UNIVERSITY OF CALIFORNIA, IRVINE

Gender Differences on the Relationship among Resting Heart Rate Variability, Self-Reported Drug Abuse, and Difficulties in Emotion Regulation

THESIS

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MASTER OF ARTS

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by

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DEDICATION

To

First and foremost, God. Everything I have ever accomplished and achieved is only possible through God's will.

My family, as they are my absolute rock and foundation. Throughout all of the struggles we have been through together, I could not be where I am today with the love and support of my parents and my brother.

My Fiancée, Pauline Wang, who has seen both the best and worst of me and continues to love and support me regardless of the circumstances. Thank you for making me a better person each and every day.

My friends who have supported me through all of the highs and lows of life, and have been a great reminder that life is best lived amongst others.

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ABSTRACT OF THE THESIS

Gender Differences on the Relationship among Resting Heart Rate Variability, Self-Reported Drug Usage, and Difficulties in Emotion Regulation

By

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Master of Arts in Psychological Science

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Early drug use might to lead to drug addiction; the earlier individuals begin to engage in risky drug use, the more likely they are to engage in later drug abuse. Therefore, early intervention is warranted. This study explored individual differences in drug use tendencies in young and healthy adults. Specifically, I examined how self-reported emotion regulation (ER) difficulties and inhibition abilities, as indexed by resting heart rate variability (HRV), might predict risky drug use tendencies in young adults. I further considered these associations stratified by women and men. Novel results showed self-reported (or perceptions of) difficulties in ER were associated with higher drug usage in the full sample and this association was significantly stronger in women than men. Among the six different facets of ER difficulties, only those related to impulse control difficulties and limited access to ER strategies were most related to risky drug usage in women but not men. The other four facets of ER difficulties were not significantly different between men and women. An indirect association was found between resting HRV and drug use, mediated by self-reported difficulties in ER, particularly in women. Overall, results indicate that lower HRV and

difficulties in ER indirectly and directly, respectively, predict risky drug use in women. These data are in line with research suggesting women might engage in risky drug use primarily for stress regulation while men might engage in risky drug activity irrespective of both resting HRV and difficulties in ER. Clinical implications are discussed.

INTRODUCTION

Drug use is unfortunately a common issue within our society, with no signs of decline. For example, according to the National Institute on Drug Abuse (NIDA), since 2018, past-year marijuana use and daily marijuana use have remained nearly the same across all age groups (8th – 12th grade). Drug use can have a wide range of short- and long-term direct and indirect effects (NIDA, 2020). Short-term effects can range from changes in appetite, wakefulness, blood pressure, and/or mood to increased chance of heart attack, stroke, psychosis, overdose, and even death. Long-term effects may include heart or lung disease, mental illness, HIV/AIDS, hepatitis, and others (NIDA, 2020). Importantly, long-term drug use can also lead to addiction (NIDA, 2020). Drug use can also have severe consequences from a social perspective. For example, drug misuse has been associated with homelessness (van Laere et al., 2009), unemployment (Henkel, 2011), and unsafe sexual practices, resulting in a higher risk of contracting sexually transmitted infections (Bastos et al., 2008; Bertoni et al., 2009).

Addiction is defined as a chronic, relapsing disorder characterized by compulsive drug seeking and use despite adverse consequences (American Psychiatric Association, 2013). Furthermore, addiction is considered a brain disorder because it involves functional changes to brain circuits involved in reward, stress, and self-control, and those changes can last a long time after a person has stopped taking drugs (Goldstein et al., 2011). According to the Substance Abuse and Mental Health Services Administration (2014), taking drugs at any age can lead to addiction. However, the earlier people begin to use drugs, the more likely they are to develop serious problems. Therefore, early intervention is necessary and warranted.

The initial decision to take drugs is typically voluntary, but with continued use, a person's ability to exert self-control can become seriously impaired (NIDA, 2020). This impairment in self-control is the hallmark of addiction (NIDA, 2020). The likelihood of developing an addiction differs from person to person, and no single factor determines whether a person will become addicted to drugs (NIDA, 2020). This study will explore individual differences in drug use tendencies in young and healthy adults. Specifically, I will examine how self-reported emotion regulation (ER) perceptions and inhibitory control, as indexed by resting heart rate variability (HRV), predict drug use tendencies in a sample of college students. Such results might lend insight into the inhibitory and motivational factors that contribute to risky drug use behavior. By studying the intricacies of such individual differences of drug use, early intervention may be possible, which may prevent the development of drug addiction and abuse.

Emotion and Drug Usage

Emotion has been defined as "a psychic and physical reaction (as an anger or fear) subjectively experienced as a strong feeling and physiologically involving changes that prepare the body for immediate vigorous action" (Webster's Ninth New Collegiate Dictionary, 1984). Due to its subjective nature, emotions or "feeling states" are interpreted in broad terms based on the organism's history and context of the situation. Drug use is one source that shapes context. Risky drug use elicits powerful emotions that can range from remarkably high states, such as pronounced euphoria, to devastatingly low negative emotional states that in the extreme cause disruption and break with homeostasis (Koob, 2015). Risky drug use also produces an abnormal activation of incentive salience/reward systems, such as the release of dopamine and opioid peptides in the extended amygdala,

which generally plays a crucial role in guiding behavior toward high-value incentives in the environment (Koob, 2015). Thus, it is clear that emotional and motivational states can serve as an alarm system for excessive engagement in the positive emotional states associated with high incentive salience/reward activity (Koob, 2015).

Given that emotional well-being is essential to one's mental health, having a healthy range of emotions has been seen as functional from an evolutionary-based perspective, ultimately increasing our chances of survival (Ekman & Davidson, 1994; Frijda, 1986; Oatley & Jenkins, 2006). However, emotions must also be regulated in accordance with goals (Aldao et al., 2010; Aldao et al., 2015; Jarymowicz, 2008). Thus, it is imperative to have adaptive ER, defined as an individual's ability to modify their emotional experiences, expressions, and subsequent physiological responses to appropriately respond to ever-changing environmental demands (Aldao, 2013). In other words, ER is a mechanism that enables better coping with environmental demands (Jarymowicz, 2002; Jarymowicz & Imbir, 2015). As such, it is possible that individuals with more difficulties in ER might also engage in riskier drug behavior. Furthermore, as it relates to self-reported difficulties in ER, one's own reports of their ER are indeed *perceptions* of their own ER capabilities, which may determine their motivation to engage in ER (Williams et al., 2018). Thus, self-reported ER difficulties may determine the extent to which otherwise healthy individuals might begin engaging in risky drug behavior.

Executive Functions and Drug Usage

Executive functions (EFs) are a collection of mental processes that allow one to focus and concentrate, rather than solely relying on instinct or intuition, which may be insufficient, impossible, or ill-advised (Burgess & Simons, 2005; Espy, 2004; Miller &

Cohen, 2001). EFs are crucial for tasks such as reasoning, problem-solving, and planning. Therefore, they are essential for success in school and life, as well as cognitive, social, and psychological development. As such, executive functions, overall, play a role in the maintenance of mental and physical health.

Inhibitory control, one of the core EFs, involves controlling one's behaviors and thoughts, potentially overriding a strong internal predisposition or external temptation and choosing the most appropriate or needed response (Diamond, 2013). Inhibitory control is also involved in managing one's emotions, and consequently, is an essential mechanism for successful ER (Williams et al., 2015). Drug addiction is a chronically relapsing disorder marked by dysregulated inhibitory control, which may exacerbate the addicted individual's ability to restrain drug-taking (Goldstein & Volkow, 2011; Kalivas & Volkow, 2005). Simply put, a core deficit in drug addiction is the inability to constrain (i.e., inhibit) maladaptive drug-seeking behavior.

