. Consistent with this, previous literature has suggested that the major mode of HIV transmission among people who use crack cocaine is sexual (Chiasson, Stoneburner, Hildebrandt, Ewing, & Telzak Jaffe, 1991; Da Silva França et al., 2018), further supporting our rationale for using the sexual risk subscale score as our primary dependent variable. Previous studies on individuals who use cocaine have also used the sexual risk subscale index score as their measure for risky sexual behavior in this population (Hayaki, Anderson, & Stein, 2006). The RAB's internal reliability was not calculated in this analysis, since it measures the frequency of different types of sexual risk behaviors (e.g. how many men have you had sex

with in the past six months, how many women have you had sex with in the past six months) that might fit different profiles of individuals. We would not expect some of the RAB's items to be correlated with each other (in fact, some are likely to be anti-correlated), thus internal reliability is not an applicable metric for the RAB.

2. <u>Cocaine use severity</u>

The Addiction Severity Index (ASI; McLellan et al., 1992) is a semi-structured interview that assesses for problems in various domains, including medical, employment, alcohol/drugs, legal status, family/social relationships, and psychiatric status. The ASI's question regarding participants' cocaine use in the past month was used as our dependent variable for the second analysis on cocaine use severity, with higher scores reflecting greater severity. Previous studies on individuals who use cocaine and heroin have found associations between cocaine use in the past 30 days and risky sexual behavior (Hayaki et al., 2006).

3. <u>Difficulties in Emotion Regulation Scale</u>

The Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004) is a 36item self-report questionnaire used to assess emotion regulation. Previous studies included in the introduction have used this measure to examine the relationship between emotion regulation difficulties and risky sexual behavior among patients with substance use disorders (Tull et al., 2012). The DERS includes six subscales: nonacceptance, goals, impulse, awareness, strategies, and clarity. Example items include, "I am clear about my feelings" and "when I'm upset, my emotions feel overwhelming." Respondents rate themselves on a 5-point Likert-style scale (1 = "almost never" to 5 = "almost always). Higher scores reflect greater difficulties with emotion regulation. The DERS's total score was used as our measure for emotion regulation. The DER's internal reliability in this study was Cronbach's $\alpha = 0.93$.

4. Avoidance and Inflexibility Scale

The Avoidance and Inflexibility Scale (AIS; Gifford et al., 2004) is a 13-item self-report questionnaire utilized to measure experiential avoidance and inflexibility. The items ask about participants' thoughts (e.g., "I wish I could use right now"), feelings (e.g., stress, depressed mood), and bodily sensations (e.g., physical cravings, withdrawal symptoms) that may encourage them to use substances. Example items include, "how likely is it that these thoughts will lead you to use substances" and "do you need to reduce how often you have these thoughts in order to not use substances." Participants base their responses on a 5-point Likert-style scale (1 = "Not at all" to 5 = "Very much"). Higher scores reflect greater levels of avoidance and inflexibility. The AIS's total score was used as our measure for experiential avoidance. The AIS's internal reliability in this study was Cronbach's $\alpha = 0.91$.

5. Distress Tolerance Scale

The Distress Tolerance Scale (DTS; Simons & Gaher, 2005) is a 15-item self-report questionnaire used to evaluate individuals' emotional distress tolerance. Studies presented in the introduction have used the DTS to assess the relationship between distress intolerance and risky sexual behavior (Van Eck et al., 2015). This measure includes four components: tolerance, appraisal, absorption, and regulation. Example items include, "feeling distressed or upset is unbearable to me" and "I'll do anything to stop feeling distressed or upset." Participants respond based on a 5-point Likert-type scale (1 = "strongly agree" to 5 "strongly disagree"). Higher total scores indicate greater levels of distress tolerance. The DTS's total score was used as our measure for distress tolerance. The DTS's internal reliability in this study was Cronbach's $\alpha = 0.90$.

