Now or Later? Emotional Factors and Decision-Making in Cocaine Use Disorder

BY

JENNIFER K. HOOTS

B.A. Cornell University, 2016

THESIS

Submitted as partial fulfillment of the requirements

for the degree of Master of Arts in Psychology

in the Graduate College of the University of Illinois at Chicago, 2020

Chicago, Illinois

Defense Committee:

Margaret C. Wardle, Chair and Advisor

Robin Mermelstein

Jin Yoon, The University of Texas Health Science Center at Houston

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ANOVA	Analysis of Variance
AUC	Area under the curve
BDI-II	Beck Depression Inventory Second Edition
CPT	Cold Pressor Task
CUD	Cocaine use disorder
DTS	Distress Tolerance Scale
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
SHAPS	Snaith-Hamilton Pleasure Scale

SUMMARY

Cocaine use disorder (CUD) remains a major public health concern, contributing significantly to death and disability. One defining feature of CUD is the repeated use of cocaine at the expense of alternative rewards. Importantly, the timescale on which drug rewards and alternate rewards are delivered typically differs. While use of cocaine quickly leads to rewarding effects, working towards alternative, long-term goals tends to involve more delay until reward receipt. Rewards are generally perceived as worth less when people must wait longer to receive them, and this phenomenon is called delay discounting. Individuals with CUD show relatively steep delay discounting, indicating that they perceive the value of the reward as quickly decreasing as the delay increases. Identifying modifiable factors that drive delay discounting will help to target treatments to this key decision-making dysfunction. While some cognitive factors have been investigated in relation to delay discounting, less is known about the roles of emotional functioning and reward processing in the steep delay discounting seen in CUD. The current study focuses on the relationship of delay discounting with distress tolerance and depression symptoms. These factors are functionally significant areas of deficit in CUD and show promise for future treatment approaches. Based on previous work on emotional functioning, reward processing, and substance use disorders, we hypothesized: (1) lower distress tolerance would relate to steeper delay discounting in treatment-seeking individuals with CUD and (2) higher levels of depression symptoms and anhedonia would relate to steeper delay discounting in treatment-seeking individuals with CUD. We also tested for possible quadratic relationships of depression and anhedonia with discounting to evaluate alternative hypotheses.

Participants included 75 treatment-seeking individuals with CUD. Distress tolerance was measured using both a self-report questionnaire (Distress Tolerance Scale) and a behavioral

measure of pain tolerance (Cold Pressor Task). Broad depression symptoms were self-reported on the Beck Depression Inventory Second Edition, and anhedonia, a particularly relevant subset of depressive symptoms, was self-reported on the Snaith-Hamilton Pleasure Scale. To assess the relationship between these factors and temporal decision-making, we used multiple regression analyses with AUClog and log *k* from the delay-discounting task as dependent variables.

We found that while self-reported distress tolerance showed no relationship with delay discounting, a behavioral measure showed that lower levels of tolerance for physical pain was associated with steeper delay discounting in treatment-seeking individuals with CUD. Results also showed that depressive symptoms had a quadratic relationship with delay discounting, such that low and high levels of depression were associated with steeper delay discounting compared to moderate levels. Anhedonia showed a quadratic relationship with delay discounting as well, but moderate levels of anhedonia were associated with steeper delay discounting in comparison to low and high levels of anhedonia.

These findings provide meaningful insight into the distinct role which tolerating physical distress may have in delay discounting. Further multi-method assessment of distress tolerance will continue to clarify the distinctions noted here between self-reported distress tolerance and physical pain tolerance as it pertains to temporal decision-making in CUD. Interestingly, the relationships reported here for depression and anhedonia with delay discounting oppose each other. This may reflect unique influences of negative mood versus reward-processing (hedonic response and motivation) in decision-making in CUD. Collectively, these findings push the field forward toward a deeper understanding of problematic decision-making in this treatment-seeking population and offer a variety of potential treatment targets for further analysis.

1. INTRODUCTION

Cocaine use disorder (CUD) is the fourth most common illicit substance use disorder in the United States (Lipari & Park-Lee, 2019). Although less prevalent than marijuana, opioid, or methamphetamine use disorders, CUD contributes significantly to health burdens through disability and death, with these harms disproportionately affecting minority communities (Degenhardt et al., 2014; Shiels et al., 2018). The United States reported a 3.5-fold increase in the total number of deaths involving cocaine between 2010 and 2017 and an estimated 14,666 overdose deaths involving cocaine in 2018 (Centers for Disease Control and Prevention (CDC) & National Center for Health Statistics (NCHS), 2020). Thus, cocaine use remains a pressing public health concern. Understanding the processes that perpetuate the cycle of drug use in CUD is critical to developing better treatments.

One defining and problematic feature of CUD is the repeated use of cocaine at the expense of alternative rewards (American Psychiatric Association, 2014). Individuals with CUD appear to compulsively choose the immediate rewarding effects of cocaine to the detriment of long-term goals like maintaining good health, a steady job, reliable housing, and relationships with friends and family. This phenomenon is reflected in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) criteria for substance use disorder, which describes symptoms including failure to meet obligations, giving up or reducing involvement in non-drug activities, and use despite related physical or psychological problems (American Psychiatric Association, 2014). Furthermore, treatment-seeking individuals clearly express the desire to achieve long-term goals but still struggle to make decisions that reflect this desire in their everyday lives, especially when faced with strong cravings. Understanding the cognitive and

emotional factors that underlie these seemingly suboptimal choices could help with the design of more effective treatments for CUD.

One factor that appears to contribute to myopic decision-making in CUD is the timescale on which drug rewards and alternate rewards are typically delivered. Although the pursuit and use of drugs often quickly leads to rewarding results, working toward alternative rewards tends to involve more delay until receipt of the reward. Choosing between immediate rewards and delayed rewards is a task that all people face, and rewards are generally perceived as worth less when people must wait longer to receive them. This phenomenon is typically assessed using behavioral economic measures aimed at understanding economic decisions based on observable choices. These measures include delay-discounting tasks in which an individual is asked to choose between an immediate reward and a delayed but larger reward (Hamilton & Potenza, 2012; Volkow & Baler, 2015). These delay-discounting tasks capture the degree to which each individual discounts the value of rewards based on delays. Individuals with steep delay discounting perceive the value of the reward as quickly decreasing as the delay increases. Consistent with the characteristics of CUD described above, individuals with CUD show steep delay discounting compared to healthy controls (Coffey et al., 2003; García-Rodríguez et al., 2013; Kirby & Petry, 2004). Notably, studies suggests that those with CUD show the highest rates of discounting seen in the literature thus far (Coffey et al., 2003; García-Rodríguez et al., 2013). Additionally, steeper delay discounting has been associated with higher symptom severity in CUD (Amlung et al., 2017; Kirby & Petry, 2004). Thus, further understanding delay discounting may be important in the treatment of CUD. Identifying modifiable cognitive, emotional, and reward processing factors that drive delay discounting will help to target treatments to this key decision-making dysfunction.

Although several studies have shown that cognitive factors such as working memory, future thinking, and mindfulness are important in delay discounting (Ashe et al., 2015; Bickel et al., 2011; Kurth-Nelson et al., 2012; Szuhany et al., 2018), research to date has not fully addressed the role of emotional factors, such as feelings of depression, difficulty experiencing pleasure, and ability to tolerate distress. While emotional functioning is generally known to affect decision-making processes and outcomes (Lerner et al., 2015; Paulus & Yu, 2012), relatively few studies have investigated the role of emotional function in relation to delay discounting in substance using populations (Dennhardt & Murphy, 2011; Imhoff et al., 2014; Rung et al., 2018; Torres et al., 2013; Tressova-Van Veldhoven et al., 2020). There are numerous known deficits in emotional functioning and reward processing in individuals with CUD that could potentially play key roles in determining the problematic, steep delay discounting seen in this disorder. Here, we will specifically assess how distress intolerance and depression symptoms including anhedonia relate to delay discounting in CUD. We focus on distress intolerance and depression both because they are commonly elevated in CUD and because they show promise as modifiable targets for treatment (Black & Amaro, 2019; Daughters et al., 2008; Fahmy et al., 2018; Hatzigiakoumis et al., 2011). Understanding and addressing these factors may thus improve providers' ability to support individuals with CUD in making choices that promote long-term goals.

One factor which may influence delay-discounting rates in individuals with CUD is distress tolerance, a person's ability and willingness to endure negative experiences. Previous research has shown that substance dependent individuals have lower levels of distress tolerance than healthy controls (Özdel & Ekinci, 2014). In studies of smokers, various measures of distress tolerance have shown associations with nicotine dependence, craving, latency to smoke, smoking

propensity, withdrawal severity, and risk of early lapse during a quit attempt (Brown et al., 2009; Mathew et al., 2019; Mathew & Zhou, 2020; Otto et al., 2020; Trujillo et al., 2017). Additionally, self-reported distress tolerance was shown to predict early treatment dropout in a residential substance use treatment facility (Daughters et al., 2005). Although distress tolerance appears to be an important factor in the development and maintenance of substance use disorders broadly, less work in CUD has been published thus far. One study reported that high levels of cocaine use were associated with low distress tolerance and major life stressors (O'Cleirigh et al., 2007). A study in rats also showed that lower distress tolerance during an abstinence period predicted higher levels of cocaine taking at the beginning of a reinstatement session (Moschak et al., 2018). Taken together, previous work suggests a likely role of distress tolerance in maintenance of CUD.

We theorize that low distress tolerance in CUD may relate to steep delay discounting, as individuals with poor distress tolerance may desire to avoid distressing emotional experiences associated with delaying gratification. Previous work has shown that negative urgency, which describes an individual's tendency to act impulsively when experiencing negative affect, significantly predicted more choices of immediate reward in a mixed sample of healthy controls, pathological gamblers, and cocaine dependent individuals (Torres et al., 2013). This suggests that impulsive choices for immediate reward may be associated with increased urges to alleviate negative emotional states. Consistent with the idea that low distress tolerance may drive steep delay discounting in addictions, studies of alcohol use have shown a relationship between distress tolerance and delay discounting. For example, one study found that low distress tolerance was related to steeper discounting of delayed rewards, although only in individuals with more problematic alcohol use (Rung et al., 2018). Dennhardt & Murphy (2011) also found

that low distress tolerance, high delay discounting, and alcohol problems were interrelated in a sample of college students (although these relationships were only observed among African American students, not European American students). Furthermore, lower levels of distress tolerance have been associated with lower task-specific functional connectivity in the prefrontal cortex in individuals regularly using cocaine and nicotine (Daughters et al., 2017). These brain regions, which contribute to goal-directed behavior and decision-making, represent a pathway by which distress and one's ability to tolerate it may affect delay discounting. These findings indicate that relationships between distress tolerance and delay discounting may be particularly striking in substance use disorders. However, the relationship between these factors has not been comprehensively studied in treatment-seeking individuals with CUD.

Other factors that could contribute to delay discounting in CUD are symptoms of depression and particularly anhedonia. Negative mood and anhedonia are the two primary symptoms associated with major depressive disorder (American Psychiatric Association, 2014). Negative mood is a non-specific factor in mood disorders defined by the experience of negative emotions and captured by symptoms of depression such as sadness, pessimism, feelings of guilt, self-dislike, crying, feelings of punishment, and feelings of worthlessness (Joiner et al., 2003). Anhedonia is defined as a loss of interest or pleasure in response to natural rewards, including food, sex, and social interactions (Destoop et al., 2019). In one study of prevalence of depressive symptoms in crack-cocaine smokers, 80% of the sample reported more than minimal depression and 55% reported symptoms of moderate to severe depression (Falck et al., 2002). While anhedonia can be a key symptom of depression, not all individuals with elevated symptoms of depression experience anhedonia, which distinctly captures features of reward functioning that other symptoms of depression do not. As compared to symptoms of depression more broadly,

anhedonia's specific hedonic and motivational dimensions may contribute to distinct relationships with goal-directed behavior such as delay discounting. Studies have shown that individuals with CUD experience elevated levels of anhedonia (Destoop et al., 2019; Garfield et al., 2014; Leventhal et al., 2010), and that anhedonia is related to worse treatment outcomes for individuals with CUD (Crits-Christoph et al., 2018; Wardle et al., 2017). Experiencing either negative mood or a lack of pleasure in response to commonly rewarding experiences could influence an individual's decision making when choosing between immediate and delayed rewards. Several hypotheses for these relationships are discussed below.