According to the fifth edition of the *Diagnostic and Statistical Manual for Mental Disorders* (DSM-5, American Psychiatric Association, 2013), impulsivity is defined as an aspect of *disinhibition*. It is considered an immediate reaction to stimuli or an unplanned reaction at the spur of the moment with little regard for possible consequences. Thus, impulsivity, which is marked by deficiencies in inhibition, is a vital construct as it pertains to risky behaviors and the inability to constrain maladaptive drug-seeking behavior, as well as the diagnostic criterion for several psychiatric disorders (Moeller et al., 2001). In general, impulsivity is one symptom often linked to many different types of disorders, such as hyperactivity disorder, depression, and anxiety disorders, as well as personality disorders, specifically cluster B disorders (antisocial personality disorder and borderline

personality disorder) (Barkley, 1997; Moeller et al., 2001). Furthermore, those who are impulsive have problems adhering to restrictions and have a constant sense of urgency and desire to engage in self-harming behavior, especially during times of emotional turmoil, and are thus considered to have maladaptive ER (Bakhshani, 2014). As such, impulsivity is widely recognized as a risk factor for many negative health behaviors and psychiatric disorders. Importantly, impulsivity is strongly related to the initiation of drug use and risky drug behavior (Brady et al. 1998; de Wit, 2009). It is, therefore, plausible that inhibition and perceptions of one's own emotion dysregulation, particularly in the domain of impulsivity, predict vulnerability to drug use.

In sum, adaptive inhibitory control as an EF is crucial in adequately regulating both emotions and impulses. In contrast, maladaptive inhibitory control, marked by emotion dysregulation and impulsiveness, is represented by responses inconsistent with environmental demands and subsequently predicts disease and mortality (Thayer & Lane, 2000; Thayer et al., 2012). To elucidate the psychophysiological mechanisms connecting inhibition with overall health, Thayer and Lane (2000) proposed that characteristic beat-to-beat variability in the heart rate (HR) time series - heart rate variability (HRV) - serves not only as an index of healthy heart function (Thayer & Lane, 2007), but also as a readily available index and measure of inhibitory control, ER ability (Williams, 2015), and overall self-regulatory (e.g., self-control) abilities.

Resting Heart Rate Variability

Executive function is primarily controlled by brain regions such as the prefrontal cortex. These regions exert an inhibitory influence on subcortical structures, such as the amygdala, which allow the organism to respond to environmental demands adaptively, and

effectively organize its emotional and behavioral responses (Thayer et al., 2012). Theoretically, at rest, active cortical brain regions may indicate greater inhibitory control and emotion regulation (Thayer et al., 2012). In addition, it has been suggested that these neural structures are responsible for regulating autonomic nervous system (ANS) activity (Hansen et al., 2003).

The ANS is a component of the peripheral nervous system that regulates involuntary physiologic processes, including heart rate, blood pressure, respiration, digestion, and sexual arousal (Waxenbaum et al., 2020). The heart, much like many organs in the body, is dually innervated by the ANS, which exerts significant influence over HR (Thayer et al., 2012). Remarkably, when the parasympathetic and sympathetic inputs are blocked pharmacologically, intrinsic HR is higher than the normal resting HR (Jose & Collison, 1970). Thus, it can be concluded that the heart is under tonic inhibitory control by parasympathetic influences and that resting cardiac autonomic balance favors energy conservation by way of parasympathetic domination over sympathetic influences (Thayer et al., 2012).

HRV is essentially the variability in the timing of the heartbeat, calculated by the sequence of time intervals between heartbeats. The time between heartbeats, or interbeat intervals (IBI), is determined by the aforementioned dually innervated qualities of the heart by way of the ANS. Increases in sympathetic activity are associated with heart rate increases, and relative increases in parasympathetic activity are associated with heart rate decreases (Thayer et al., 2012). Concurrent relative sympathetic increases cause the IBI to become shorter, whereas relative parasympathetic increases cause the IBI to become longer, with the latter indicative of regulating influence.

Several neuroimaging and pharmacological studies have identified the link between inhibitory executive brain regions and cardiac parasympathetic activity as indexed by resting HRV (Ahern et al., 2001; Lane et al., 2009; Thayer et al., 2012). The Neurovisceral Integration Model (NIM) postulates that HRV is an index of parasympathetic activity, and thus *resting* HRV serves as a readily available measure and as an index of the degree to which the brain's integrative system for adaptive regulation provides flexible control over the periphery (Williams et al., 2015). Specifically, higher resting HRV is associated with better prefrontal function that supports flexible and adaptive responses to environmental demands (Thayer & Lane, 2000; Thayer et al., 2009). For instance, individuals with higher resting HRV have been shown to exhibit effective behavioral responses (e.g., faster response times and better accuracy) on executive cognitive tasks (Hansen et al., 2003) as well as more flexible and adaptive emotional responding relative to individuals with lower resting HRV (Ruiz-Padial et al., 2003; Thayer et al., 2009). In contrast, individuals with the latter pattern exhibit hypoactive prefrontal brain activation, which results in hyperactive subcortical structures that are believed to contribute to maladaptive cognitive and emotional self-regulation (Thayer et al., 2012). Essentially individuals with lower resting HRV cannot easily recognize safety cues and have difficulties habituating to novel, neutral stimuli (Friedman, 2007; Hansen et al., 2003; Park et al., 2012a). Those same individuals respond to neutral stimuli with a heightened startle and neural responses as if the stimuli were emotionally negative (Brosschot et al., 2018; Park et al., 2012a; Ruiz-Padial et al., 2003). Finally, lower HRV is associated with greater alcohol abuse (Ralevski et al., 2019) and as such, resting HRV might likewise be associated with individuals' drug use tendencies. Ultimately, this typical reciprocal inhibitory cortico-subcortical neural circuit

may serve as the structural link between psychological processes such as ER and health-related physiological processes, and this circuit can be indexed by HRV (Thayer et al., 2012).

Gender Differences

According to the NIDA, men are more likely than women to use almost all types of illicit drugs (methamphetamines, cannabis, inhalants, tranquilizers, cocaine, narcotics, and hallucinogens) (Center for Behavioral Health Statistics and Quality, 2017). Furthermore, illicit drug use is more likely to result in emergency department visits or overdose deaths for men than women (Center for Behavioral Health Statistics and Quality, 2017). However, the gender gap has been decreasing over the past few decades (Mendrek, 2014). Although men are still known to have an overall greater dependence on drugs like alcohol, cannabis, and nicotine, the gender differences in the use of stimulants and opiates seem to have all but disappeared (Mendrek, 2014). There have been numerous socio-cultural factors that are associated with the decreasing gender gap. From a more Western, socio-cultural perspective, drug use among women, although still not accepted (especially if one is pregnant), has seen less gender-specific stigma.

Notably, a large proportion of men are known to initiate drug use to induce feelings of elation, energy, or focus. In contrast, women frequently start taking drugs to alleviate pre-existing mental health problems, including high-stress levels, feelings of alienation, depression, anxiety, or post-traumatic stress disorder (Mendrek, 2014). Consequently, this maladaptive self-medication strategy often results in a faster transition to habitual drug use and eventually a more severe dependence. There are some hints that psychophysiological processes may also contribute to gender differences, although without

more research, these hints are tentative. Most importantly, psychosocial factors such as discrimination (Hackett et al., 2019) and/or gender roles (Williams et al. 2018) may indirectly contribute to such pre-existing mental health difficulties, and potentially subsequent drug use.

As mentioned, lower resting HRV is thought to reflect poorer functioning of the neurophysiological pathways underlying ER. Some evidence suggests that women may have higher resting HRV than men, despite having greater HR in comparison with men (Koenig & Thayer, 2016). Thus, differences in HRV might explain the vastly different reasons behind the risky behavior of drug use between men and women (i.e., women generally have greater inhibitory control). Moreover, additional studies have shown that the negative association between HRV and both self-reported difficulties in ER (Williams et al., 2018) and HR (Williams et al., *under* review) is stronger in women than men; these data suggest that basic psychophysiological differences between women and men may be associated with drug abuse tendencies. As mentioned, self-reported difficulties in ER are essentially *perceptions* of an individual's own ER capabilities, which may determine their motivation to engage in ER (Williams et al., 2018). Therefore, Williams et al.'s (2018) findings suggest that ER ability, as indexed by resting HRV, and ER motivation, as indexed by self-reported difficulties in ER, are more closely related in women than men. Consequently, there is a possibility of gender differences in the relationships among resting HRV, self-reported difficulties in ER, and drug use tendencies in young and healthy individuals.