6. Five-Facet Mindfulness Questionnaire

The Five-Facet Mindfulness Questionnaire (FFMQ; Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006) is a 39-item self-report questionnaire used to assess mindfulness. Previous studies described in the introduction have used this measure to examine the relationship between mindfulness and risky sexual behavior (Roberts & Danoff-Burg, 2011). The FFMQ includes five facets: observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience. Example items include, "I tell myself I shouldn't be feeling the way I'm feeling," and "I am easily distracted." Respondents rate themselves on a 5-point Likert-style scale (1 = "never or very rarely true" to 5 = "very often or always true"). Higher total scores indicate greater levels of mindfulness. The FFMQ's total score was used as our measure for mindfulness. The FFMQ's internal reliability in this study was Cronbach's $\alpha = 0.89$.

7. Delay Discounting Task

The delay discounting task is a behavioral economic measure of the extent to which individuals prefer short-term rewards over long-term rewards. This task has been used with individuals who are dependent on cocaine (Coffey et al., 2001). In this computerized task, participants were presented with hypothetical monetary outcomes. Participants were presented with two options, an immediate reward of \$5 to \$955 or a delayed reward of \$1,000. The delayed reward ranged from 1 day to 25 years. Area under the curve with a log-transformation of the delay values (AUClog), which were determined based on indifference points, were used as our measure for delay discounting (Borges, Kuang, Milhorn, & Yi, 2016). Lower AUC scores suggested greater levels of delay discounting.

D. **Procedure**

Our measures are from the screening evaluation intake and baseline visit of the clinical trial. On average, the screening and baseline sessions were separated by 9.72 days (SD = 5.38)

for the risky sexual behavior analysis and by 9.78 days (SD = 5.37) for the cocaine use severity analysis. The screening is a two to three-day intake that occurs before participants enroll in the clinical trial. During the screening visit, participants completed the Risk Assessment Battery, Difficulties in Emotion Regulation Scale, Addiction Severity Index, Structured Clinical Interview for DSM-5 (SCID-5) to establish substance and psychiatric diagnoses, a medical screening, blood draw, and provided a urine sample. The screening evaluation results were presented to participants within two days of completion, and participants had the option to enroll in the clinical trial. During the baseline visit of the clinical trial, participants completed the Avoidance and Inflexibility Scale, Distress Tolerance Scale, Five-Facet Mindfulness Questionnaire, and Delay Discounting task. This study is underway at the Treatment Research Clinic of the Center for Neurobehavioral Research on Addiction (CNRA), a university-supported center within the UTHealth Department of Psychiatry.

III. ANALYTIC APPROACH

Our analysis included five predictors, experiential avoidance, emotion regulation, distress tolerance, mindfulness, and delay discounting. We analyzed the relationship between our predictor variables and our outcomes of sexual risk behavior and cocaine use severity using multiple linear regression. We used R for all analyses (Version 4.0.1; R Core Team, 2020).

Pre-analysis, we tested the internal reliability for each measure by calculating Cronbach's alpha. The R-package *psych* was used to calculate Cronbach's alpha (Version 1.9.12.31). Cronbach alpha values \geq .70 indicate good internal reliability (Kline, 1999). All applicable scales in this analysis met this criteria.

Additionally, tests of systematicity based on Johnson and Bickel (2008) were conducted to identify non-systematic delay discounting data. Predictive mean matching was used for missing data. After total scores were calculated, we assessed whether our predictors and outcome variable were normally distributed. We analyzed the zero-order correlations between the predictor variables and assessed for multicollinearity by calculating variance inflation factors (VIF). The R-Studio package *car* was used to assess for Multicollinearity (Version 3.0-8).

Possible covariates included gender, age, education, income, sexual preference, and race. We included a variable as a covariate if it was significantly related to any one of the predictor variables and the outcome variable (Pocock, Assmann, Enos, & Kasten, 2002). To address our main hypothesis, we conducted a linear regression analysis to examine the relationship between the predictor variables, experiential avoidance, emotion regulation, distress tolerance, mindfulness, and delay discounting and the outcome variable, sexual risk behavior, while controlling for any identified covariates. To address our second hypothesis, we conducted an additional linear regression analysis to examine the relationship between the five predictor variables and cocaine use severity, while controlling for any identified covariates. We considered our models significant if p < .05 for the contribution of our predictors of interest, above and beyond any identified covariates.