Increased negative mood may relate to steeper delay discounting. Individuals who are experiencing high levels of negative mood could be more motivated to seek an immediate reward in an attempt to improve their mood. These individuals may experience short-sightedness and low desire to wait for larger rewards, especially if low mood is accompanied by feelings of hopelessness or low expectations of ever receiving a larger-later reward. Indeed, previous work has shown that depressive symptoms are correlated with steeper discounting rates in non-CUD populations (Imhoff et al., 2014; Mies et al., 2016; Pulcu et al., 2014; Szuhany et al., 2018; Yoon et al., 2007). Similarly, negative experiences such as exposure to prolonged socioeconomic hardship and elevated stress are associated with steeper delay discounting (Fields et al., 2014; Oshri et al., 2019). Additionally, individuals with intensive heroin use showed increased delay discounting during the imagined negative state of heroin withdrawal (Stoltman et al., 2015). This effect may be even more pronounced in substance use populations, as one study found that perceived stress only significantly predicted delay discounting in heavy smokers, but not nonsmokers (Carim-Todd et al., 2016). These findings incorporating measures of depression and

negative mood states suggest that higher levels of negative mood may be associated with steeper delay discounting in CUD.

Similarly, increased anhedonia may relate to steeper delay discounting. Individuals with high levels of anhedonia may have increased desire to obtain immediate rewards in hopes of experiencing pleasure that feels otherwise absent. Furthermore, if individuals experiencing high levels of anhedonia perceive rewards as inherently less valuable, delay discounting in these individuals may reflect the magnitude effect, in which rewards are more steeply discounted when the reward magnitude is smaller overall (Amlung & MacKillop, 2011; Green et al., 1997). This suggests that individuals experiencing more anhedonia may have steeper delay discounting. Indeed, a recent study showed a positive correlation between anhedonia and delay discounting in patients with an alcohol use disorder but not healthy controls (Tressova-Van Veldhoven et al., 2020). Olson et al. (2018) showed that anhedonia is positively associated with steeper delay discounting in trauma-exposed individuals. Research on smokers showed a relationship between higher levels of anhedonia and quicker smoking initiation when delayed smoking was monetarily rewarded (Leventhal et al., 2014). Studies have also shown that those with higher levels of anhedonia experience stronger effects of urgency on nicotine dependence (Roys et al., 2016) and of deprivation on smoking urges (Leventhal et al., 2009), suggesting that higher anhedonia may be associated with urges to pursue the immediately rewarding effects of smoking. In contrast, while Mies et al. (2016) found a positive relationship between delay-discounting rate and depressive symptoms broadly, they did not find a significant relationship between delay discounting rate and anhedonia as measured by a single-item in a self-report measure of depressive symptoms. However, this work studied a non-clinical sample, and it may be that

individuals with substance use disorders who have higher levels of anhedonia do experience steeper delay discounting.

While findings largely suggest that higher levels of depression and anhedonia are related to steeper delay discounting, there are also alternative hypotheses. Less negative mood may relate to steeper delay discounting. Individuals with very low symptoms of depression may have a particularly strong desire to pursue salient, immediate rewards and therefore may also exhibit steep delay discounting. One study found an interaction indicating that individuals who were highly extraverted and experiencing a positive mood showed the steepest delay discounting (Hirsh et al., 2010). Another study showed that mood moderates the relationship between self-reported impulsiveness and delay discounting such that positive mood strengthens the relationship (Koff & Lucas, 2011). These findings support the possibility that positive mood and particularly low levels of depressive symptoms may actually be associated with steeper delay discounting in CUD.

Likewise, less anhedonia may relate to steeper delay discounting. Individuals with low levels of anhedonia may prefer immediate rewards due to increased approach motivation and appetitive urges. Indeed, Lempert & Pizzagalli (2010) showed a negative correlation between levels of anhedonia and delay-discounting rate in a healthy student population, suggesting that low levels of anhedonia could actually be associated with steep delay discounting in individuals with CUD.

Finally, it is also possible that both of these relationships are true, which would produce a more complex quadratic (U-shaped or inverted U-shaped) effect with delay discounting. Although directionality is unclear, previous reports have shown quadratic effects for depressive symptoms predicting risky sexual behavior in select populations (Millar et al., 2017; Shiu et al.,

2014). Another study found that a biomarker for depression has shown a quadratic relationship with delay discounting (Kimura et al., 2013). Studies have also shown a quadratic relationship between reward sensitivity and body mass index (Davis & Fox, 2008; Verdejo-Roman et al., 2017). Thus, the possibility of quadratic relationships of depression and anhedonia with delay discounting in individuals with CUD merits further investigation. For example, both low and high levels of depression symptoms may be related to steep delay discounting, with some individuals motivated to seek immediate rewards due to low mood while others might display an increased desire to pursue salient rewards associated with positive mood. Additionally, low anhedonia may indicate high motivation for rewards while high anhedonia may indicate reward hyposensitivity, yet both of these conditions will produce steeper delay discounting than average levels of anhedonia. Alternatively, the opposite may be true: low anhedonia may produce reward hypersensitivity while high anhedonia produces low motivation, such that both will have less steep delay discounting than those with average anhedonia. Testing both simple linear and more complex quadratic relationships will help clarify these relationships in the CUD population.

The aims of the current study are thus (1) to determine if distress tolerance is associated with decision making in a delay-discounting task in individuals with CUD and (2) to determine if depressive symptoms, and particularly anhedonia, are associated with decision making in a delay-discounting task in individuals with CUD. Based on previous work on reward processing, emotional functioning, and substance use disorders, we hypothesize: (1) lower distress tolerance will relate to steeper delay discounting in treatment-seeking individuals with CUD and (2) higher levels of depression symptoms and anhedonia will relate to steeper delay discounting in treatment-seeking individuals with CUD. However, we will also test for possible quadratic relationships of depression and anhedonia with discounting, as described above.

2. METHODS

2.1 Overall Design

This study was conducted in the context of a parent trial investigating contingency management, Acceptance and Commitment Therapy, and modafinil as treatments for CUD (ClinicalTrials.gov Identifier: NCT02896712). This analysis used behavioral and self-report measures obtained during a general eligibility screening and a baseline session for the parent study to assess delay discounting, distress tolerance, depression symptoms, and anhedonia. These sessions included a medical examination, urine toxicology screen, and a clinical interview using the Structured Clinical Interview for DSM-5 (SCID-5) administered by trained licensed professional counselors under the supervision of a licensed clinical psychologist that were used to establish inclusion and exclusion criteria. They also included a battery of self-report measures and behavioral tests that provide the primary measures used in this study. This study provides a secondary analysis of this baseline data using multiple regressions to examine how distress tolerance and depression symptoms, including anhedonia, relate to delay discounting in individuals with CUD.

2.2 Participants

Participants were drawn from a parent study conducted at the Center for Neurobehavioral Research on Addictions within the Louis A. Faillace, MD, Department of Psychiatry and Behavioral Sciences at McGovern Medical School at The University of Texas Health Science Center at Houston. Recruitment strategies included newspaper and newsletter articles, public service announcements on TV and radio, notices mailed to local professionals, and billboards located throughout the local community.

Participants were treatment-seeking individuals, 18 to 60 years old, who met current DSM-5 criteria for CUD of at least moderate severity (≥4 symptoms). To qualify, participants also submitted at least one positive urine toxicology screen for the cocaine metabolite benzoylecgonine (BE ≥ 150 ng/mL) during screening, which ensured enrollment of only individuals actively using cocaine. This sample reported using cocaine an average of 17.97 days (*SD* = 9.30) in the previous 30 days, and they reported an average of 15.47 years (*SD* = 8.61) of regular cocaine use. This sample's primary route of cocaine administration was smoking (90.67%), but some individuals reported intranasal administration (9.33%).

Exclusion criteria included: 1. Meeting criteria for moderate or severe Substance Use Disorders for substances other than cocaine, marijuana, alcohol, or nicotine; 2. Meeting criteria for physiological dependence on alcohol requiring detoxification or other substance use that makes participation medically unsafe; 3. The presence of significant and unstable psychiatric disorders including active psychosis, dementia, or other axis I psychiatric or neurological conditions requiring ongoing treatment or making study participation unsafe; 4. Medical conditions or using medications known to be contraindicated for modafinil pharmacotherapy (due to the medication used in the main study). Individuals with a past psychiatric history but not reporting symptoms within the past 12 months prior to assessment or with stable medical conditions or medications compatible with modafinil use were eligible. Included female participants of childbearing potential agreed to use an acceptable method of birth control (includes non-hormonal methods of contraception such as barrier contraceptives, intrauterine devices, and steroid contraceptives) during the study, and pregnant women were excluded.

Participant eligibility was first determined in an eligibility screening, then eligible individuals were invited to participate in the primary study and complete the baseline session.

The self-report measure of anhedonia was administered during the screening, while all other measures included in this analysis were administered at the baseline session. The screening and baseline sessions were permitted to occur a few days apart.

All participants provided informed consent prior to their participation in the study, and the study procedures were approved by The University of Texas Health Science Center at Houston Institutional Review Board. The present analysis was determined by the University of Illinois at Chicago Institutional Review Board as an activity that does not engage the University of Illinois at Chicago. A Data Transfer and Use Agreement for a limited data set was established between The University of Texas Health Science Center at Houston and University of Illinois at Chicago.

2.3 Measures

2.3.1 Delay-Discounting Task

The delay-discounting task is a behavioral economic measure which describes how a reward loses value as a function of increasing delay to its receipt (Amlung et al., 2017; Bickel & Marsch, 2001). In the computerized task, participants were presented with repeated choices between two hypothetical monetary outcomes. Previous work has shown high convergence between delay discounting of hypothetical and real monetary outcomes (Lagorio & Madden, 2005; Matusiewicz et al., 2013) indicating the validity of using tasks with choices between hypothetical rewards. The participants repeatedly chose between $1,000 after a fixed delay or a smaller, immediate option ranging from $10 to $990. The value of the immediate option began at $10 and was titrated to a point of subjective equality (the indifference point) at each fixed delay (delay values range between 1 day and 25 years) based on the participant's responding (García-Rodríguez et al., 2013). This allowed for a complete characterization of the delay-discounting

function which was used to determine an indifference point for each participant. We described delay discounting using AUClog, a variation of the atheoretical area under the curve method which is particularly useful for representing high discounters like those often seen in substance using populations (Borges et al., 2016; Coffey et al., 2003; Yoon et al., 2017, 2018). To calculate AUClog values, we first log-transformed the delay values then entered them into the equation $AUClog = (D_{i+1} - D_i)\big((V_i + V_{i+1})/2\big)$, where D_i and D_{i+1} are consecutive delays and V_i and V_{i+1} are the associated indifference points (Borges et al., 2016; Yoon et al., 2018). The AUClog represents how much the value of the reward is affected by the delay, and a smaller AUClog indicates steeper delay discounting. Additionally, we calculated log *k* derived from Mazur's (1987) hyperbolic equation $V = A/(1 + kD)$ and ran analyses using this dependent variable to confirm that the findings were robust in both measurements of delay discounting (Yoon et al., 2017).

2.3.2 Distress Tolerance

We used two measures of distress tolerance in this study, one self-report scale and one behavioral task. Using both allows for comparison of the two types of measures which have occasionally (Vujanovic et al., 2018), but not typically (Macatee et al., 2015; Marshall-Berenz et al., 2010; Mathew & Zhou, 2020; McHugh et al., 2011), converged in the past. We were thus able to determine if either method of measuring this construct is a strong predictor of delay discounting in CUD.

2.3.2.1 Distress Tolerance Scale (DTS)

The DTS (Simons & Gaher, 2005) is a 15-item self-report measure which indicates the extent to which an individual believes they can experience and withstand distressing emotional states. Each item (e.g. "I can't handle feeling distressed or upset") was scored on a 5-point Likert

scale ranging between 1 (Strongly Agree) and 5 (Strongly Disagree). Factor analysis has shown that the DTS consists of a second-order factor, Global Distress Tolerance, and four first-order factors: Tolerance, Appraisal, Absorption, and Regulation (Simons & Gaher, 2005). The primary outcome variable was the Global Distress Tolerance score which was calculated as the average of the items, and higher scores indicate greater distress tolerance. Previous work has reported the internal consistency of the DTS to be ≥ .82 (Simons & Gaher, 2005).

2.3.2.2 Cold Pressor Task (CPT)

While the DTS measures self-reported distress tolerance, this characteristic can also be measured behaviorally with tasks such as the CPT which has been widely implemented as a measure of physical distress tolerance (Hayes et al., 1999). In this task, the participant's hand was exposed to ice water (1℃, 33℉ verified by thermometer) intended to be safe but aversive (Burns et al., 2004). The CPT has reliably induced increases in subjective pain, cortisol, beta-endorphin, adrenocorticotropic hormone, blood pressure, and heart rate, indicating its strong activation of the hypothalamic-pituitary-adrenal axis (Al'Absi et al., 2002; Bullinger et al., 1984; Edelson & Robertson, 1986; Suzuki et al., 2007). Tolerance was defined as the length of time (in seconds) until the participant reported that the discomfort was no longer tolerable or removed their hand from the ice water, with a maximum time of 300 seconds.

2.3.3 Depressive Symptoms

We used two self-report measures of depressive symptoms in this study. One captured information about symptoms of depression broadly, including both negative mood and anhedonia, as has been done in previous work on depression and delay discounting in substance use disorders. The other examined symptoms of anhedonia only, which may be more specifically related to reward valuation and delay discounting.