Present Study

Research has yet to consider the association among self-reported ER difficulties, resting HRV, and drug usage in young and healthy adults. Therefore, this project sought to evaluate the association between drug use and resting HRV and self-reported difficulties in ER and whether gender moderates these associations.

If inhibitory control is crucial in successful ER, and HRV in a resting state serves as an index of inhibitory and ER abilities, it can then be hypothesized that resting HRV will have a significant inverse relationship with drug usage. Moreover, self-reported difficulties in ER might serve as an important psychological predictor in drug usage, as those who perceive greater difficulties in ER might be more likely to engage in drug use. Finally, and as mentioned, there is an increasing adoption and acceptance of drug use among women. Taken together, the association between drug usage and both HRV and ER difficulties might be stronger in women compared to men, in so far as women might engage in risky drug use to regulate stress, compared to thrill-seeking purposes for men (Mendrek, 2014).

METHODS

Participants

Archival data from two pooled studies conducted within the Emotions and Quantitative Psychophysiology lab at The Ohio State University were combined for the current study. Participants were recruited via two primary methods: (1) a Research Experience Program (REP) pool at The Ohio State University, which allowed students to participate in research for partial class credit in an introductory level psychology course, and (2) cash compensation for individuals' participation outside of the research pool. The original study samples contained 210 participants. Most participants scored either as no risk (zero), or risky (one and two) points on the Drug Abuse Screening Test (DAST). Twenty participants scored three or higher. They were considered to be statistical outliers through box plots and removed. Outliers were not determined via the standard deviation method as the data was not normally distributed. The final sample thus contained a total of 190 participants (102 males, 88 females; 88 ethnic minorities; M_{age} = 20.07, SD = 2.87, age range: 18 – 38 years).

Procedure

Participants were asked not to smoke, undergo vigorous physical activity, or drink caffeine six hours before the experiment. Each study was approved by the Institutional Review Board (IRB) at The Ohio State University, and all participants signed written informed consent. In both studies, participants were placed in a soundproof experimental room equipped with a camera and microphone for safety and instructional reasons and a high-definition TV for stimuli presentation. Participants were given a detailed explanation of the procedures that would occur without indicating the specific hypothesis under the

study or manipulations applied. Electrocardiogram (ECG) leads were attached to the subjects, and while in a separate control room, the experimenter led the subjects to the initial phases of the experiment. All participants first completed a 5-min baseline-resting period, which included viewing a blank, gray screen. They were told not to move or fall asleep and just relax and breathe. Participants then completed a set of self-report questionnaires.

Resting Heart Rate Variability

Cardiac activity data were recorded continuously throughout each experiment via a 3-lead ECG at a 1000Hz sampling rate using a Mindware™ 2000D (MW2000D) Impedance Cardiograph package. Resting vmHRV was assessed during a 5-min baseline (spontaneous breathing and resting state) period prior to any experimental task. Electrodes were placed (1) below the right clavicle, (2) on the left side of the abdomen (below the heart), and (3) on the right side of the abdomen. The variability between successive R-spikes (or variability within inter-beat-intervals, IBIs) was obtained from ECG recordings to calculate HRV. Participants' successive IBIs, in milliseconds, were extracted using HRV 2.51 Analysis software. IBIs were written in a text file and analyzed using Kubios HRV analysis package 2.0 (Tarvainen et al., 2014), allowing for the calculation of time-and frequency-domain indices of HRV. Artifacts within the R-to-R series were visually detected. An artifact correction level that would differentiate and remove artifacts (differing abnormal IBIs from the mean IBI) using a piecewise cubic spline interpolation method was employed. The root mean square of successive differences (RMSSD), measured in milliseconds, was calculated and is considered to be a stable (Li et al., 2009) and valid (Thayer & Sternberg, 2010) time-domain measure of HRV. Autoregressive estimates were also calculated, yielding high-

frequency power HRV (HF-HRV, 0.15 – 0.4 Hz) (Thayer & Sternberg, 2010). In the present study, RMSSD correlated highly with HF power ($r = 0.90$, $p < 0.001$). For ease of interpretation, only HRV results using HF-HRV are reported. Results were identical using RMSSD. HF-HRV values were natural log-transformed (ln) to fit assumptions of linear analyses (Thayer et al., 2010).

Self-report Questionnaires

Perceived difficulties in ER were assessed using the *Difficulties in Emotion Regulation Scale* (DERS; completed within 30 minutes of the baseline-resting period described above). The DERS is comprised of 36-items and six sub-scales designed to measure different facets of difficulties in ER (Gratz & Roemer, 2004). Participants are asked to respond on a scale from 1 (*almost never*) to 5 (*almost always)* regarding how much these statements are reflective of them (example item: "When *I'm upset, I believe that I will end up feeling very depressed"*). Subscales included (a) *difficulties in controlling impulsive behavior when experience negative emotions* (impulse); (b) *lack of strategies to regulate emotions* (strategies); (c) *lack of emotional awareness* (awareness); (d) *nonacceptance of emotional responses* (non-accept); (e) *lack of emotional clarity* (clarity); and (f) *difficulties engaging in goal-oriented behavior when experience negative emotions* (goals). The DERS total score is based on all 36-items, whereas the subscales are scored based on different combinations of the 36-items (See Figure #1 for the DERS subscale scoring method).

Drug use was assessed using the Short Form Drug Abuse Screening Test (DAST-10), a 10-item self-report scale designed to provide a brief, self-report instrument for population screening, clinical case finding, and treatment evaluation research, adapted from the original 28-item DAST (Skinner, 1982). Participants answer YES or NO on each of

the ten questions. A score of "1" is given for each YES response, and a score of "0" is given for each NO response. Higher scores are indicative of a higher risk of drug use. According to this scale, score labels are as follows: score of zero - No Risk; score of 1-2 Risky; score of 3 – Harmful; and score of 4 or above - Severe. All participants included in this study scored between 0-2, and thus, all individuals fell between “no risk” and “risky." Participants who scored 3 and above were a small clinical sample that doesn’t vary greatly and was ultimately not the focus. As mentioned, these statistical outliers were excluded via box plot analysis as they varied significantly from the mean.

Covariates

Ethnicity has also been related to resting HRV (Choi et al., 2006; Hill et al., 2015). Thus, ethnicity was included as a covariate in applicable analyses (ethnicity coded as 1 = White, 2 = Black, 3 = Asian, 4 = Hispanic, 5 = Middle Eastern, 6 = Other). Higher body mass index is also associated with decreased resting HRV (e.g., Koenig et al., 2014; Molfino et al., 2009); in the current sample, men showed greater body mass index (BMI) in comparison with women (see Results section for details). Thus, BMI was also used as a covariate in applicable analyses. Gender was also included as a covariate for all analyses that did not include gender as a predictor variable.

Statistical Analyses

All statistical tests were conducted using SPSS (ver. 27, IBM, Chicago, IL.). All tests were two-tailed, and significance levels were evaluated using an alpha of .05.

Participants were stratified into groups based on their reported gender (men = 1 and women = 2). Subjects were also stratified into high (coded as 2) and low HRV (coded as 1) groups based on a median split. Previous studies (Thayer et al., 2009), when viewing

HRV as an independent variable, has considered resting HRV as an individual difference, and groups were created using a median split. Therefore, low and high HRV groups were created using this method. In addition to keeping DAST scores as a "continuous" variable (scores 0-2), participants were divided into two groups, based on their DAST scores; those who scored a total score of zero were considered to be the "no risk" group, and those who scored one or two points were grouped as "risky" drug use group.

Mean and standard deviations for all variables of interest for the entire sample are presented. Additionally, HRV, drug use, gender group differences in these variables were analyzed and reported using Independent samples t-tests. A multivariate one-way analysis of variance (MANOVA) was conducted to explore potential group differences controlling covariates (see covariate section above) on all variables of interest.

Analysis of variance (ANOVA) was used to determine potential interactions between these grouping variables. F-values, eta values (noted as "r"), and *p* values are reported. Spearman's rank correlation coefficient (rho) was used to create correlation matrices for the entire and split by gender, HRV, and drug use group variables.

Spearman's Rho correlation tests were used to assess the relationship between DAST scores (not normally distributed) and other variables of interest. All other correlation values reported reflect Pearson's r correlation coefficients. Correlations were conducted in the entire sample as well as for men and women separately.