If the results indicated that the overall models were significant, we then addressed our sub-hypotheses. We considered the relationship between each predictor and our outcome variables to be significant if p < .05.

To address our exploratory aim, we assessed for the relative importance of each predictor, experiential avoidance, emotion regulation, distress tolerance, mindfulness, and delay discounting on our outcome variable, sexual risk behavior. The R-Studio package *relaimpo* was used to assess relative importance (Version 2.2-3). We parsed the influence to determine how much variance each predictor accounted for in our total model. We then bootstrapped the confidence intervals of each predictor's influence. This determined which predictor was most strongly related to sexual risk-taking among individuals with cocaine use disorder.

IV. RESULTS

Prior to the main analyses, tests for systematicity based on Johnson and Bickel (2008) identified non-systematic delay discounting data. Non-systematic data (n = 5) was excluded from future analyses. Influential observations (n = 3) were also identified and excluded from the final risky sexual behavior analysis using Cook's distance, and (n = 1) participant was excluded due to missing data on the dependent variable, risky sexual behavior. The final risky sexual behavior analysis included 87 participants. For the cocaine use severity analysis, (n = 1) influential observation was identified and excluded. The final cocaine use severity analysis included 90 participants. Descriptive statistics for the final samples are presented in Table 1.

Our sample reported an average sexual risk score of 0.25 (SD = 0.14), which was similar to previous studies on individuals who use cocaine 0.30 (SD = 0.18) (Hayaki et al., 2006). On average, our sample reported using cocaine 17.95 days (SD = 9.18) in the last month. There were no indicators of multicollinearity present (all variance inflation factors < 4) for both analyses.

	Analysis 1 ($N = 87$)		Analysis 2 ($N = 90$)	
	M(SD)	n	M(SD)	n
Sex				
Female		15		18
Male		72		73
Age (years)	50(7.62)		49.85(7.62)	
Race				
African American		70		72
Asian		1		1
White		12		14
More than one race		1		1
Unknown/not reported		3		3
Education (years)	12.86(1.53)		12.83(1.52)	
Sexual Preference				
Heterosexual		83		87

Other		4	
RAB Sexual Risk	0.25(0.14)		
Cocaine use severity			
(days used in last			17.95(9.18)
month)			

Note: Analysis 1 = risky sexual behavior analysis. Analysis 2 = cocaine use severity analysis. RAB = Risk Assessment Battery.

A. <u>Multiple Regression Analyses</u>

1. Analysis 1: Risky Sexual Behavior

To test our primary hypothesis, a multiple regression analyzed the effect of experiential avoidance, emotion regulation difficulties, distress tolerance, mindfulness, and delay discounting on risky sexual behavior. All independent variables and potential covariates (age, education, income) were centered. Age, education, gender, race, sexual preference, and income were not included in our final model as covariates, since these variables were not significantly related to both sexual risk behavior and any of our independent variables.

The results from the multiple regression were not statistically significant F(5, 81) = 0.97, p = 0.43, see Table 2. Experiential avoidance, emotion regulation difficulties, distress tolerance, mindfulness, and delay discounting accounted for R²= 0.06 of the variance in risky sexual behavior. The analysis revealed that there were no significant effects of experiential avoidance (b = -0.002, p = 0.27), emotion regulation difficulties (b = 0.001, p = 0.13), distress tolerance (b = 0.017, p = 0.40), mindfulness (b = -0.00, p = 0.59), or delay discounting (b = 0.066, p = 0.50) on risky sexual behavior.

Relative importance analyses were conducted to determine the proportion of variance explained by each predictor. Emotion regulation difficulties contributed to the most variance in the model (lmg = 0.45), followed by avoidance (lmg = 0.21), mindfulness (lmg = 0.19), distress tolerance (0.09), and delay discounting (lmg = 0.06).

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	b	SE	р
Experiential Avoidance	-0.002	0.001	0.27
Emotion regulation difficulties	0.001	0.000	0.13
Distress tolerance	0.017	0.020	0.40
Mindfulness	-0.000	0.001	0.59
Delay discounting	0.066	0.097	0.50
R ²			0.06
Adj. R2			0.00

Table 2. Multiple regression analysis on risky sexual behavior (N = 87)

Note: SE = standard error * $p \le .05$. ** $p \le .01$. *** $p \le .001$.