2.3.3.1 Beck Depression Inventory Second Edition (BDI-II)

The BDI-II (Beck et al., 1996) is a 21-item self-report inventory that assesses the severity of a wide range of depressive symptoms including both sadness and loss of pleasure. Each item was rated on a 4-point scale ranging between 0 (e.g. "I get as much pleasure as I ever did from the things I enjoy") and 3 (e.g. "I can't get any pleasure from the things I used to enjoy"). The primary outcome variable was a summary score which ranged between 0 and 63 with higher scores indicating more severe symptoms of depression. The BDI-II has high internal reliability and improved validity over previous versions (Dozois et al., 1998; Wang & Gorenstein, 2013).

2.3.3.2 Snaith-Hamilton Pleasure Scale (SHAPS)

The SHAPS (Snaith et al., 1995) is a 14-item self-report scale that measures anhedonia. The items asked participants how much they would enjoy pleasurable experiences across four domains: social interaction, food and drink, sensory experience, and interest/pastimes. Each item was rated by the participant on a 4-point Likert scale ranging between 0 (strongly disagree) and 3 (strongly agree), then reverse coded, and summed. The primary outcome variable was the summed SHAPS score which ranges between 0 and 42 with higher scores indicating greater anhedonia. We chose this continuous variable with a wide range rather than the original SHAPS clinical cutoff scores which use categorization of symptoms as "clinically significant" and have a smaller range (0-14). The SHAPS has high internal consistency, test-retest stability, and convergent validity in this modified scoring format, including in individuals with substance use disorders (Franken et al., 2007).

2.4 Analytic Approach

First, we determined if any demographic factors should be included as covariates. Potential covariates included ethnicity (De Wit et al., 2007; Dennhardt & Murphy, 2011),

income (Epstein et al., 2014), years of education (De Wit et al., 2007), smoking status (Weidberg et al., 2015), and alcohol use (Takahashi & Ohmura, 2009). We examined all potential covariates for relationships with delay discounting, DTS, CPT, BDI-II, and SHAPS outcome variables. Any demographic factor found to be highly related to both the outcome (delay discounting) and any one of the predictor variables (DTS, CPT, BDI-II, SHAPS) would be entered into analyses. This approach of predetermining empirical criteria for covariate inclusion has been recommended for analyses of the relation of baseline data to clinical outcomes (Assmann et al., 2000; Pocock et al., 2002).

While it is not necessary for the predictors in a multiple regression to be normally distributed, we assessed normality in the dependent variables, AUClog and log *k* from the delay-discounting task, using the Shapiro-Wilk test to determine if transformations were necessary. Additionally, we removed any nonsystematic delay-discounting data as identified by the algorithm presented by Johnson and Bickel (2008).

We used multiple regression models to assess whether distress tolerance measures or symptoms of depression, particularly anhedonia, predict behavior in the delay-discounting task. We analyzed the correlations between our potential predictors (DTS, CPT, BDI-II, SHAPS) to determine if any of these variables were highly correlated. If predictors were found to be highly correlated, they would be collapsed to represent one common construct by averaging z-scores on the predictors in question. We then ran separate hierarchical multiple regression models predicting the delay-discounting AUClog and log *k*, including any covariates in Step 1, and our predictors of interest in Step 2, to assess the unique contribution of our predictors of interest above and beyond demographic covariates. Regarding our predictors of interest, as noted above, we tested linear relationships with the DTS and CPT, representing our primary hypothesis about

the relationship between distress tolerance and delay discounting and tested both linear and quadratic relationships with the BDI-II and SHAPS scores, representing both our primary hypotheses about the relationships between depression and anhedonia with delay discounting as well as alternative hypotheses. We examined Cook's distance to test for multivariate outliers and re-ran analyses with outliers removed to test the robustness of the findings. We also tested for heteroscedasticity in our models and planned to address it if found by fitting power polynomials or transforming the predictor(s) according to an exponential, power law, logarithmic, or reciprocal model. The overall models capturing the unique contribution of our predictors of interest above and beyond any covariates were tested for significance at an alpha level of 0.05. Planned follow up tests examining individual beta weights for each predictor were also considered significant at an alpha level of 0.05.

We used R (R Core Team, 2018), R Studio (RStudio Team, 2015), and the following R packages: afex (Singmann et al., 2020), car (Fox & Weisberg, 2019), moments (Komsta & Novomestky, 2015), psych (Revelle, 2019), tidyverse (Wickham et al., 2019), and jtools (Long, 2019).

3. RESULTS

3.1 Demographics

75 participants completed the DTS, CPT, BDI-II, SHAPS, and delay-discounting measures and were considered to have systematic delay-discounting data according to the Johnson and Bickel (2008) criteria. Demographic characteristics are presented in Table 1. The sample's mean age was 49.68 years (*SD* = 7.66), and the mean number of years of education was 12.71 (*SD* = 1.50). Income information was only available for 74 individuals in the sample, but mean income in the previous month was $1792 (*SD* = 3707.17). The sample was 21.33%

Female, and self-identified race was 78.67% African American, 14.67% White, 1.33% Asian, 1.33% More than one race, and 4% Unknown/Not reported race. 8% of individuals reported Hispanic/Latino ethnicity. In the sample, 68% of individuals reported they were current smokers. The sample reported using alcohol an average of 8.09 days (SD = 9.11) in the previous 30 days, and they reported an average of 15.57 years (SD = 12.74) of regular alcohol use (3 or more days per week).

We examined these demographic characteristics to determine if any should be included as covariates. As shown in Table 1, there were no significant relationships between measures of delay discounting and age, years of education, gender, race, ethnicity, income, smoking status, or alcohol use, indicating that these factors should not be included as covariates (Assmann et al., 2000; Pocock et al., 2002). Thus, no demographic covariates were entered into analyses.

3.2 Reliability and Validity

The selected self-report questionnaires showed good reliability in this sample. Internal consistency was high in the DTS (15 items; $\alpha = 0.88$), BDI-II (21 items; $\alpha = 0.94$), and SHAPS (14 items; $\alpha = 0.93$). As shown in Table 2, scores on the DTS and BDI-II were negatively correlated ($r = -0.51$, $p < 0.001$), indicating that individuals reporting lower distress tolerance also reported more symptoms or higher severity of depressive symptoms. Although this relationship is significant, the correlation was not strong enough to result in problems with multicollinearity, thus the DTS and BDI-II were included as separate predictors in the regression analyses. There were no other significant correlations between predictors in the analyses, indicating that the DTS and CPT ($r = -0.10$, $p = 0.41$) measure unique aspects of distress tolerance and the BDI-II and SHAPS ($r = 0.17$, $p = 0.15$) measure distinct symptoms of depression.

Table 1

Demographic Characteristics and Relationships with Delay Discounting

		AUClog		Log *k*	
Demographic	Mean (±SD) or *N* (%)	Statistic	*p*	Statistic	*p*
Age (years)	49.68 (7.66)	$r = 0.04$	0.71	$r = -0.09$	0.44
Education (years)	12.71 (1.50)	$r = 0.17$	0.14	$r = -0.09$	0.44
Income (previous month)	1792.00 (3707.17)	$r = -0.04$	0.75	$r = 0.04$	0.76
Gender		$t = 1.33$	0.19	$t = -1.53$	0.13
Female	16 (21.33%)				
Male	59 (78.67%)				
Race		$F = 0.22$	0.93	$F = 0.07$	0.99
African American	59 (78.67%)				
White	11 (14.67%)				
Asian	1 (1.33%)				
More than one race	1 (1.33%)				
Unknown/Not reported	3 (4%)				
Ethnicity		$t = -1.29$	0.23	$t = 1.28$	0.24
Hispanic	6 (8%)				
Not Hispanic	69 (92%)				
Smoking status		$t = 1.49$	0.14	$t = -1.71$	0.09
Smoker	51 (68%)				
Non-smoker	24 (32%)				
Alcohol use					
Days in previous 30 days	8.09 (9.11)	$r = 0.11$	0.36	$r = -0.02$	0.89
Years of regular use [a]	15.57 (12.74)	$r = 0.0003$	0.998	$r = 0.04$	0.74

Note. We used Pearson correlations to evaluate continuous variables, Welch's t-tests to evaluate variables with two groups, and one-way between-subjects ANOVAs to evaluate variables with more than two groups. For descriptive statistics, $N = 75$ for age, education, gender, race, ethnicity, smoking status, and alcohol use; $N = 74$ for income. For AUClog and log *k* statistics, $N = 72$ for age, education, gender, race, ethnicity, smoking status, and alcohol use; $N = 71$ for income.

[a] Regular use is defined as drinking alcohol on 3 or more days per week.

Table 2

Descriptive Statistics and Correlations for Model Predictors

Variable	*M*	*SD*	1. DTS	2. CPT	3. BDI-II	4. SHAPS
1. DTS	2.83	0.97	-			
2. CPT	56.01	83.79	-0.10	-		
3. BDI-II	15.17	12.28	-0.51***	-0.01	-	
4. SHAPS	12.56	8.81	-0.06	0.12	0.17	-

Note. $N = 75$.

***p < 0.001, **p < 0.01, *p < 0.05

3.3 Delay Discounting

We used multiple regression models to assess whether distress tolerance or symptoms of depression, including anhedonia, predict behavior in the delay-discounting task. The dependent variable, AUClog from the delay-discounting task, was normally distributed. Using the algorithm from Johnson and Bickel (2008) for determining nonsystematic delay-discounting data, we found 4 instances of data identified by Criteria 1 (any indifference point is greater than the preceding one by a magnitude greater than 20% of the larger later reward) and 5 instances identified by Criteria 2 (the last indifference point is not less than the first one by at least 10% of the larger later reward). These 9 cases of nonsystematic delay discounting were removed prior to analyses ($N = 75$).

The initial regression models accounted for 21.64% of the variance in AUClog ($R^2 = 0.2164$, $F(6,68) = 3.13$, $p = 0.009$) and 21.52% of the variance in log k ($R^2 = 0.2152$, $F(6,68) =$

3.11, $p = 0.009$). Based on Cook's distance, three multivariate outliers were removed in each analysis ($N = 72$). For DTS, BDI-II, and SHAPS, the model findings remained the same with outliers removed, indicating that these findings are not solely attributable to the influence of outliers in the sample. However, while the relationship between CPT and AUClog was not significant in the initial model ($\beta = 0.0004$, $p = 0.053$), this effect was significant after removal of outliers ($\beta = 0.0005$, $p = 0.03$). The relationship between CPT and log k was significant with ($\beta = -0.005$, $p = 0.049$) and without outliers ($\beta = -0.005$, $p = 0.03$). Table 3 reports models with multivariate outliers removed ($N = 72$), and all reported models passed testing for heteroscedasticity.

The final models accounted for 20.44% of the variance in AUClog ($R^2 = 0.2044$, $F(6,65) = 2.78$, $p = 0.018$) and 24.01% of the variance in log k ($R^2 = 0.2401$, $F(6,65) = 3.42$, $p = 0.005$). As these results were substantively similar in the final models for AUClog and log k, only the final model with AUClog is reported in depth below.

3.3.1 Relationship with Distress Tolerance

We tested linear relationships with the DTS and CPT to evaluate the hypothesis that lower distress tolerance relates to steeper delay discounting in treatment-seeking individuals with CUD. Scores of self-reported distress tolerance as measured by the DTS did not significantly relate to delay-discounting behavior (Figure 1A; $\beta = -0.028$, $p = 0.19$). Analyses did reveal a significant relationship between distress tolerance as measured by the CPT and delay discounting (Figure 1B; $\beta = 0.0005$, $p = 0.03$). As hypothesized, low distress tolerance in the CPT was related to steeper delay discounting.

3.3.2 Relationship with Depressive Symptoms

To test our hypotheses that higher depressive symptoms, particularly anhedonia, are associated with steeper delay discounting in treatment-seeking individuals with CUD, we tested for independent, linear relationships of BDI-II and SHAPS with delay discounting. We additionally assessed alternative hypotheses by testing for a quadratic relationship between depressive symptoms on the BDI-II and delay discounting as well as a quadratic relationship between anhedonia measured by the SHAPS and delay discounting.

While there was no significant linear effect of the BDI-II with delay discounting (β = -0.014, p = 0.94), there was a significant quadratic relationship between scores on the BDI-II and delay discounting (Figure 1C; β = -0.303, p = 0.047). In line with an alternative hypothesis, this relationship shows that relatively low and high levels of depressive symptoms on the BDI-II were related to steeper delay discounting (smaller AUClog values) as compared to average scores on the BDI-II in this sample.

Analyses revealed no significant linear effect of the SHAPS with delay discounting (β = 0.016, p = 0.92). However, there was a significant quadratic relationship between scores on the SHAPS and delay discounting (Figure 1D; β = 0.489, p = 0.004). Contrary to the hypothesis, average levels of anhedonia in the sample were related to steeper delay discounting (smaller AUClog values) as compared to relatively low and high levels of anhedonia on the SHAPS.