To test if gender indeed moderates the relationship between resting HRV and DERS scores, the SPSS macro-PROCESS was used (Hayes, 2012). In the program PROCESS, "Model 1" was used to test the conditional effect of the independent variables (IV; HF-HRV, DERS), a conditional effect of the moderator (M; gender), and an interaction effect of the two on

the dependent variable (DV; DAST scores) (see Figure #2 for conceptual representation). In addition, conditional effects were used to assess the impact of gender on the link between resting HF-HRV and DERS scores. High and low values for the predictor variables are derived using +/- 1 SD from the mean, allowing the PROCESS program to yield predicted DV values at varying levels of the predictor variable via regions of significance and simple slope analyses. Model "4" was also used to probe potential mediation effects between HRV, DERS, and DAST scores. In this test, the "M" variable represents the mediating variable (DERS scores), with HRV as the IV and DAST scores as the DV (see Figure #3 for conceptual representation). Finally, gender will be considered the "W" variable in "Model 58", which represents moderated mediations; in other words, it is the mediation model proposed among HRV, DERS, and DAST scores significant in one gender compared to the other. (See Figure #4 for conceptual representation.) For both Models 4 and 58, statistics for Paths A (IV-M), B (M-DV), C (direct IV-DV), and C' (indirect IV-DV) are reported. Statistics include unstandardized beta (B) coefficients, standard errors (SE; in brackets), 95% bootstrapping confidence intervals (95% boot CI in square brackets, 5,000 samples; Hayes, 2012), partial correlation coefficients (for main effects and interactions), and *p*- values.

RESULTS

Participant Demographics

For the current sample of 190 participants who scored two or below on the DAST (either considered “no risk” or “risky”). There were one hundred and two males (54%) and 88 females (46%); their ages ranged from 18 and 38 years (M = 20.07, SD = 2.87). They were ethnically diverse with 102 White, 42 Black, 25 Asian, two Latinx, and 19 "other." Mean and standard deviations for all variables of interest are displayed in Table 1. Among the total sample, BMI (M = 24.78, SD = 6.13); resting HF-HRV (M = 6.74, SD = 1.01); DERS (M = 82.07, SD = 17.98); and DAST (M = 0.46, SD = 0.69).

Stratified by Gender. Gender differences are also presented in Table 1. Women had marginally higher DERS (M=84.47, SD=20.15) and strategies subscale (M=16.32, SD=6.29) scores compared to men (DERS: M=80.00, SD=15.69; M=14.83, SD=4.64). There were no significant differences between men and women on resting HRV, heart rate, and DAST scores.

Zero-Order Correlations among Variables of Interest

Correlations among the variables of interest in the entire sample are presented in Table 2. Spearman’s correlation tests were conducted. In the full sample, higher DAST scores were related to higher DERS (ρ = .196, p < .01) and impulse subscale (ρ = .202, p < .01) scores. Resting HRV was not significantly correlated with any variables of interest at a bivariate level.

Stratified by Gender. Split by gender, significant correlations emerged among women but not men. Resting HRV was negatively correlated with DERS (r = -.238, p < .05) and strategies subscale scores (r = -.288, p < .01) for women. Drug use scores were

positively correlated with DERS (ρ = .336, p = .001), impulse subscale (ρ = .346, p = .001), and strategies subscale (ρ = .222, p < .05) scores for women.

Group Comparisons

In the full sample, total DAST scores that correspond to the "risky" group were significantly higher than the "no risk" group on DERS (F (1, 188) = 6.49, p < .05, r = .182), impulse subscale (F (1, 188) = 8.31, p < .01, r = .205), strategies subscale (F (1, 188) = 4.37, p < .05, r = .152), and goals subscale scores (F (1, 188) = 109.78, p < .01, r = .207). Split by gender, associations emerged again primarily in women, such that the "risky" group scored higher than the "no risk" group on DERS in addition to the impulse, strategies and goals subscales (each p < .05). Only one significant difference was evident for men; BMI was higher for the non-risk group than the risky group (see Table 3).

There was a marginally significant difference between low and high HRV groups in DERS scores (F (1, 188) = 3.82, p = .052, η^2 = .02 [For the low HRV group, M = 84.57 (19.61); for the high HRV group, M = 79.51 (15.85)]. However, there was no difference between HRV groups on DAST scores F(1, 188) = .286, p = .594, η^2 = .002 [For the low HRV group, M = .49 (.71); for the high HRV group, M = .44 (.67)].

There was no significant interaction effect among DAST and HRV group on DERS scores, (F(1, 186) = .238, p = .626, η^2 = .001) or on the DERS subscales. However, in the low HRV group, risk and no-risk groups showed a significant difference on impulse control (F (1, 94) = 5.75, p < .05, η^2 = .058) and on total DERS scores (F (1, 94) = 3.81, p = .054, η^2 = .039). These differences were not significant for those who had higher resting HRV (see Figures 5 and 6).

HRV groups stratified by gender showed a significant interaction on the strategies subscale only (F (1, 186) = 5.08, $p < .05$, $\eta^2 = .027$). There was no difference between high [M = 14.94 (4.39)] and low [M = 14.73 (4.91)] HRV group among men on the strategies subscale. However, for women, those in the high [M = 14.66 (4.30)] HRV group had lower strategy scores than those in the low [M = 17.98 (7.49)] HRV group.

Drug use groups stratified by gender were compared on variables of interest. There was a significant interaction effect of drug group and gender on DERS (F(1, 186) = 4.28, $p < .05$, $\eta^2 = .022$) and impulse subscale (F(1, 186) = 3.99, $p < .05$, $\eta^2 = .021$) scores (see Figures 7 and 8).

No significant or notable interactions were found with resting HRV and drug use groups on DERS.

Moderation, Mediation, and Moderated-Mediation Analyses

Moderation analysis showed that gender significantly moderated the association between drug use and DERS (B = 12.67 (5.35), 95% boot CI [2.11, 23.24], $r_{partial}$ =.30, $p < .05$). Conditional analyses showed that women (B = 12.74 (3.82), 95% boot CI [5.21, 20.27], $p < .01$) compared with men (B = .07 (3.72), 95% boot CI [-7.28, 7.41], $p = .99$) showed a stronger association between drug use and DERS. BMI and ethnicity were used as covariates (see Figure 9). A similar moderation effect of gender was also found on the association between drug use and difficulties in impulse control (B = 2.75 (1.2), 95% boot CI [.39, 5.11], $r_{partial}$ =.30, $p < .05$). Conditional analyses showed that women (B = 3.05 (.85), 95% boot CI [1.36, 4.73], $p < .001$) compared with men (B = .29 (.83), 95% boot CI [-1.35, 1.94], $p = .72$) showed a stronger association between drug use and impulse control. BMI

and ethnicity were used as covariates (see Figure 10). Significant or notable gender moderations were found with HRV as the predictor.

Finally, in the full sample, DERS mediated an *indirect* association between resting HRV and DAST scores (B = .0069 (.0028), 95% boot CI [.0014, .0123], $p < .05$), such that lower resting HRV was associated with higher DERS scores (Path A: B = -1.88 (1.30), 95% boot CI [-4.44, .6763], $p = .1485$), higher DERS scores were associated with higher DAST scores (Path B: B = .0069 (.0028), 95% boot CI [.0014, .0123], $p < .05$), and the indirect effect was significant (Path C': B = -.0130 (.0092), 95% boot CI [-.0347, .0015]). It is important to note that, as expected given correlation analyses, the direct effect is not significant (Path C: B = .0068 (.0494), 95% boot CI [-.0906, .1043], $p = .89$). However, gender also moderated this mediation analysis (B = 40.08 (17.60), 95% boot CI [5.35, 74.81], $p < .05$) such that this indirect effect was present only in women (B = -4.93 (1.95), 95% boot CI [-8.78, -1.09], $p < .05$) but not men (B = .34 (1.69), 95% boot CI [-3.01, 3.68], $p = .84$).