2. <u>Analysis 2: Cocaine Use Severity</u>

To test our second hypothesis, a multiple regression analyzed the effect of experiential avoidance, emotion regulation difficulties, distress tolerance, mindfulness, and delay discounting on cocaine use severity. All independent variables and potential covariates (age, education, income) were centered. Age, education, gender, race, sexual preference, and income were not included in our final model as covariates, since these variables were not significantly related to both cocaine use severity and any of our independent variables.

The results from the multiple regression were not statistically significant F(5, 84) = 1.15, p = 0.34, see Table 3. Experiential avoidance, emotion regulation difficulties, distress tolerance, mindfulness, and delay discounting accounted for R²= .06 of the variance in cocaine use severity. The analysis revealed that there were no significant effects of experiential avoidance (b = 0.05, p = 0.59), emotion regulation difficulties (b = 0.01, p = 0.82), distress tolerance (b = -0.28, p = 0.83), mindfulness (b = -0.08, p = 0.19), or delay discounting (b = -6.93, p = 0.29) on cocaine use severity.

	b	SE	р
Experiential Avoidance	0.05	0.09	0.59
Emotion regulation difficulties	0.01	0.06	0.82
Distress tolerance	-0.28	1.29	0.83
Mindfulness	-0.08	0.06	0.19
Delay discounting	-6.93	6.53	0.29
R ²			0.06
Adj. R2			0.00

Table 3. Multiple regression analysis on cocaine use severity (N = 90)

Note: SE = standard error

* $p \le .05$. ** $p \le .01$. *** $p \le .001$.

V. DISCUSSION

This sample's average self-reported risky sexual behavior was comparable to other studies on sexual risk behavior among individuals who use cocaine (Hayaki et al., 2006). Contrary to our hypotheses, emotion regulation, experiential avoidance, distress tolerance, mindfulness, and delay discounting did not predict risky sexual behavior or cocaine use severity in individuals with cocaine use disorder.

The results from this secondary analysis may differ from the literature, despite using the same measures, due to several reasons. Two possible explanations may be the use of subscales in previous studies, and their decision to complete analyses at the item level. Previous study findings suggested that risky sexual behavior was not related to some of the emotional processes as a whole construct (e.g., mindfulness) and was only correlated with subscales, which we did not analyze but could be possible in our sample as well (Roberts & Danoff-Burg, 2011). In our analyses, we did not use subscales since most of the studies cited explored these relationships by analyzing constructs as a whole. Future studies may focus on examining whether the subscales used in previous literature relate to risky sexual behavior among individuals who use cocaine. Also, study results have found the mechanisms we tested (e.g., emotion regulation difficulties) to be significantly related to specific items (e.g., number of sexual partners, condom use) presented on the RAB (Tull et al., 2012). However, we did not complete any analyses at the item level, because we were interested in examining high risk sexual behaviors in general in this population. Thus, in our analysis, we examined the relationship between the mechanisms of interest and the RAB's sexual risk subscale as a whole. Not taking this into account in our analyses may have contributed to the discrepancy between our results and the literature. To better understand these

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relationships, future studies may analyze how these mechanisms relate to specific risky sexual practices on the RAB (e.g., number of sexual partners, condom use).

In addition, other potential explanations for these differences include the failure to include interactions or consider possible mediational relationships in our analyses. Some previous studies also did not find main effects on risky sexual behavior for some of the processes examined (e.g., distress tolerance), but rather found significant interactions with other symptoms (e.g., MDD and distress tolerance, ADHD symptoms and distress tolerance) that influenced risky sexual behavior (Tull & Gratz, 2013; Van Eck et al., 2015). Studies have also incorporated depression, anxiety, and PTSD symptoms in their analyses when examining interactions and when analyzing the emotional and behavioral processes as potential mediators for compulsive sexual behavior (Brem et al., 2017, 2018). As such, it is possible we did not find significant effects for these five mechanisms, since we did not take into account possible relationships with measures of depression, anxiety, or PTSD. Future studies can explore these relationships further by examining interactions, the mechanisms as mediators, and also exploring cardinal features of MDD, such as the relationship between anhedonia and risky sexual behavior among individuals with cocaine use disorder.