Table 3

Statistical Results for Multiple Regression Models of Delay Discounting

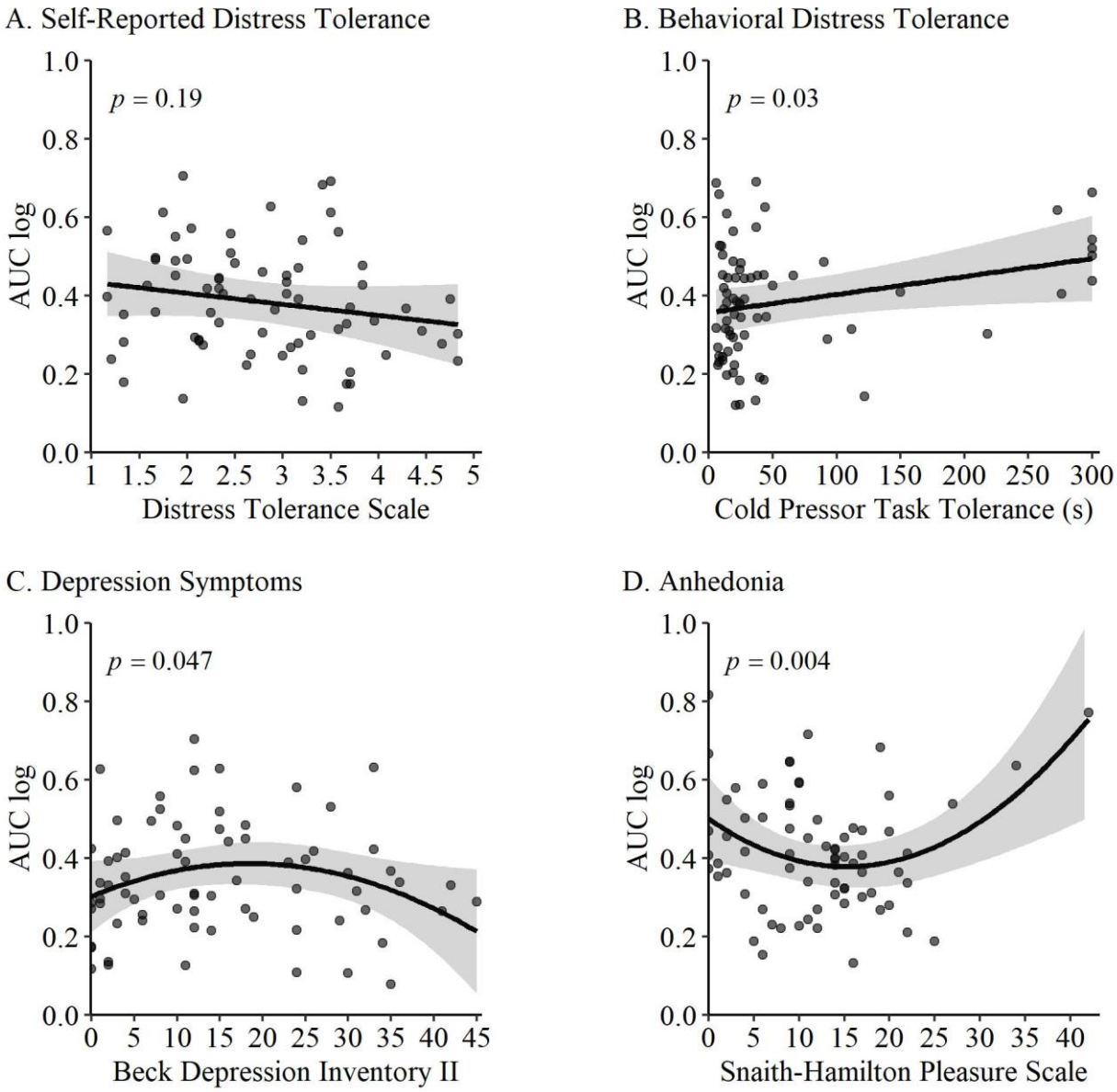
Effect	AUClog			Log *k*		
	Estimate	*SE*	*p*	Estimate	*SE*	*p*
Intercept	0.374	0.017	<0.001***	-3.253	0.189	<0.001***
DTS (linear)	-0.028	0.021	0.19	0.297	0.229	0.20
CPT (linear)	0.0005	0.0002	0.03*	-0.005	0.002	0.03*
BDI-II (linear)	-0.014	0.179	0.94	0.021	1.955	0.99
BDI-II (quadratic)	-0.303	0.150	0.047*	4.317	1.650	0.01*
SHAPS (linear)	0.016	0.153	0.92	-1.941	1.664	0.25
SHAPS (quadratic)	0.489	0.164	0.004**	-4.855	1.798	0.009**
R^2		0.2044			0.2401	
Adjusted R^2		0.1309			0.1699	
Observations		72			72	
F-statistic		2.783			3.422	
p		0.018*			0.005**	

Note. Beta estimates and standard errors (*SE*) are presented.

***p < 0.001, **p < 0.01, *p < 0.05

Figure 1.

Effects of Distress Tolerance and Depression Symptoms on Delay Discounting



Note. Data presented are predicted values from final regression model with 95% confidence intervals shaded.

4. DISCUSSION

This secondary analysis on emotional factors and decision-making in individuals with CUD helps clarify complex relationships which may contribute to the maintenance of this disorder. The aims of the current study were (1) to determine if distress tolerance is associated with decision making in a delay-discounting task in individuals with CUD and (2) to determine if depressive symptoms, and particularly anhedonia, are associated with decision making in a delay-discounting task in individuals with CUD. We found that while self-reported distress tolerance showed no relationship with delay discounting, lower levels of distress tolerance for physical pain were associated with steeper delay discounting. We found that depressive symptoms had a quadratic relationship with delay discounting, such that low and high levels of depression were associated with steeper delay discounting than moderate levels. Anhedonia also showed a quadratic relationship with delay discounting, but in this case, moderate levels were associated with steeper delay discounting in comparison to low and high levels of anhedonia.

This analysis yielded interesting findings related to distress tolerance in CUD. In contrast with previous research, we found that self-reported distress tolerance did not significantly relate to delay discounting. Previous work showed that self-reported distress tolerance was significantly correlated with delay discounting in heavy-drinking college students (Dennhardt & Murphy, 2011; Rung et al., 2018) and predicted alcohol-related problems in African American students (Dennhardt & Murphy, 2011). Notably, these previous studies examined samples younger in age (M = 19.51 years, SD =1.99 in Dennhardt & Murphy, 2011; Median = 22 years, range =18-54 in Rung et al., 2018) than in the present study. This may have contributed to the difference in outcome, as older age has been associated with higher distress tolerance (Rung et al., 2018) and delay discounting typically becomes less steep in individuals over the age of 30

due to the maturation of brain areas related to decision-making and impulsivity (Green et al., 1996; Ross et al., 2013; Yoon et al., 2007). Additionally, these previous studies failed to see these effects generalize to their full sample of college students (Rung et al., 2018) or European American students (Dennhardt & Murphy, 2011), which indicates some instability in these effects.

Using a behavioral measure of distress tolerance, we found that lower tolerance for physical pain was related to steeper delay discounting. This finding suggests that an inability to tolerate negative physiological experiences may confer difficulty in resisting immediate rewards and making decisions associated with long-term benefits. Similarly, Mathew et al. (2019) found that tolerance of physical pain was uniquely related to smoking choice in adult daily smokers, while measures of respiratory distress and psychological distress were not. Given the lack of convergence of measures of distress tolerance in relation to cessation-related outcomes in smokers (Mathew & Zhou, 2020), these findings provide useful evidence distinguishing between self-reported distress tolerance and physical pain tolerance as they relate to decision-making in CUD.

In this sample, we found no significant correlation between scores on the self-report measure of distress tolerance and the behavioral measure of physical pain tolerance. This indicates that these two aspects of distress tolerance are dissociable in this sample and supports the finding that only self-reported distress tolerance was associated with delay discounting in our analyses. While these measures have occasionally shown overlap (Vujanovic et al., 2018), our finding is consistent with numerous investigations showing divergence between self-report measures of distress tolerance and behavioral measures of physical distress tolerance (Macatee et al., 2015; Marshall-Berenz et al., 2010; Mathew & Zhou, 2020; McHugh et al., 2011).

Further comprehensive, multi-method assessments of distress tolerance in CUD will be needed to replicate these findings and solidify connections with ecologically valid factors related to abstinence and relapse, such as choice of cocaine over other delayed rewards. Additionally, Torres et al. (2013) showed a relationship between negative urgency and preference for sooner-smaller rewards in a mixed sample of healthy controls, pathological gamblers, and individuals with cocaine dependence. Direct analysis of negative urgency as a mediator of the connection between low distress tolerance and delay discounting will shed additional light on the contextual meaning of this initial finding in CUD. In addition to this analysis of decision-making regarding gained rewards, it may be useful to assess the relationship of distress tolerance with delay discounting for aversive consequences in this population. This can be done with procedures that ask participants to choose between a small loss immediately and a larger loss at a delay. In such studies, individuals typically discount future losses less than future gains, and this is referred to as the sign effect (Estle et al., 2006; Mies et al., 2016; Thaler, 1981). Previous work has shown that delay discounting for losses, but not gains, relates to frequency of alcohol use (Takahashi & Ohmura, 2009). In individuals with CUD, it may be that distress tolerance is uniquely related to delay discounting for losses which may be associated with more distress than gains.

Our findings did not support the primary hypotheses that depressive symptoms and delay discounting have a linear relationship in treatment-seeking individuals with CUD. The results did, however, reveal a significant quadratic relationship between depressive symptoms and delay discounting, such that relatively low and high levels of depressive symptoms were related to steeper delay discounting as compared to average levels of depressive symptoms in this sample.

One explanation for those experiencing little to no symptoms of depression is that steep delay discounting may be due to relatively positive mood associated with a desire to urgently

pursue salient rewards. This aligns with the finding that, in individuals who were highly extraverted, experiencing a positive mood was associated with steeper delay discounting (Hirsh et al., 2010). Another study found that positive mood strengthens the relationship between self-reported impulsiveness and delay discounting in undergraduate students (Koff & Lucas, 2011). Perhaps underlying personality traits may also moderate the effect seen here.

Interestingly, in this sample of treatment seeking individuals with CUD, self-reported moderate depression symptoms were associated with increased preference for the delayed rewards compared to those reporting minimal depression or more severe depression. It is possible that moderately negative mood may be protective in this population when temporal decision making is concerned. Consistent with this, in a sample of cocaine polysubstance-using individuals, exposure to negative affective images was associated with a preference for risk-averse choices in the Iowa Gambling Task to such a degree that this group was comparable to controls (Fernández-Serrano et al., 2011). Those in the study who were exposed to positive, drug-related, and neutral images showed patterns of maladaptive risky choices in the task and performed significantly poorer than controls.

Furthermore, individuals with CUD who are highly depressed likely show steep delay discounting due to an increased preference for immediate rewards to compensate for low mood. This explanation for high levels of depression associated with steep delay discounting follows the bulk of the literature which also reflects this relationship in non-CUD populations. A 2014 study showed that delay discounting and depression were positively correlated, and individuals classified as non-depressed non-smokers discounted significantly less than those who were smokers, depressed, or both (Imhoff et al., 2014). Depressive symptoms were also associated with steeper discounting in students (Mies et al., 2016), pregnant women (Yoon et al., 2007), and

community populations (Szuhany et al., 2018). Finally, diagnoses of major depressive disorder was significantly related to steeper delay discounting, and severity of depression symptoms was correlated with steeper delay discounting (Pulcu et al., 2014). It should be noted that none of these studies evaluating the relationship between depression and delay discounting reported investigating quadratic effects. It is possible that published studies may have missed significant quadratic effects of depression symptoms and delay discounting due to only testing linear relationships in their samples.

While published studies using direct measures of depressive symptoms such as self-report questionnaires and clinical interviews have not previously found a quadratic relationship with delay discounting, one study did find such an effect when measuring C-reactive protein, a biomarker for depression (Kimura et al., 2013). C-reactive protein is a nonspecific acute-phase protein positively associated with depressive symptoms including mild symptoms in non-clinical individuals (Howren et al., 2009). Kimura et al.'s research showed a significant quadratic effect where steeper delay discounting rates were associated with low and high baseline concentrations of C-reactive protein. Although this study does not directly measure depressive symptoms, this evidence does align with the current finding and provides a potential biological mechanism by which the effect could be mediated.

For anhedonia, our findings again did not support the primary hypothesis of a linear relationship with delay discounting. Rather, we found a significant quadratic relationship between the two factors. In this case, moderate levels of anhedonia in the sample were related to steeper delay discounting as compared to relatively low and high levels of anhedonia. This finding notably contrasts with the results for depression symptoms broadly. This divergence

suggests unique functional roles of these constructs in CUD, with depression symptoms likely reflecting the role of mood while anhedonia specifically indicates the role of reward functioning.