DISCUSSION

The present study sought to examine the relationship between inhibition control (indexed by HRV), self-reported ER difficulties, and drug use tendencies. Since it is known that inhibitory control is crucial in successful ER (Williams et al., 2015), lower resting HRV was hypothesized to be associated with more risky drug behaviors. It was also expected that more risky drug behaviors would be associated with higher self-reported ER difficulties. Finally, these potential associations were hypothesized to be stronger in women compared to men.

Results partially supported hypotheses. First, results replicated the Williams et al. (2018) report showing that the association between HRV and difficulties in ER was more robust in women compared to men. Notably, group, correlation, and moderation analyses supported the hypothesis that self-reported (or perceptions of) difficulties in ER are associated with higher drug usage in the full sample, and this association was significantly stronger in women than men. Among the six different facets of ER difficulties, only those related to impulse control difficulties and limited access to ER strategies were most related to drug usage in women but not men. The other four facets of ER difficulties were not significantly different between men and women. Finally, while correlational and group-based analyses confirm resting HRV was not *directly* associated with DAST in the full sample or stratified by gender, mediation results suggest an *indirect* association between resting HRV and drug use mediated by self-reported difficulties in ER. However, this mediated association was also moderated by gender, such that this model was statistically reliable in women but not men.

Overall, this is the first study to explore how both resting HRV and difficulties in ER are related to drug usage and how these associations may differ as a function of gender. As mentioned, men initiate drug use for the thrill, drive, and fun of the experience, whereas women initiate drug use primarily for stress regulation (Mendrek, 2014). My data are in line with this idea, as lower resting HRV in women may influence perceived ER abilities and thus, influence drug usage in women but not men. Importantly, self-reported difficulties in ER appears to be an important factor linking resting HRV with drug usage, in addition to predicting risky drug behavior in a young and healthy sample of women. Such data might provide additional insight in decreasing risky drug behavior in women. Additional research is needed to understand how to decrease risky drug behavior in men from an ER standpoint, as the data suggest that such risky behavior is not directly related to psychological well-being. In sum, these findings suggest that differences between men and women exist as it relates to the potential catalyst of drug use; perceived ER difficulties may drive risky drug behavior for women more than men, which might be indirectly linked with resting HRV. These data have clinical implications, as the target of decreasing risky drug use tendencies in women might be stress and ER-related, whereas, for men it may be based on motivational factors unrelated to ER (i.e., thrill seeking).

Implications

The current sample did not include individuals who struggle with addiction, which has been defined as a chronic, relapsing disorder that consists of three major factors. These include 1) a compulsion to seek and take drugs, 2) loss of control over drug intake, and 3) emergence of a negative emotional state (e.g., dysphoria, anxiety, and irritability). Thus, these three characteristics define a motivational withdrawal syndrome when access to the

drug is prevented (Koob & Le Moal, 1997). Furthermore, there is a three-stage cycle that conceptualizes what addiction is, including 1) a binge/intoxication stage, 2) a withdrawal/negative affect stage, and 3) a preoccupation/anticipation stage, which worsens in severity over time and involves allostatic changes in the brain reward and stress systems. Therefore, perceptions of one's own difficulties in ER may determine the likelihood of becoming addicted. In fact, one of the most important components of impulsivity is thought to be *negative urgency*, at least as it relates to problematic drug use during adolescence and young adulthood (Verdejo-Garcia et al., 2007). This makes logical sense when reiterating what *negative urgency* is, which is essentially acting rashly when one is in a negative mood. Thus, difficulties in ER should be considered when targeting variables for preventing and treating riskier drug behavior (Kelly et al., 2016). It will be imperative for future work to understand how such interventions might impact both difficulties in ER and resting HRV to avoid initial drug use and/or relapse.

Higher heart rate (HR) is related to cardiovascular and other related diseases such as atherosclerosis and hyperinsulinemia (Palatini et al., 2004). Interestingly, women have consistently displayed greater HR than men, without showing increased mortality and morbidity rates compared to men (Cordero et al., 2006). This paradoxical finding is possibly explained by the fact that despite having greater HR than men, women have greater resting HRV (Koenig & Thayer, 2016). Higher resting HRV is associated with more efficient functioning of the prefrontal-subcortical inhibitory circuit, which supports flexible and adaptive responses to environmental demands (Thayer & Lane, 2000; Thayer et al., 2009). Thus, research posits that women might compensate for increased psychopathology and HR compared to men, and this compensation is reflected in greater resting HRV

relative to men (Koenig & Thayer, 2016; Williams et al., 2018; Williams et al., *under review*). The present data extend this idea to the domain of drug use. Specifically, women appear to be aware and mindful of their ER capabilities and motivations, as indicated by a stronger correlation between resting HRV and self-reported difficulties in ER. Drug use tendencies were also more strongly related to difficulties in ER, and indirectly with resting HRV, in women compared to men. On the other hand, men appear to engage in risky drug behavior irrespective of both ER abilities and motivation, as indexed by resting HRV and self-reported ER difficulties, respectively. Taken together, these results highlight the importance of compensation in women, since less compensation, marked by lower resting HRV and more ER difficulties, is associated with more drug use tendencies.

Limitations and Future Directions

One major limitation of the current study is that it was cross-sectional by nature, and thus the cause of current and future drug use could not be determined. It would be interesting to conduct a longitudinal follow-up study to determine future drug use behavior as it relates to HRV and difficulties in ER. Another potential limitation is the fact that all participants fell between the "no risk" or "risky" category based on the Short Form DAST-10. There was no one within the "Harmful" or "Severe" category. Thus, a more direct effect of HRV on DAST may exist had we had a larger, more diverse (and variable) sample. However, it must be noted that this study suggests that in a young, healthy population within a non-pathological range of drug usage, perceptions of difficulties in ER may predict risky drug use behaviors, especially among women. Future studies should work to examine the association between resting HRV and drug usage in pathological populations (i.e.,

individuals who score greater than 3 on the DAST) and individuals of different age and ethnic groups.

Conclusions

Exploring psychophysiological predictors of drug use and risky drug behavior is clearly warranted. Moreover, as the gender gap of drug use closes with more acceptance of drug use among women (Mendrek, 2014), it is necessary to explore differences in drug use tendencies by gender. Men are known to initiate drug use for the thrill of the experience as well as for the feelings of elation and energy, whereas women, on the other hand, are known to initiate drug use primarily to reduce stress (Mendrek, 2014). The current study is the first to show that self-reported ER difficulties are associated with less drug use tendencies and that this relationship is present in women but not men. Moreover, self-reported difficulties in ER carried the indirect association between lower HRV and higher drug use tendencies in women only. Overall, it can be concluded that lower HRV and difficulties in ER indirectly and directly, respectively, are associated with risky drug use in women. On the other hand, men might engage in illicit drug activity irrespective of both resting HRV and difficulties in ER. Future investigations should adopt a more diverse sample and longitudinal model in order to predict future drug use in men and women independently.

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TABLES

Table 1. *Comparisons between Men and Women*

	Total	Men	Women	*F*	*r*	*p*
N	190	102	88			
Total DERS	82.07 (17.98)	80.00 (15.69)	84.47 (20.15)	2.94	.122	.088
Impulse	11.03 (4.02)	10.75 (3.14)	11.35 (4.85)	1.04	.077	.308
Strategies	15.52 (5.50)	14.83 (4.64)	16.32 (6.29)	3.48	.134	.064
Awareness	18.85 (4.02)	18.98 (4.83)	18.70 (4.84)	0.15	.032	.695
Non-Accept	11.58 (5.39)	10.80 (4.86)	12.48 (5.84)	4.65	.155	.032
Clarity	11.99 (3.09)	11.70 (2.96)	12.34 (3.23)	2.06	.104	.152
Goals	13.09 (3.69)	12.93 (3.33)	13.27 (4.09)	0.40	.044	.527
BMI	24.78 (6.13)	25.14 (4.96)	24.36 (7.27)	0.77	.063	.380
HF-HRV	6.74 (1.01)	6.720 (1.03)	6.760 (.97)	0.09	.000	.760
Mean HR	75.50 (11.45)	75.04 (11.79)	76.03 (11.45)	0.35	.044	.554
Drug abuse	.46 (.69)	0.440 (.70)	0.490 (.68)	0.22	.032	.636

Table 2. *Correlation Matrices for the Entire Sample and Split by Gender*

Table 2| Correlation Matrix of Entire Sample (N = 190)