Regarding cocaine use severity, drug use in the past 30 days has been found to be significantly associated with risky sexual behavior (Hayaki et al., 2006; Meade, McDonald, & Weiss, 2009; Rasch et al., 2000). However, when examining drug use severity in relation to the mechanisms tested, few studies have used 30 day frequency as a measure when exploring these relationships (Strickland et al., 2017). Although the emotional and behavioral processes in our analysis were not significantly related to cocaine use in the past 30 days, it is plausible that they are related to different aspects of substance use, including initiation, lifetime use, drug use

quantity, number of DSM CUD symptoms endorsed, and other substance use severity. In fact, previous studies have found some of the mechanisms we tested (e.g., delay discounting) to not be significant predictors of past month drug use, but significant predictors of other aspects of drug use such as number of DSM symptoms endorsed (Strickland et al., 2017). Additionally, past literature has used other drug use outcomes (e.g., success in treatment) when analyzing the relationship between the mechanisms and drug use (Stotts et al., 2015; Zvolensky et al., 2014). Given these findings, it would be important for future studies to examine these relationships further.

Other explanations for the difference in results, even in analyses that used the same measures as previous studies, are sample differences. For instance, some of the previously reported studies were conducted among adolescent populations, which is different from our sample. Several studies on each of the mechanisms presented in the introduction also used larger sample sizes than the one in our analyses. Some of these studies included as many as 752 participants (Messman-Moore et al., 2010). Based on a power analysis, for analysis 1 on risky sexual behavior, we would need a sample size of 222 to detect this effect at 0.05 significance level. For analysis 2 on cocaine use severity, we would need a sample size of 193 to detect this effect at 0.05 significance level.

This secondary analysis has the following limitations. First, we recognize that taking measures from two different points in time (i.e., baseline and intake) represents a limitation. Thus, we reported the average delay between these two sessions to allow evaluation of this, which was a brief period of time. Second, given the focus on unhealthy behaviors, it is possible that severity of drug use and other drug use (e.g., alcohol, smoking, THC) may be associated with the emotional and behavioral processes. As such, not having a more comprehensive

measure for severity of drug use and other drug use (e.g., Timeline Followback) was a limitation in this analysis. Third, using hypothetical money in the delay discounting task is a limitation; however, several studies on delay discounting have shown no difference between hypothetical and real outcomes (Johnson & Bickel, 2002). Fourth, a measure of sexual discounting was not included in the initial study design, thus it was not included in this secondary analysis. Future studies may examine whether there are differences between delay discounting for hypothetical monetary rewards and sexual rewards in regard to their relationship with risky sexual behavior.

Overall, this sample endorsed risky sexual practices that are important to address in psychotherapy for individuals with cocaine use disorder. If these results are accurate and there is no relationship or a small relationship between these five mechanisms and risky sexual behavior/cocaine use, these mechanisms may not be the best targets in dual interventions. Therefore, it is crucial to examine additional emotional or behavioral processes that may relate to sexual risk-taking and cocaine use to tailor dual interventions for this population.

VI. CITED LITERATURE

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CONFERENCE POSTERS AND PRESENTATIONS	Nunez, C., Schepers, S.T., Bower, M., Wardle, M.C., & de Wit, H. (2020, June 20-24). <i>Nicotine Does Not Alter Willingness to Exert Effort for Monetary Rewards</i> [Oral presentation canceled]. The Annual Meeting of The College on Problems of Drug Dependence, Hollywood, FL.
	Torres, T. K., Slonecker, E., Nunez, C., Sakr, S., Eales, L., Lukowski, A. (2017, October). <i>Associations between Parent-</i> <i>Reported Sleep Problems and English Language Production in 24- to</i> <i>30-Month-Old Children</i> . Poster presented at Cognitive Development Society, Portland, OR.
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