One explanation for those with low levels of anhedonia centers around the magnitude effect. Because individuals with low levels of anhedonia have intact reward responsivity, they perceive reward magnitudes more accurately than those with more anhedonia who perceive them as smaller. Previous work has shown that rewards with larger magnitude are less steeply discounted by delay (Amlung & MacKillop, 2011; Green et al., 1997). This magnitude effect may thus explain the higher preference for the later, larger rewards seen in individuals with little to no anhedonia and CUD. A recent study showed that reward sensitivity was indeed inversely related to anhedonia in individuals with alcohol use disorder and controls (Tressova-Van Veldhoven et al., 2020). They also saw a positive correlation between anhedonia and delay discounting in the alcohol use disorder group only. Another study showed that higher reward sensitivity is related to more rational decision-making on the Iowa Gambling Task in healthy volunteers (Franken & Muris, 2005).

Individuals with moderate levels of anhedonia may be influenced by reduced reward sensitivity and perception of reward magnitude as compared to those with little to no anhedonia. In addition, those with moderate anhedonia may still have intact motivation and appetitive urges compared to those with high levels of anhedonia. This specific combination of influences may then confer higher vulnerability to steep delay discounting in these individuals as compared to those with low and high anhedonia. We found that the average levels of anhedonia in this sample of treatment-seeking individuals with CUD contributed to the most problematic pattern of delay discounting with a preference for smaller, sooner rewards over delayed gratification.

However, those with even higher levels of anhedonia in this sample showed a preference for choosing later, larger rewards in the delay-discounting task. This relationship may potentially be due to decreased approach motivation and appetitive urges associated with high levels of anhedonia. A study of individuals with major depressive disorder found that levels of anticipatory anhedonia predicted motivation to exert effort for the rewards (Sherdell et al., 2012). Another study in a college student sample showed that anhedonia was negatively associated with self-report of approach motivation (Germans & Kring, 2000). These studies show that deficits in anticipation of rewards reduce motivation for rewards, and this suggests that individuals with CUD and high levels of anhedonia may experience low motivation to pursue the immediate rewards offered. This explanation is also supported by Lempert & Pizzagalli's (2010) work which showed a negative correlation between levels of anhedonia and delay-discounting rate in a healthy student population. Future studies will benefit from further consideration of quadratic effects related to the complex symptom of anhedonia and its impact on behaviors. Studies may also add to this work by assessing levels of anhedonia as they relate to temporal decision-making for rewards in ecologically valid contexts for individuals with CUD. Additional measures distinguishing between hedonic response and motivation for rewards may also clarify the underlying processes contributing to this finding.

Further indications of the differences between depression symptoms broadly and anhedonia specifically can improve our understanding of these divergent results for their relationships with delay discounting. Despite their shared connection in measuring symptoms of major depressive disorder, scores on the BDI-II and SHAPS were not correlated in this sample. This demonstrates minimal overlap between reports of broad depression symptoms and specific experiences of anhedonia in these self-report questionnaires. Indeed, measures of depression

symptoms largely assess indicators of mood while measures of anhedonia particularly probe for reward-related interests, behaviors, and responses. This divergence indicates the need to measure distinct symptoms of heterogenous disorders such as depression, especially when considering the impact of these symptoms on other disorders including CUD where specific symptoms such as anhedonia are likely to show unique effects.

It is worth noting that scores on the BDI-II and DTS were moderately correlated in this sample, such that higher severity of depression was associated with lower distress tolerance. This finding aligns with previous reports of significant correlations between these measures in samples of patients with substance dependence (Özdel & Ekinci, 2014), individuals in residential substance use treatment (Magidson et al., 2013), and cocaine-dependent adults (Vujanovic et al., 2016). This relationship appears widely generalizable, including to treatment-seeking individuals with CUD.

Limitations of this study include generalizability to individuals with certain common comorbid conditions (e.g., opioid use disorder, alcohol use disorder with physical dependence, major cardiovascular disease) due to exclusion criteria necessary to ensure participant safety for the main study from which this data was obtained. In particular, the study's sample does not include individuals with moderate or severe polydrug use (other than cocaine, marijuana, alcohol, or nicotine), physiological dependence on alcohol, or medical conditions or medications contraindicated for modafinil pharmacotherapy. Furthermore, all measures are cross-sectional. Due to this study design, causal relationships between variables cannot be inferred. The temporal relationships between drug use, delay discounting, and difficulties with distress tolerance or depression symptoms remain unclear. It is also possible that the significant relationships reported here may be artifacts produced by the outcomes of a common variable that was not assessed. For

example, early life adversity is related to increased anhedonia, poorer emotion regulation, and steeper delay discounting according to a review by Duffy et al., 2018. One particular study found that individuals with CUD who had been put in foster care and/or put up for adoption showed steeper delay discounting than others with CUD (Ross et al., 2013). Previous studies have also found that steeper delay discounting is associated with lower scores on measures of intelligence (Olson et al., 2007; Shamosh et al., 2008) which could present as a confounding factor here.

Despite these limitations, this study does indicate that steep delay discounting is associated with physical distress tolerance, depression symptoms broadly, and anhedonia in treatment-seeking individuals with CUD. Establishing the relationships between these variables is a key first step in suggesting potential ways to ameliorate steep delay discounting in treatment of CUD. Future studies should seek to replicate these novel findings and assess the potential for meaningfully incorporating this information into effective treatment approaches. Studies should address whether treatments targeting physical pain tolerance, depression, or anhedonia also affect delay discounting in CUD. Research should also assess if interventions aimed at these constructs are more effective for those who particularly struggle with distress tolerance, depression, or anhedonia during treatment for CUD.

In relation to distress tolerance deficits in this population, acceptance-based training may be beneficial as it was shown to significantly decrease discounting of monetary rewards and increase distress tolerance in an undergraduate sample (Morrison et al., 2014). Additionally, there is evidence that therapeutic dose of a mindfulness-based intervention relates significantly with improved distress tolerance in women with substance use disorders (Black & Amaro, 2019). Another study found that a mindfulness-based intervention was associated with improved distress tolerance in individuals with opioid use disorder (Fahmy et al., 2018). These

interventions are likely to also impact distress tolerance in treatment-seeking individuals with CUD and may additionally impact its relationship with temporal decision-making in this population.

Prior research suggests that individuals with addiction may also benefit from treatment focused on anhedonia (Destoop et al., 2019; Hatzigiakoumis et al., 2011), and the findings reported here provide evidence for delay discounting as one mechanism that could potentially contribute to this relationship. Behavioral activation, a well-established treatment for depression, focuses on increasing engagement in meaningful activities (Nagy et al., 2020), and the evidence supports its effectiveness for this purpose in individuals with substance use disorders (Daughters et al., 2008). There is also evidence that behavioral activation reduces anhedonia (Walsh et al., 2019) and may be particular effective at treating depression in individuals with elevated anhedonia (Carl et al., 2016). Further, dopaminergic medications show promise for addressing anhedonia in individuals struggling with CUD (Hatzigiakoumis et al., 2011). These are promising avenues for interventions focused on anhedonia and promoting reward-related behaviors consistent with treatment goals for individuals with CUD.

Additionally, further study is needed of delay discounting and the effect of potential treatments for this key factor on symptoms of distress tolerance, depression, and anhedonia. Working memory training has been related to improvements in delay discounting in people with stimulant addictions (Bickel et al., 2011). Episodic future thinking, which promotes cognitive engagement with distant future rewards, is another promising approach to treating delay discounting in substance use disorders (Snider et al., 2016; Stein et al., 2016).

In summary, in treatment-seeking individuals with CUD, results suggest that self-reported distress tolerance does not relate to delay discounting, but lower tolerance for physical

pain in a behavioral task is associated with steeper delay discounting. Low and high levels of depression symptoms appear to be associated with steeper delay discounting while only moderate levels of anhedonia are associated with steeper delay discounting. These findings push the field forward toward a deeper understanding of problematic decision-making in this treatment-seeking population.

5. REFERENCES

Al'Absi, M., Petersen, K. L., & Wittmers, L. E. (2002). Adrenocortical and hemodynamic predictors of pain perception in men and women. *Pain*, *96*(1–2), 197–204. https://doi.org/10.1016/S0304-3959(01)00447-X

American Psychiatric Association. (2014). Diagnostic and Statistical Manual of Mental Disorders, 5th ed. (DSM-V). *American Journal of Pyschiatry*. https://doi.org/10.1111/phil.12034

Amlung, M., & MacKillop, J. (2011). Delayed Reward Discounting and Alcohol Misuse: The Roles of Response Consistency and Reward Magnitude. *Journal of Experimental Psychopathology*, *2*(3), 418–431. http://www.ncbi.nlm.nih.gov/pubmed/25191534

Amlung, M., Vedelago, L., Acker, J., Balodis, I., & MacKillop, J. (2017). Steep Delay Discounting and Addictive Behavior: A Meta-Analysis of Continuous Associations. *Addiction*, *112*(1), 51–62. https://doi.org/10.1111/ADD.13535

Ashe, M. L., Newman, M. G., Wilson, S. J., & Building, M. (2015). Delay Discounting and the use of Mindful Attention versus Distraction in the Treatment of Drug Addiction: A Conceptual Review. *J Exp Anal Behav*, *103*(1), 234–248. https://doi.org/10.1002/jeab.122

Assmann, S. F., Pocock, S. J., Enos, L. E., & Kasten, L. E. (2000). Subgroup analysis and other (mis)uses of baseline data in clinical trials. *The Lancet*, *355*(9209), 1064–1069. https://doi.org/10.1016/S0140-6736(00)02039-0

Beck, A., Steer, R., & Brown, G. (1996). *Manual for the Beck Depression Inventory-II*. Psychological Corporation.

Bickel, W. K., & Marsch, L. A. (2001). Toward a behavioral economic understanding of drug dependence: delay discounting processes. *Addiction*, *96*(1), 73–86.

https://doi.org/10.1046/j.1360-0443.2001.961736.x

Bickel, W. K., Yi, R., Landes, R. D., Hill, P. F., & Baxter, C. (2011). Remember the Future: Working Memory Training Decreases Delay Discounting Among Stimulant Addicts. *Biological Psychiatry*, *69*, 260–265. https://doi.org/10.1016/j.biopsych.2010.08.017

Black, D. S., & Amaro, H. (2019). Moment-by-Moment in Women's Recovery (MMWR): Mindfulness-based intervention effects on residential substance use disorder treatment retention in a randomized controlled trial. *Behaviour Research and Therapy*, *120*, 103437. https://doi.org/10.1016/j.brat.2019.103437

Borges, A. M., Kuang, J., Milhorn, H., & Yi, R. (2016). An alternative approach to calculating Area-Under-the-Curve (AUC) in delay discounting research. *Journal of the Experimental Analysis of Behavior*, *106*(2), 145–155. https://doi.org/10.1002/jeab.219

Brown, R. A., Lejuez, C. W., Strong, D. R., Kahler, C. W., Zvolensky, M. J., Carpenter, L. L., Niaura, R., & Price, L. H. (2009). A prospective examination of distress tolerance and early smoking lapse in adult self-quitters. *Nicotine & Tobacco Research*, *11*(5), 493–502. https://doi.org/10.1093/ntr/ntp041

Bullinger, M., Naber, D., Pickar, D., Cohen, R. M., Kahn, N. H., Pert, A., & Bunney, W. E. (1984). Endocrine Effects of the Cold Pressor Test: Relationships to Subjective Pain Appraisal and Coping. *Psychiatry Research*, *12*, 227–233.

Burns, J. W., Bruehl, S., & Caceres, C. (2004). Anger management style, blood pressure reactivity, and acute pain sensitivity: Evidence for "trait × situation" models. *Annals of Behavioral Medicine*, *27*(3), 195–204. https://doi.org/10.1207/s15324796abm2703_7

Carim-Todd, L., Mitchell, S. H., & Oken, B. S. (2016). Impulsivity and Stress Response in Nondependent Smokers (Tobacco Chippers) in Comparison to Heavy Smokers and

Nonsmokers. *Nicotine & Tobacco Research*, *18*(5), 547–556. https://doi.org/10.1093/ntr/ntv210

Carl, H., Walsh, E., Eisenlohr-Moul, T., Minkel, J., Crowther, A., Moore, T., Gibbs, D., Petty, C., Bizzell, J., Dichter, G. S., & Smoski, M. J. (2016). Sustained anterior cingulate cortex activation during reward processing predicts response to psychotherapy in major depressive disorder. *Journal of Affective Disorders*, *203*, 204–212. https://doi.org/10.1016/j.jad.2016.06.005

Centers for Disease Control and Prevention (CDC), & National Center for Health Statistics (NCHS). (2020). *Multiple Cause of Death 1999-2018 on CDC WONDER*.