	1	2	3	4	5	6	7	8	9	10	11
[1] DRUG ABUSE	--										
[2] DERS	**.196****	--									
[3] IMPULSE	**.202****	**.822****	--								
[4] STRATEGIES	.126	**.870****	**.729****	--							
[5] AWARENESS	.021	**.292****	.091	-.015	--						
[6] NON-ACCEPT	.084	**.746****	**.549****	**.663****	-.067	--					
[7] CLARITY	.107	**.631****	**.490****	**.445****	**.313****	**.215****	--				
[8] GOALS	**.202****	**.680****	**.497****	**.630****	-.123	**.496****	**.317****	--			
[9] HF-HRV	-.019	-.105	-.08	-.128	-.069	-.133	.054	.004	--		
[10] RMSSD-HRV	-.009	-.108	-.059	**-.146***	-.079	-.133	.03	.03	**.949****	--	
[11] BMI	.034	.104	**.444****	.084	.08	.05	.101	.101	**-.147***	-.115	--

Note:

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

a. Women (N = 88)

Table 2| Correlation Matrix of Entire Sample (N = 190)

	1	2	3	4	5	6	7	8	9	10	11
[1] DRUG ABUSE	--										
[2] DERS	**.336****	--									
[3] IMPULSE	**.346****	**.853****	--								
[4] STRATEGIES	**.222***	**.898****	**.767****	--							
[5] AWARENESS	.052	.172	-.017	-.116	--						
[6] NON-ACCEPT	.174	**.817****	**.654****	**.759****	-0.06	--					
[7] CLARITY	.158	**.656****	**.567****	**.531****	**.223***	**.279****	--				
[8] GOALS	**.408****	**.648****	**.479****	**.615****	**-.227***	**.505****	**.292****	--			
[9] HF-HRV	- .071	**-.238***	- .14	**-.288****	.02	**-.305****	.017	- .168	--		
[10] RMSSD-HRV	- .088	**-.225***	- .126	**-.293****	.031	**-.283****	- .003	- .138	**.961****	--	
[11] BMI	- .065	.118	.072	.183	.043	.147	.06	- .095	**-.274****	**-.283****	--

Note:

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

b. Men (N = 102)

Table 2| Correlation Matrix of Entire Sample (N = 190)

	1	2	3	4	5	6	7	8	9	10	11
[1] DRUG ABUSE	--										
[2] DERS	.052	--									
[3] IMPULSE	.067	**.776****	--								
[4] STRATEGIES	.03	**.822****	**.661****	--							
[5] AWARENESS	-.006	**.443****	**.245***	.112	--						
[6] NON-ACCEPT	-.013	**.643****	**.385****	**.515****	-.069	--					
[7] CLARITY	.064	**.596****	**.385****	**.324****	**.407****	.118	--				
[8] GOALS	-.007	**.723****	**.531****	**.655****	-.011	**.484****	**.341****	--			
[9] HF-HRV	.023	.022	-.015	.033	-.14	.021	.082	.171	--		
[10] RMSSD-HRV	.069	.011	.019	.005	-.166	.01	.066	.192	**.943****	--	
[11] BMI	.145	.108	**.232***	-.058	.126	-.07	.179	.129	-.002	.059	--

Note:

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

Table 3

Comparisons between Risk and No Risk drug groups Split by Gender

	Total Sample (N = 190)				
	Risky	No-Risk	*F*	η^2	*p*
BMI	25.03 (5.92)	24.64 (6.27)	6.51	.001	.678
HF-HRV	6.74 (1.12)	6.74 (.945)	.000	.000	.989
DERS	86.51 (19.19)	79.65 (16.89)	6.49	.033	**.012***
Impulse	12.15 (4.79)	10.42 (3.40)	8.31	.042	**.004****
Strategies	16.64 (6.36)	14.91 (4.90)	4.37	.023	**.038***
Awareness	19.00 (4.89)	18.77 (4.80)	2.25	.001	.757
Non-Acceptance	12.09 (5.61)	11.30 (5.26)	26.98	.005	.336
Clarity	12.51 (3.20)	11.71 (3.01)	27.21	.015	.092
Goals	14.12 (4.01)	12.53 (3.40)	109.78	.043	**.004****

a. Women (N = 88)

	Women (N = 88)				
	Risky	No-Risk	*F*	η^2	*p*
BMI	23.51 (5.54)	24.89 (8.17)	.754	.009	.388
HF-HRV	6.66 (1.04)	6.83 (.94)	.578	.007	.989
DERS	92.0 (20.5)	79.72 (18.58)	8.41	.089	**.005****
Impulse	13.15 (5.52)	10.22 (4.03)	8.23	.087	**.005****
Strategies	18.03 (7.05)	15.24 (5.57)	4.25	.047	**.042***
Awareness	18.85 (5.14)	18.61 (4.68)	.821	.001	.821
Non-Acceptance	13.62 (5.85)	11.76 (5.77)	2.14	.024	.147
Clarity	13.03 (3.71)	11.91 (2.83)	2.57	.029	.113
Goals	15.32 (3.90)	11.98 (3.68)	16.45	.161	**.000****

b. Men (N = 102)

	Men (N = 102)				
	Risky	No-Risk	*F*	η^2	*p*
BMI	26.59 (5.97)	24.44 (4.27)	.754	.042	**.040***
HF-HRV	6.82 (1.21)	6.67 (.95)	.578	.005	.498
DERS	80.85 (16.15)	79.59 (15.57)	.142	.001	.708
Impulse	11.12 (3.71)	10.58 (2.84)	.662	.007	.418
Strategies	15.21 (5.3)	14.65 (4.33)	.322	.003	.571
Awareness	19.15 (4.69)	18.90 (4.92)	.821	.001	.806
Non-Acceptance	10.52 (4.96)	10.94 (4.84)	2.14	.002	.680
Clarity	11.57 (3.16)	11.97 (2.52)	2.57	.004	.521
Goals	12.88 (3.78)	12.96 (3.12)	16.45	.000	.913

FIGURES

Figure 1.
Difficulties in Emotion Regulation Scale (DERS): Subscale scoring method

SUBSCALE SCORING:** The measure yields a total score (SUM) as well as scores on six sub-scales:

1. Nonacceptance of emotional responses (NONACCEPT): 11, 12, 21, 23, 25, 29
2. Difficulty engaging in Goal-directed behavior (GOALS): 13, 18, 20R, 26, 33
3. Impulse control difficulties (IMPULSE): 3, 14, 19, 24R, 27, 32
4. Lack of emotional awareness (AWARENESS): 2R, 6R, 8R, 10R, 17R, 34R
5. Limited access to emotion regulation strategies (STRATEGIES): 15, 16, 22R, 28, 30, 31, 35, 36
6. Lack of emotional clarity (CLARITY): 1R, 4, 5, 7R, 9

Total score: sum of all subscales

**"R" indicates reverse scored item

Figure 2.
PROCESS "Model #1"

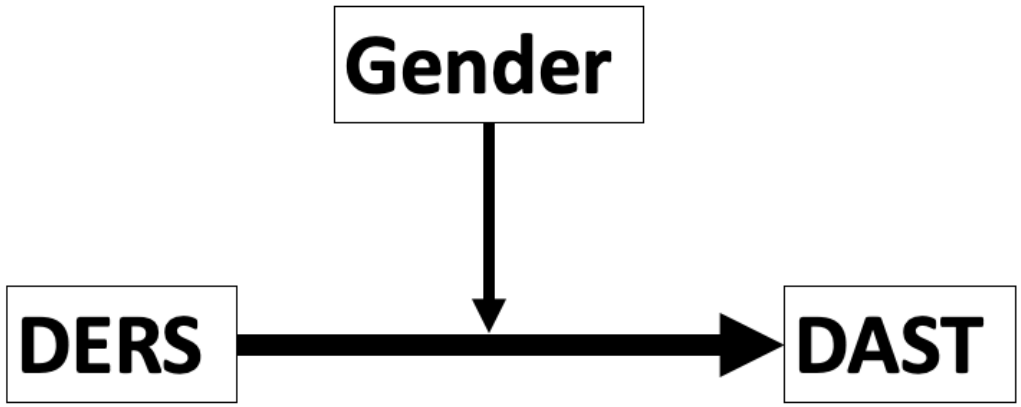

Figure 3.
PROCESS "Model #4"