Coffey, S. F., Gudleski, G. D., Saladin, M. E., & Brady, K. T. (2003). Impulsivity and Rapid Discounting of Delayed Hypothetical Rewards in Cocaine-Dependent Individuals. *Experimental and Clinical Psychopharmacology*, *11*(1), 18–25. https://doi.org/10.1037/1064-1297.11.1.18

Crits-Christoph, P., Wadden, S., Gaines, A., Rieger, A., Gallop, R., McKay, J. R., & Gibbons, M. B. C. (2018). Symptoms of anhedonia, not depression, predict the outcome of treatment of cocaine dependence. *Journal of Substance Abuse Treatment*, *92*, 46–50. https://doi.org/10.1016/j.jsat.2018.06.010

Daughters, S. B., Braun, A. R., Sargeant, M. N., Reynolds, E. K., Hopko, D. R., Blanco, C., & Lejuez, C. W. (2008). Effectiveness of a brief behavioral treatment for inner-city illicit drug users with elevated depressive symptoms: The Life Enhancement Treatment for Substance Use (LETS Act!). *Journal of Clinical Psychiatry*, *69*(1), 122–129. https://doi.org/10.4088/JCP.v69n0116

Daughters, S. B., Lejuez, C. W., Bornovalova, M. A., Kahler, C. W., Strong, D. R., & Brown, R.

A. (2005). Distress Tolerance as a Predictor of Early Treatment Dropout in a Residential Substance Abuse Treatment Facility. *Journal of Abnormal Psychology*, *114*(4), 729–734. https://doi.org/10.1037/0021-843X.114.4.729

Daughters, S. B., Ross, T. J., Bell, R. P., Yi, J. Y., Ryan, J., & Stein, E. A. (2017). Distress Tolerance among Substance Users is Associated with Functional Connectivity between Prefrontal Regions during a Distress Tolerance Task. *Addict Biol*, *22*(5), 1378–1390. https://doi.org/10.1111/adb.12396

Davis, C., & Fox, J. (2008). Sensitivity to reward and body mass index (BMI): Evidence for a non-linear relationship. *Appetite*, *50*, 43–49. https://doi.org/10.1016/j.appet.2007.05.007

De Wit, H., Flory, J. D., Acheson, A., Mccloskey, M., & Manuck, S. B. (2007). IQ and nonplanning impulsivity are independently associated with delay discounting in middle-aged adults. *Personality and Individual Differences*, *42*, 111–121. https://doi.org/10.1016/j.paid.2006.06.026

Degenhardt, L., Baxter, A. J., Lee, Y. Y., Hall, W., Sara, G. E., Johns, N., Flaxman, A., Whiteford, H. A., & Vos, T. (2014). The global epidemiology and burden of psychostimulant dependence: Findings from the Global Burden of Disease Study 2010. *Drug and Alcohol Dependence*, *137*, 36–47. https://doi.org/10.1016/j.drugalcdep.2013.12.025

Dennhardt, A. A., & Murphy, J. G. (2011). Associations between depression, distress tolerance, delay discounting, and alcohol-related problems in European American and African American college students. *Psychology of Addictive Behaviors*, *25*(4), 595–604. https://doi.org/10.1037/a0025807

Destoop, M., Morrens, M., Coppens, V., & Dom, G. (2019). Addiction, anhedonia, and

comorbid mood disorder. A narrative review. *Frontiers in Psychiatry*, *10*. https://doi.org/10.3389/fpsyt.2019.00311

Dozois, D. J. A., Dobson, K. S., & Ahnberg, J. L. (1998). A psychometric evaluation of the Beck Depression Inventory-II. *Psychological Assessment*, *10*(2), 83–89. https://doi.org/10.1037/1040-3590.10.2.83

Duffy, K. A., Mclaughlin, K. A., & Green, P. A. (2018). Early life adversity and health-risk behaviors: Proposed psychological and neural mechanisms. *Annals of the New York Academy of Sciences*, *1428*(1), 151. https://doi.org/10.1111/nyas.13928

Edelson, J. T., & Robertson, G. L. (1986). The effect of the cold pressor test on vasopressin secretion in man. *Psychoneuroendocrinology*, *11*(3), 307–316. https://doi.org/10.1016/0306-4530(86)90016-8

Epstein, L. H., Jankowiak, N., Lin, H., Paluch, R., Koffarnus, M. N., & Bickel, W. K. (2014). No food for thought: moderating effects of delay discounting and future time perspective on the relation between income and food insecurity. *Am J Clin Nutr*, *100*, 884–890. https://doi.org/10.3945/ajcn.113.079772

Estle, S. J., Green, L., Myerson, J., & Holt, D. D. (2006). Differential effects of amount on temporal and probability discounting of gains and losses. *Memory and Cognition*, *34*(4), 914–928. https://doi.org/10.3758/BF03193437

Fahmy, R., Wasfi, M., Mamdouh, R., Moussa, K., Wahba, A., Wittemann, M., Hirjak, D., Kubera, K. M., Wolf, N. D., Sambataro, F., & Wolf, R. C. (2018). Mindfulness-based interventions modulate structural network strength in patients with opioid dependence. *Addictive Behaviors*, *82*, 50–56. https://doi.org/10.1016/j.addbeh.2018.02.013

Falck, R. S., Wang, J., Carlson, R. G., Eddy, M., & Siegal, H. A. (2002). The prevalence and

correlates of depressive symptomatology among a community sample of crack-cocaine smokers. *Journal of Psychoactive Drugs*, *34*(3), 281–288. https://doi.org/10.1080/02791072.2002.10399964

Fernández-Serrano, M. J., Moreno-López, L., Pérez-García, M., Viedma-Del Jesús, M. I., Sánchez-Barrera, M. B., & Verdejo-García, A. (2011). Negative mood induction normalizes decision making in male cocaine dependent individuals. *Psychopharmacology*, *217*, 331–339. https://doi.org/10.1007/s00213-011-2288-2

Fields, S. A., Lange, K., Ramos, A., Thamotharan, S., & Rassu, F. (2014). The relationship between stress and delay discounting: A meta-analytic review. *Behavioural Pharmacology*, *25*(5–6), 434–444. https://doi.org/10.1097/FBP.0000000000000044

Fox, J., & Weisberg, S. (2019). *An {R} Companion to Applied Regression* (Version 3.0-6). Sage. https://socialsciences.mcmaster.ca/jfox/Books/Companion/

Franken, I. H. A., & Muris, P. (2005). Individual differences in decision-making. *Personality and Individual Differences*, *39*, 991–998. https://doi.org/10.1016/j.paid.2005.04.004

Franken, I. H. A., Rassin, E., & Muris, P. (2007). The assessment of anhedonia in clinical and non-clinical populations: Further validation of the Snaith–Hamilton Pleasure Scale (SHAPS). *Journal of Affective Disorders*, *99*(1–3), 83–89. https://doi.org/http://dx.doi.org/10.1016/j.jad.2006.08.020

García-Rodríguez, O., Secades-Villa, R., Weidberg, S., & Yoon, J. H. (2013). A systematic assessment of delay discounting in relation to cocaine and nicotine dependence. *Behavioural Processes*, *99*, 100–105. https://doi.org/10.1016/j.beproc.2013.07.007

Garfield, J. B. B., Lubman, D. I., & Yücel, M. (2014). Anhedonia in substance use disorders: A systematic review of its nature, course and clinical correlates. *Australian & New Zealand*

Journal of Psychiatry, *00*(0), 1–16. https://doi.org/10.1177/0004867413508455

Germans, M. K., & Kring, A. M. (2000). Hedonic deficit in anhedonia: Support for the role of approach motivation. *Personality and Individual Differences*, *28*(4), 659–672. https://doi.org/10.1016/S0191-8869(99)00129-4

Green, L., Myerson, J., Lichtman, D., Rosen, S., & Fry, A. (1996). Temporal Discounting in Choice Between Delayed Rewards: The Role of Age and Income. *Psychology and Aging*, *11*(1), 79–84.

Green, L., Myerson, J., & McFadden, E. (1997). Rate of temporal discounting decreases with amount of reward. *Memory & Cognition*, *25*(5), 715–723. http://www.ncbi.nlm.nih.gov/pubmed/9337589

Hamilton, K. R., & Potenza, M. N. (2012). Relations among delay discounting, addictions, and money mismanagement: implications and future directions. *The American Journal of Drug and Alcohol Abuse*, *38*(1), 30–42. https://doi.org/10.3109/00952990.2011.643978

Hatzigiakoumis, D. S., Martinotti, G., DiGiannantonio, M., & Janiri, L. (2011). Anhedonia and Substance Dependence: Clinical Correlates and Treatment Options. *Frontiers in Psychiatry*, *2*(10), 1–12. https://doi.org/10.3389/fpsyt.2011.00010

Hayes, S. C., Bissett, R. T., Korn, Z., Zettle, R. D., Rosenfarb, I. S., Cooper, L. D., & Grundt, A. M. (1999). The Impact of Acceptance Versus Control Rationales on Pain Tolerance. *The Psychological Record*, *49*(1), 33–47. https://doi.org/10.1007/BF03395305

Hirsh, J. B., Guindon, A., Morisano, D., & Peterson, J. B. (2010). Positive Mood Effects on Delay Discounting. *Emotion*, *10*(5), 717–721. https://doi.org/10.1037/a0019466

Howren, M. B., Lamkin, D. M., & Suls, J. (2009). Associations of depression with c-reactive protein, IL-1, and IL-6: A meta-analysis. *Psychosomatic Medicine*, *71*(2), 171–186.

https://doi.org/10.1097/PSY.0b013e3181907c1b

Imhoff, S., Harris, M., Weiser, J., & Reynolds, B. (2014). Delay discounting by depressed and non-depressed adolescent smokers and non-smokers. *Drug and Alcohol Dependence, 135*, 152–155. https://doi.org/10.1016/j.drugalcdep.2013.11.014

Johnson, M. W., & Bickel, W. K. (2008). An Algorithm for Identifying Nonsystematic Delay-Discounting Data. *Exp Clin Psychopharmacol, 16*(3), 264–274. https://doi.org/10.1037/1064-1297.16.3.264

Joiner, T. E., Brown, J. S., & Metalsky, G. I. (2003). A test of the tripartite model's prediction of anhedonia's specificity to depression: patients with major depression versus patients with schizophrenia. *Psychiatry Research, 119*, 243–250. https://doi.org/10.1016/S0165-1781(03)00131-8

Kimura, K., Izawa, S., Sugaya, N., Ogawa, N., Yamada, K. C., Shirotsuki, K., Mikami, I., Hirata, K., Nagano, Y., & Hasegawa, T. (2013). The biological effects of acute psychosocial stress on delay discounting. *Psychoneuroendocrinology, 38*, 2300–2308. https://doi.org/10.1016/j.psyneuen.2013.04.019

Kirby, K. N., & Petry, N. M. (2004). Heroin and cocaine abusers have higher discount rates for delayed rewards than alcoholics or non-drug-using controls. *Addiction, 99*(4), 461–471. https://doi.org/10.1111/j.1360-0443.2003.00669.x

Koff, E., & Lucas, M. (2011). Mood moderates the relationship between impulsiveness and delay discounting. *Personality and Individual Differences, 50*(7), 1018–1022. https://doi.org/10.1016/J.PAID.2011.01.016

Komsta, L., & Novomestky, F. (2015). *moments: Moments, cumulants, skewness, kurtosis, and related tests* (Version 0.14). https://cran.r-project.org/package=moments

Kurth-Nelson, Z., Bickel, W., & David Redish, A. (2012). A theoretical account of cognitive effects in delay discounting. *European Journal of Neuroscience*, *35*(7), 1052–1064. https://doi.org/10.1111/j.1460-9568.2012.08058.x

Lagorio, C. H., & Madden, G. J. (2005). Delay discounting of real and hypothetical rewards III: Steady-state assessments, forced-choice trials, and all real rewards. *Behavioural Processes*, *69*(2), 173–187. https://doi.org/10.1016/J.BEPROC.2005.02.003

Lempert, K. M., & Pizzagalli, D. A. (2010). Delay Discounting and Future-directed Thinking in Anhedonic Individuals. *Journal of Behavior Therapy and Experimental Psychiatry*, *41*(3), 258–264. https://doi.org/10.1016/j.jbtep.2010.02.003

Lerner, J. S., Li, Y., Valdesolo, P., & Kassam, K. S. (2015). Emotion and Decision Making. *Annu. Rev. Psychol*, *66*, 799–823. https://doi.org/10.1146/annurev-psych-010213-115043

Leventhal, A. M., Brightman, M., Ameringer, K. J., Greenberg, J., Mickens, L., Ray, L. A., Sun, P., & Sussman, S. (2010). Anhedonia associated with stimulant use and dependence in a population-based sample of American adults. *Experimental and Clinical Psychopharmacology*, *18*(6), 562–569. https://doi.org/10.1037/a0021964

Leventhal, A. M., Trujillo, M., Ameringer, K. J., Tidey, J. W., Sussman, S., & Kahler, C. W. (2014). Anhedonia and the Relative Reward Value of Drug and Nondrug Reinforcers in Cigarette Smokers. *J Abnorm Psychol*, *123*(2), 375–386. https://doi.org/10.1037/a0036384

Leventhal, A. M., Waters, A. J., Kahler, C. W., Ray, L. A., & Sussman, S. (2009). Relations between anhedonia and smoking motivation. *Nicotine & Tobacco Research*, *11*(9), 1047–1054. https://doi.org/10.1093/ntr/ntp098

Lipari, R. N., & Park-Lee, E. (2019). *Key Substance Use and Mental Health Indicators in the United States: Results from the 2018 National Survey on Drug Use and Health*.

https://www.samhsa.gov/data/

Long, J. A. (2019). *jtools: Analysis and Presentation of Social Scientific Data* (Version 2.0.1). https://cran.r-project.org/package=jtools

Macatee, R. J., Sarawgi, S., Norr, A. M., Oglesby, M. E., Lejuez, C. W., & Cougle, J. R. (2015). Behavioral assessment of risk-taking under uncertain threat: Associations with affect and pain tolerance. *Personality and Individual Differences*, *87*, 256–260. https://doi.org/10.1016/J.PAID.2015.08.019

Magidson, J. F., Listhaus, A. R., Seitz-Brown, C. J., Anderson, K. E., Lindberg, B., Wilson, A., & Daughters, S. B. (2013). Rumination mediates the relationship between distress tolerance and depressive symptoms among substance users. *Cognitive Therapy and Research*, *37*(3), 456–465. https://doi.org/10.1007/s10608-012-9488-x

Marshall-Berenz, E. C., Vujanovic, A. A., Bonn-miller, M. O., & Zvolensky, M. J. (2010). Multimethod Study of Distress Tolerance and PTSD Symptom Severity in a Trauma-Exposed Community SAmple. *Journal of Traumatic Stress*, *23*(5), 623–630. https://doi.org/10.1002/jts.

Mathew, A. R., Heckman, B. W., Froeliger, B., Saladin, M. E., Brown, R. A., Hitsman, B., Carpenter, M. J., Clin, E., & Author, P. (2019). Multi-Method Assessment of Distress Tolerance and Smoking-Related Factors among Adult Daily Smokers. *Exp Clin Psychopharmacol*, *27*(2), 136–145. https://doi.org/10.1037/pha0000238

Mathew, A. R., & Zhou, M. (2020). Distress tolerance in relation to cessation history and smoking characteristics among adult daily smokers. *Addictive Behaviors*, *100*, 1–6. https://doi.org/10.1016/j.addbeh.2019.106124

Matusiewicz, A. K., Carter, A. E., Landes, R. D., Yi, R., & House, F. (2013). Statistical

Equivalence and Test-Retest Reliability of Delay and Probability Discounting Using Real and Hypothetical Rewards. *Behav Processes*, *100*, 116–122. https://doi.org/10.1016/j.beproc.2013.07.019

Mazur, J. (1987). An adjusting procedure for studying delayed reinforcement. In *The effect of delay and intervening events on reinforcement value* (pp. 55–73).

McHugh, R. K., Daughters, S. B., Lejuez, C. W., Murray, H. W., Hearon, B. A., Gorka, S. M., & Otto, M. W. (2011). Shared Variance among Self-Report and Behavioral Measures of Distress Intolerance. *Cognitive Therapy and Research*, *35*(3), 266–275. https://doi.org/10.1007/s10608-010-9295-1

Mies, G. W., De Water, E., & Scheres, A. (2016). Planning to make economic decisions in the future, but choosing impulsively now: are preference reversals related to symptoms of ADHD and depression? *International Journal of Methods in Psychiatric Research*, *25*(3), 178–189. https://doi.org/10.1002/mpr.1511

Millar, B. M., Starks, T. J., Grov, C., & Parsons, J. T. (2017). Sexual Risk-Taking in HIV-Negative Gay and Bisexual Men Increases with Depression: Results from a U.S. National Study. *AIDS Behav*, *21*(6), 1665–1675. https://doi.org/10.1007/s10461-016-1507-6

Morrison, K. L., Madden, G. J., Odum, A. L., Friedel, J. E., & Twohig, M. P. (2014). Altering impulsive decision making with an acceptance-based procedure. *Behavior Therapy*, *45*(5), 630–639. https://doi.org/10.1016/j.beth.2014.01.001

Moschak, T. M., Terry, D. R., Daughters, S. B., & Carelli, R. M. (2018). Low distress tolerance predicts heightened drug seeking and taking after extended abstinence from cocaine self-administration. *Addict Biol*, *23*(1), 130–141. https://doi.org/10.1111/adb.12488

Nagy, G. A., Cernasov, P., Pisoni, A., Walsh, E., Dichter, G. S., & Smoski, M. J. (2020). Reward

Network Modulation as a Mechanism of Change in Behavioral Activation. *Behavior Modification*, *44*(2), 186–213. https://doi.org/10.1177/0145445518805682

O'Cleirigh, C., Ironson, G., & Smits, J. A. J. (2007). Does Distress Tolerance Moderate the Impact of Major Life Events on Psychosocial Variables and Behaviors Important in the Management of HIV? *Behavior Therapy*, *38*(3), 314–323. https://doi.org/10.1016/j.beth.2006.11.001

Olson, E. A., Hooper, C. J., Collins, P., & Luciana, M. (2007). Adolescents' performance on delay and probability discounting tasks: Contributions of age, intelligence, executive functioning, and self-reported externalizing behavior. *Personality and Individual Differences*, *43*, 1886–1897. https://doi.org/10.1016/j.paid.2007.06.016

Olson, E. A., Kaiser, R. H., Pizzagalli, D. A., Rauch, S. L., & Rosso, I. M. (2018). Anhedonia in Trauma-Exposed Individuals: Functional Connectivity and Decision-Making Correlates. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *3*(11), 959–967. https://doi.org/10.1016/j.bpsc.2017.10.008

Oshri, A., Hallowell, E., Liu, S., Mackillop, J., Galvan, A., Kogan, S. M., & Sweet, L. H. (2019). Socioeconomic hardship and delayed reward discounting: Associations with working memory and emotional reactivity. *Developmental Cognitive Neuroscience*, *37*, 1–11. https://doi.org/10.1016/j.dcn.2019.100642

Otto, M. W., Rosenfield, D., Gorlin, E. I., Hoyt, D. L., Patten, E. A., Bickel, W. K., Zvolensky, M. J., & Doan, S. N. (2020). Targeting cognitive and emotional regulatory skills for smoking prevention in low-SES youth: A randomized trial of mindfulness and working memory interventions. *Addictive Behaviors*, *104*, 1–9. https://doi.org/10.1016/j.addbeh.2019.106262

Özdel, K., & Ekinci, S. (2014). Distress intolerance in substance dependent patients. *Comprehensive Psychiatry*, *55*, 960–965. https://doi.org/10.1016/j.comppsych.2013.12.012

Paulus, M. P., & Yu, A. J. (2012). Emotion and decision-making: affect-driven belief systems in anxiety and depression. *Trends Cogn Sci*, *16*(9), 476–483. https://doi.org/10.1016/j.tics.2012.07.009

Pocock, S. J., Assmann, S. E., Enos, L. E., & Kasten, L. E. (2002). Subgroup analysis, covariate adjustment and baseline comparisons in clinical trial reporting: Current practice and problems. *Statistics in Medicine*, *21*(19), 2917–2930. https://doi.org/10.1002/sim.1296

Pulcu, E., Trotter, P. D., Thomas, E. J., Mcfarquhar, M., Juhasz, G., Sahakian, B. J., Deakin, J. F. W., Zahn, R., Anderson, I. M., & Elliott, R. (2014). Temporal discounting in major depressive disorder. *Psychological Medicine*, *44*, 1825–1834. https://doi.org/10.1017/S0033291713002584

R Core Team. (2018). *R: A language and environment for statistical computing* (Version 3.5.2). R Foundation for Statistical Computing. https://www.r-project.org/

Revelle, W. (2019). *psych: Procedures for Psychological, Psychometric, and Personality Research* (Version 1.9.12). https://cran.r-project.org/package=psych

Ross, E. L., Yoon, J. H., Mahoney, J. J., Omar, Y., Newton, T. F., & De La Garza, R. (2013). The impact of self-reported life stress on current impulsivity in cocaine dependent adults. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *46*, 113–119. https://doi.org/10.1016/j.pnpbp.2013.06.002

Roys, M., Weed, K., Carrigan, M., & Mackillop, J. (2016). Associations between nicotine dependence, anhedonia, urgency and smoking motives. *Addictive Behaviors*, *62*, 145–151. https://doi.org/10.1016/j.addbeh.2016.06.002

RStudio Team. (2015). *RStudio: Integrated Development for R. RStudio, Inc.* http://www.rstudio.com/

Rung, J. M., Johnson, P. S., & Madden, G. J. (2018). Differential Relations Between Delay Discounting and Distress Tolerance as a Function of Opportunity Cost and Alcohol Use. *Experimental and Clinical Psychopharmocology*, *26*(3), 278–289. https://doi.org/10.17605/OSF.IO/HN4JC

Shamosh, N. A., DeYoung, C. G., Green, A. E., Reis, D. L., Johnson, M. R., A Conway, A. R., Engle, R. W., & Braver, T. S. (2008). *Individual Differences in Delay Discounting: Relation to Intelligence, Working Memory, and Anterior Prefrontal Cortex* (Vol. 19, Issue 9).

Sherdell, L., Waugh, C. E., & Gotlib, I. H. (2012). Anticipatory Pleasure Predicts Motivation for Reward in Major Depression. *J Abnormal Psychol, 121*(1), 51–60. https://doi.org/10.1037/a0024945

Shiels, M. S., Freedman, N. D., Thomas, D., & De Gonzalez, A. B. (2018). Trends in U.S. Drug overdose deaths in non-hispanic black, hispanic, and non-hispanic white persons, 2000-2015. *Annals of Internal Medicine, 168*(6), 453–455. https://doi.org/10.7326/M17-1812

Shiu, C. S., Chen, Y. C., Tseng, P. C., Chung, A. C., Wu, M. T., Hsu, S. T., & Ko, N. Y. (2014). Curvilinear relationship between depression and unprotected sexual behaviors among men who have sex with men. *Journal of Sexual Medicine*, *11*(10), 2466–2473. https://doi.org/10.1111/jsm.12638

Simons, J. S., & Gaher, R. M. (2005). The Distress Tolerance Scale: Development and Validation of a Self-Report Measure. *Motivation and Emotion*, *29*(2), 83–102. https://doi.org/10.1007/s11031-005-7955-3

Singmann, H., Bolker, B., Westfall, J., Aust, F., & Ben-Shachar, M. S. (2020). *afex: Analysis of Factorial Experiments* (Version 0.26-0). https://cran.r-project.org/package=afex

Snaith, R. P., Hamilton, M., Morley, S., Humayan, A., Hargreaves, D., & Trigwell, P. (1995). A Scale for the Assessment of Hedonic Tone the Snaith–Hamilton Pleasure Scale. *British Journal of Psychiatry*, *167*(01), 99–103. https://doi.org/10.1192/bjp.167.1.99

Snider, S. E., LaConte, S. M., & Bickel, W. K. (2016). Episodic Future Thinking: Expansion of the Temporal Window in Individuals with Alcohol Dependence. *Alcoholism: Clinical and Experimental Research*, *40*(7), 1558–1566. https://doi.org/10.1111/acer.13112

Stein, J. S., Wilson, A. G., Koffarnus, M. N., Daniel, T. O., Epstein, L. H., & Bickel, W. K. (2016). Unstuck in time: episodic future thinking reduces delay discounting and cigarette smoking. *Psychopharmacology*, *233*, 3771–3778. https://doi.org/10.1007/s00213-016-4410-y

Stoltman, J. J. K., Woodcock, E. A., Lister, J. J., Lundahl, L. H., & Greenwald, M. K. (2015). Heroin delay discounting: modulation by pharmacological state, drug-use impulsivity and intelligence. *Exp Clin Psychopharmacol*, *23*(6), 455–463. https://doi.org/10.1037/pha0000054

Suzuki, K., Maekawa, K., Minakuchi, H., Yatani, H., Clark, G. T., Matsuka, Y., & Kuboki, T. (2007). Responses of the hypothalamic-pituitary-adrenal axis and pain threshold changes in the orofacial region upon cold pressor stimulation in normal volunteers. *Archives of Oral Biology*, *52*(8), 797–802. https://doi.org/10.1016/j.archoralbio.2007.01.008

Szuhany, K. L., Mackenzie, D., & Otto, M. W. (2018). The impact of depressed mood, working memory capacity, and priming on delay discounting. *Journal of Behavior Therapy and Experimental Psychiatry*, *60*, 37–41. https://doi.org/10.1016/j.jbtep.2018.03.001

Takahashi, T., & Ohmura, Y. (2009). Alcohol use and discounting of delayed and probabilistic gain and loss. *Neuro Endocrinology Letters*, *30*(6), 749–752.