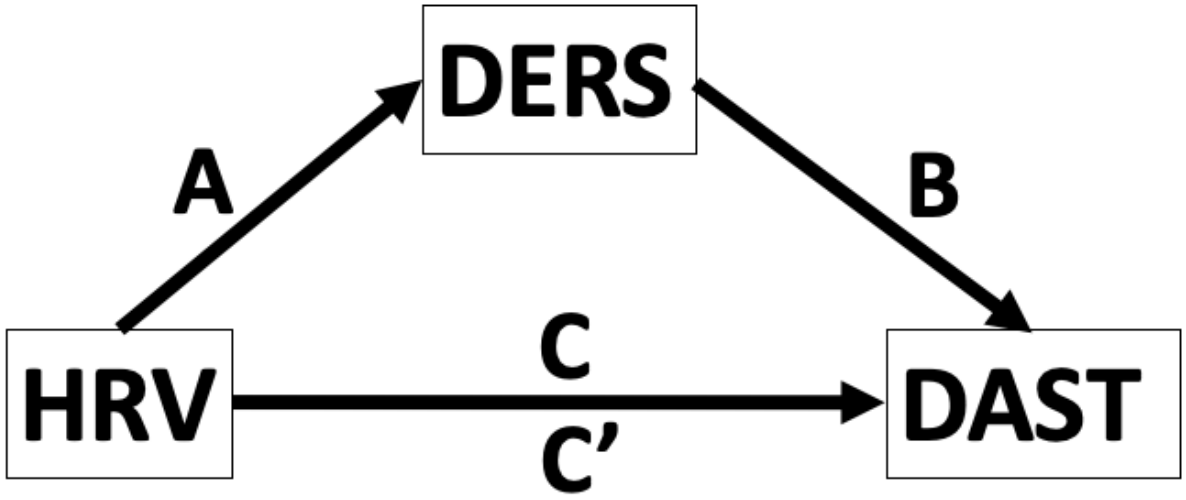

Figure 4.
PROCESS "Model #58"

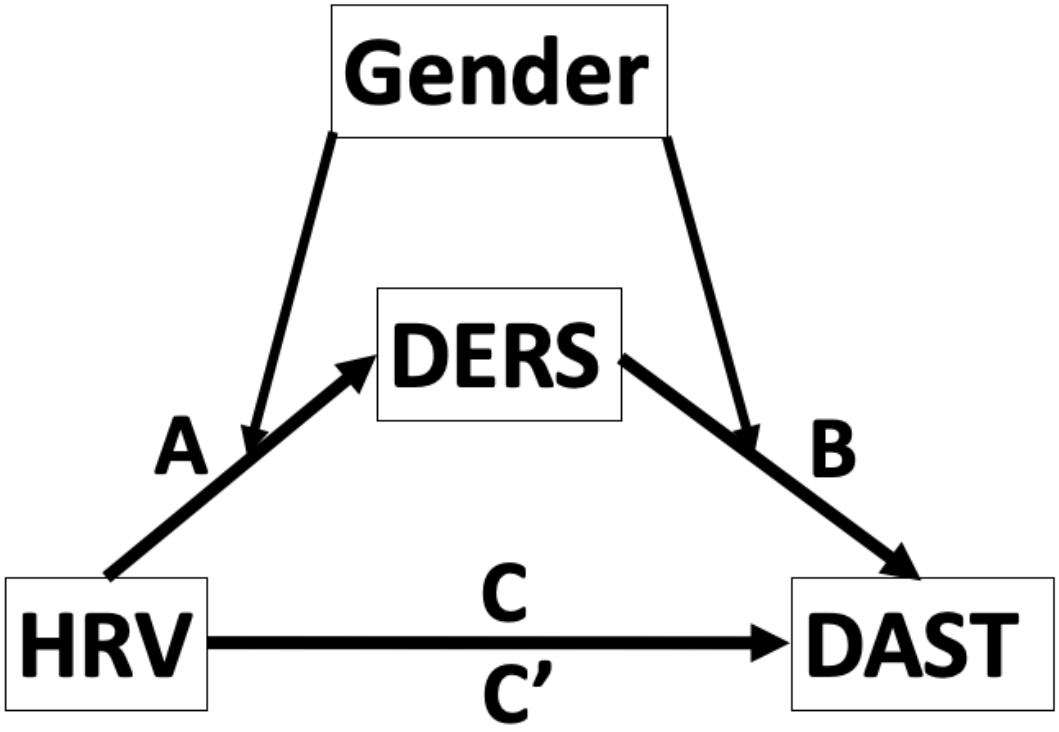

Figure 5. Drug users and non-users' Impulse scores for the low and high HRV groups