Thaler, R. (1981). Some empirical evidence on dynamic inconsistency. *Economics Letters*, *8*(3), 201–207. https://doi.org/10.1016/0165-1765(81)90067-7

Torres, A., Catena, A., Megías, A., Maldonado, A., Cándido, A., Verdejo-García, A., & Perales, J. C. (2013). Emotional and non-emotional pathways to impulsive behavior and addiction. *Frontiers in Human Neuroscience*, *7*, 43. https://doi.org/10.3389/fnhum.2013.00043

Tressova-Van Veldhoven, D., Roozen, H., & Vingerhoets, A. (2020). The Association between Reward Sensitivity and Activity Engagement: the Influence of Delay Discounting and Anhedonia. *Alcohol and Alcoholism*, *55*(2), 215–224. https://doi.org/10.1093/alcalc/agz105

Trujillo, M. A., Khoddam, R., Greenberg, J. B., Dyal, S. R., Ameringer, K. J., Zvolensky, M. J., & Leventhal, A. M. (2017). Distress Tolerance as a Correlate of Tobacco Dependence and Motivation: Incremental Relations over and above Anxiety and Depressive Symptoms HHS Public Access. *Behav Med*, *43*(2), 120–128. https://doi.org/10.1080/08964289.2015.1110559

Verdejo-Roman, J., Vilar-Lopez, R., Navas, J. F., Soriano-Mas, C., & Verdejo-Garcia, A. (2017). Brain Reward System's Alterations in Response to Food and Monetary Stimuli in Overweight and Obese Individuals. *Human Brain Mapping*, *38*, 666–667. https://doi.org/10.1002/hbm.23407

Volkow, N. D., & Baler, R. D. (2015). NOW vs LATER brain circuits: implications for obesity and addiction. *Trends in Neurosciences*, *38*(6), 345–352. https://doi.org/10.1016/j.tins.2015.04.002

Vujanovic, A. A., Rathnayaka, N., Amador, C. D., & Schmitz, J. M. (2016). Distress Tolerance:

Associations With Posttraumatic Stress Disorder Symptoms Among Trauma-Exposed, Cocaine-Dependent Adults. *Behavior Modification*, *40*(2), 120–143. https://doi.org/10.1177/0145445515621490

Vujanovic, A. A., Wardle, M. C., Bakhshaie, J., Smith, L. J., Green, C. E., Lane, S. D., & Schmitz, J. M. (2018). Distress tolerance: Associations with trauma and substance cue reactivity in low-income, inner-city adults with substance use disorders and posttraumatic stress. *Psychology of Addictive Behaviors*, *32*(3), 264–276. https://doi.org/10.1037/adb0000362

Walsh, E. C., Eisenlohr-Moul, T. A., Minkel, J., Bizzell, J., Petty, C., Crowther, A., Carl, H., Smoski, M. J., & Dichter, G. S. (2019). Pretreatment brain connectivity during positive emotion upregulation predicts decreased anhedonia following behavioral activation therapy for depression. *Journal of Affective Disorders*, *243*, 188–192. https://doi.org/10.1016/j.jad.2018.09.065

Wang, Y.-P., & Gorenstein, C. (2013). Psychometric properties of the Beck Depression Inventory-II: a comprehensive review. *Revista Brasileira de Psiquiatria*, *35*, 416–431. https://doi.org/10.1590/1516-4446-2012-1048

Wardle, M. C. M. C., Vincent, J. N. J. N. N., Suchting, R., Green, C. E. C. E. E., Lane, S. D. S. D., & Schmitz, J. M. J. M. (2017). Anhedonia Is Associated with Poorer Outcomes in Contingency Management for Cocaine Use Disorder. *Journal of Substance Abuse Treatment*, *72*, 32–39. https://doi.org/10.1016/j.jsat.2016.08.020

Weidberg, S., García-Rodríguez, O., Yoon, J. H., & Secades-Villa, R. (2015). Interaction of depressive symptoms and smoking abstinence on delay discounting rates. *Psychology of Addictive Behaviors*, *29*(4), 1041–1047. https://doi.org/10.1037/adb0000073

Wickham, H., Averick, M., Bryan, J., Chang, W., D'Agostino McGowan, L., Francois, R., Grolemund, G., Hayes, A., Henry, L., Hester, J., Kuhn, M., Lin Pedersen, T., Miller, E., Milton Bache, S., Muller, K., Ooms, J., Robinson, D., Paige Siedel, D., Spinu, V., … Yutani, H. (2019). *Welcome to the tidyverse* (Version 1.3.0; p. 1686). Journal of Open Source Software. https://doi.org/https://doi.org/10.21105/joss.01686

Yoon, J. H., De, R., Garza Ii, L., Newton, T. F., Suchting, R., Weaver, M. T., Brown, G. S., Omar, Y., & Haliwa, I. (2017). A comparison of Mazur's k and area under the curve for describing steep discounters. *Psychol Rec*, *67*(3), 355–363. https://doi.org/10.1007/s40732-017-0220-9

Yoon, J. H., Higgins, S. T., Heil, S. H., Sugarbaker, R. J., Thomas, C. S., & Badger, G. J. (2007). Delay Discounting Predicts Postpartum Relapse to Cigarette Smoking Among Pregnant Women. *Experimental and Clinical Psychopharmacology*, *15*(2), 176–186. https://doi.org/10.1037/1064-1297.15.2.186

Yoon, J. H., Weaver, M. T., De La Garza, R., Suchting, R., Nerumalla, C. S., Omar, Y., Brown, G. S., Haliwa, I., & Newton, T. F. (2018). Comparison of three measurement models of discounting among individuals with methamphetamine use disorder. *The American Journal on Addictions*, *27*(5), 425–432. https://doi.org/10.1111/ajad.12761

6. VITA

NAME: Jennifer K. Hoots

EDUCATION: B.A., Biology, Cornell University, Ithaca, New York, 2016

HONORS: Outstanding Poster Award, National Institutes of Health Postbac Poster Day, 2017 & 2018

Outstanding Poster Award, National Institute on Drug Abuse Poster Day, 2017 & 2018

National Institutes of Health Postbaccalaureate Intramural Research Training Award, 2016-2018

American Heart Association Summer Undergraduate Research Fellowship, 2014

PUBLICATIONS: Soder H.E., Cooper J.A., Lopez-Gamundi P., **Hoots J.K.**, Nunez C., Lawlor V., Lane S., Treadway M.T., & Wardle M.C. (in press). Dose-response effects of d-amphetamine on effort-based decision-making and reinforcement learning. *Neuropsychopharmacology*.

Bossert, J.M., Kiyatkin, E., Korah, H., **Hoots, J.K.**, Afzal, A., Perekipskiy, D., Thomas, S., Fredriksson, I., Blough, B.E., Negus, S.S., Epstein, D.H., & Shaham, Y. (2020). In a rat model of opioid maintenance, the G protein-biased mu opioid receptor agonist TRV130 decreases relapse to oxycodone seeking and taking and prevents oxycodone-induced brain hypoxia. *Biological Psychiatry*, https://doi.org/10.1016/j.biopsych.2020.02.014

Madangopal, R., Tunstall, B.J., Komer, L.E., Weber, S.J., **Hoots, J.K.**, Lennon, V.A., Bossert, J.M., Epstein, D.H., Shaham, Y., & Hope, B.T. (2019). Discriminative stimuli are sufficient for incubation of cocaine craving. *eLife*, *8*, e44427. https://doi.org/10.7554/eLife.44427.001

Venniro, M., Zhang, M., Caprioli, D., **Hoots, J.K.**, Golden, S.A., Heins, C., Epstein, D.H., Morales, M., & Shaham, Y. (2018). Volitional social interaction prevents drug addiction in rat models. *Nature Neuroscience, 21*(11), 1520-1529. https://doi.org/10.1038/s41593-018-0246-6

Bossert, J.M., **Hoots, J.K.,** Fredriksson, I., Adhikary, S., Zhang, M., Venniro, M., & Shaham, Y. (2018). Role of mu, but not delta or kappa, opioid receptors in context-induced reinstatement of oxycodone seeking. *The European Journal of Neuroscience 50*(3), 2075-2085. https://doi.org/10.1111/ejn.13955

Pelloux, Y., **Hoots, J.K.,** Cifani, C., Adhikary, S., Martin, J., Minier-Toribio, A., Bossert, J.M., & Shaham, Y. (2018). Context-induced relapse to cocaine seeking after punishment-imposed abstinence is associated with activation of cortical and sub-cortical brain regions. *Addiction Biology, 23*(2), 699-712. https://doi.org/10.1111/adb.12527

Pelloux, Y., Minier-Toribio, A., **Hoots, J.K.,** Bossert, J.M., & Shaham, Y. (2018). Opposite effects of basolateral amygdala inactivation on context-induced relapse to cocaine seeking after extinction versus punishment. *The Journal of Neuroscience, 38*(1), 51-59. https://doi.org/10.1523/JNEUROSCI.2521-17.2017

CONFERENCE POSTERS AND PRESENTATIONS:

Hoots, J.K., Wardle, M.C., & de Wit, H. (2019, October 19-23). *Naltrexone does not alter willingness to exert effort in a monetary reward task* [Poster presentation]. Annual Meeting for the Society for Neuroscience, Chicago, IL, United States.

Bossert, J.M., Kiyatkin, E., Korah, H., **Hoots, J.K.**, Fredriksson, I., Blough, B.E., & Shaham, Y. (2019, October 19-23). *Opioid maintenance delivery of the biased agonist TRV130 decreases relapse to oxycodone seeking and prevents acute opioid-induced brain hypoxia* [Poster presentation]. Annual Meeting for the Society for Neuroscience, Chicago, IL, United States.

Weber, S.J., Komer, L.E., **Hoots, J.K.**, Tunstall, B.J., Bossert, J.M., Shaham, Y., Hope, B.T., & Madangopal, R. (2018, November 3-7). *Incubation of discriminative stimulus-induced cocaine craving*. [Poster presentation]. Annual Meeting for the Society for Neuroscience, San Diego, CA, United States.

Bossert, J.M., **Hoots, J.K.**, Negus, S.S., Blough, B.E., & Shaham, Y. (2018, November 3-7). *Modeling opioid maintenance therapy in rats: Effects of chronic buprenorphine and the biased mu-opioid receptor agonist TRV130 on relapse to oxycodone seeking*. [Poster presentation]. Annual Meeting for the Society for Neuroscience, San Diego, CA, United States.

Hoots, J.K., Negus, S.S., Blough, B., Shaham, Y., & Bossert, J.M. (2018, June 9-14). *Modeling opioid maintenance therapy in rats: Effects of chronic buprenorphine on responding for drug-paired discrete cues in a non-drug context, context-induced reinstatement of drug seeking, and reacquisition of oxycodone self-administration.* [Poster presentation]. Annual Meeting for the College on Problems of Drug Dependence, San Diego, CA, United States.

Hoots, J.K., Fredriksson, I., Cifani, C., Adhikary, S., Shaham, Y., & Bossert, J.M. (2017, November 11-15). *Effects of blockade of mu, delta, and kappa opioid receptors on context-induced reinstatement of oxycodone seeking*. [Poster presentation]. Annual Meeting for the Society for Neuroscience, Washington, D.C., United States.

Hoots, J.K., Fredriksson, I., Madangopal, R., Komer, L.E., Cifani, C., Shaham, Y., & Bossert, J.M. (2017, August 13-17). *Effects of blockade of mu, delta, and kappa opioid receptors on context-induced reinstatement of oxycodone seeking*. [Poster presentation]. Gordon Research Conference on Catecholamines, Newry, ME, United States.

ABSTRACTS:

Hoots, J.K., Soder, H.E., Lopez-Gamundi, P., Cooper, J.A., Lane, S., Treadway, M.T., Wardle, M.C. (2020). *All work, no play: Acute drug effects differentially predict wanting to take dextroamphetamine again for work versus recreation*. [Abstract accepted for poster presentation at Annual Meeting for the College on Problems of Drug Dependence].

PROFESSIONAL AFFILIATIONS:

American Psychological Association, 2018-Present
Division 28: Psychopharmacology and Substance Abuse
Division 40: Society for Clinical Neuropsychology
Society for Neuroscience, 2017-Present

SERVICE ACTIVITIES:

Letters to a Pre-Scientist, *Scientist Pen Pal*, 2019-2020

Eliminating Stigma in Addiction and Mental Illness Working Group, *Committee Member*, National Institute on Drug Abuse, 2017-2018

Biology Service Leaders, *Co-President*, Cornell University, 2014-2015