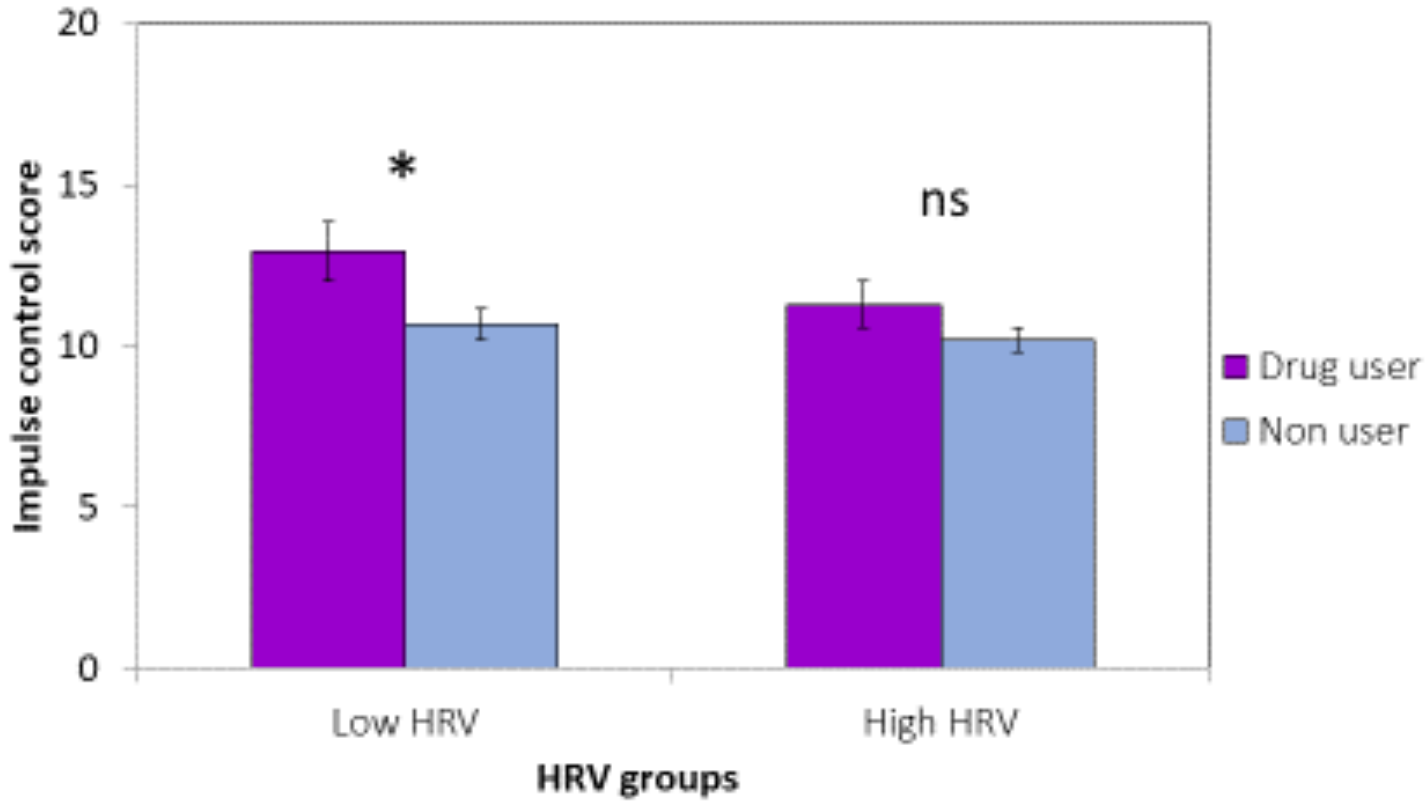

Figure 6. Drug users and non-users' DERS scores for the low and high HRV groups

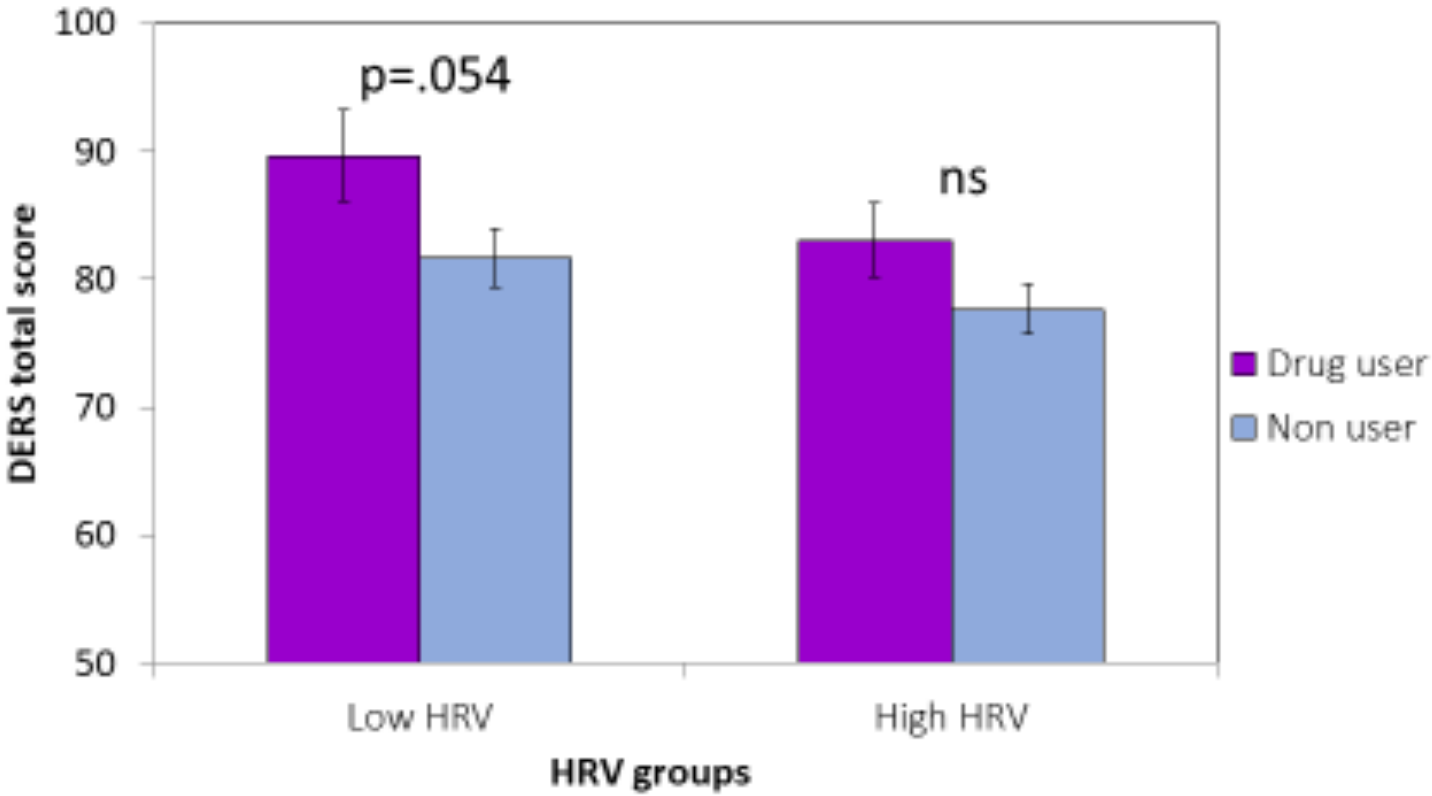

Figure 7. Drug users and non-users stratified by gender on DERS scores

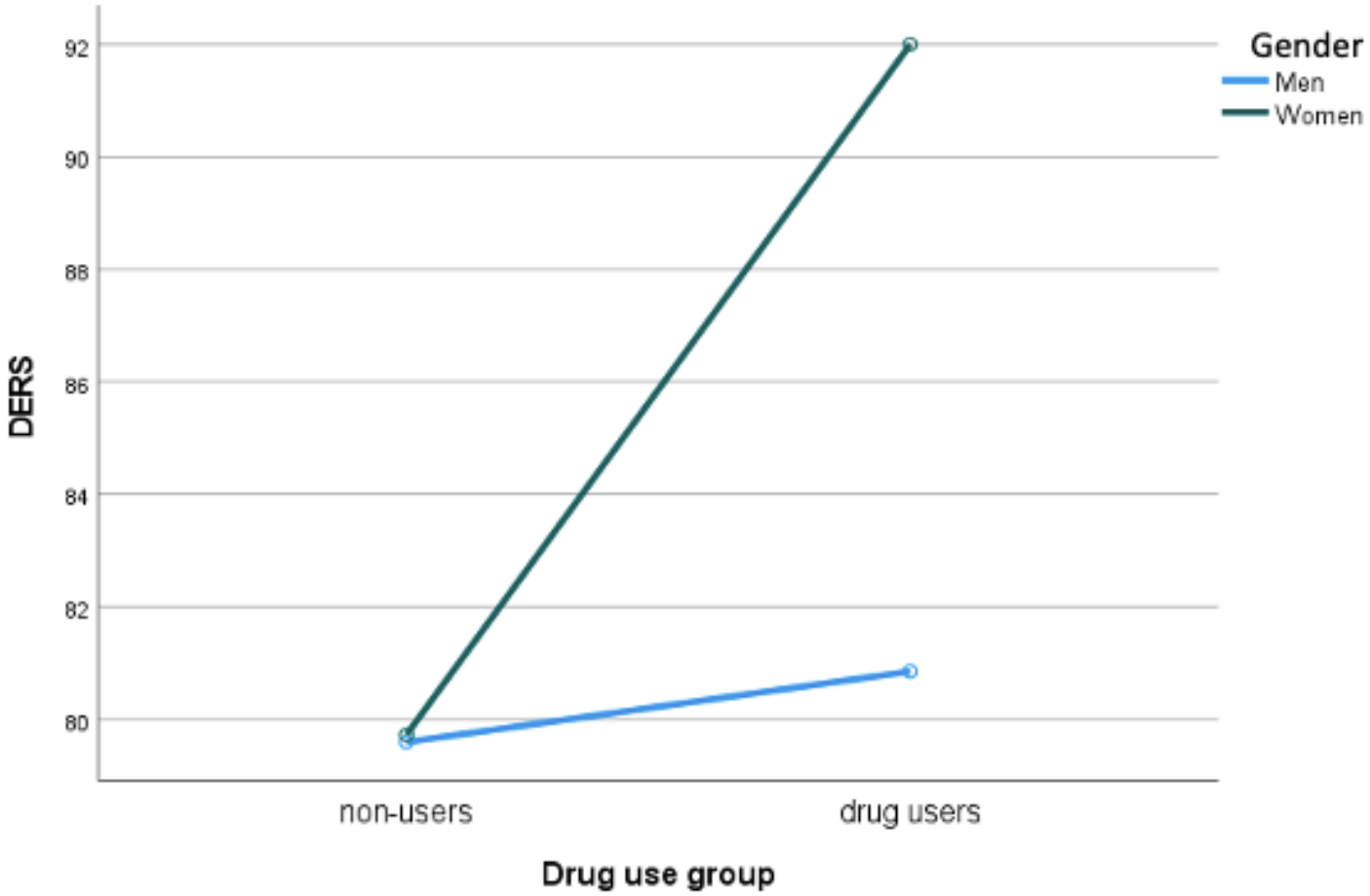

Figure 8. Drug users and non-users stratified by gender on Impulse

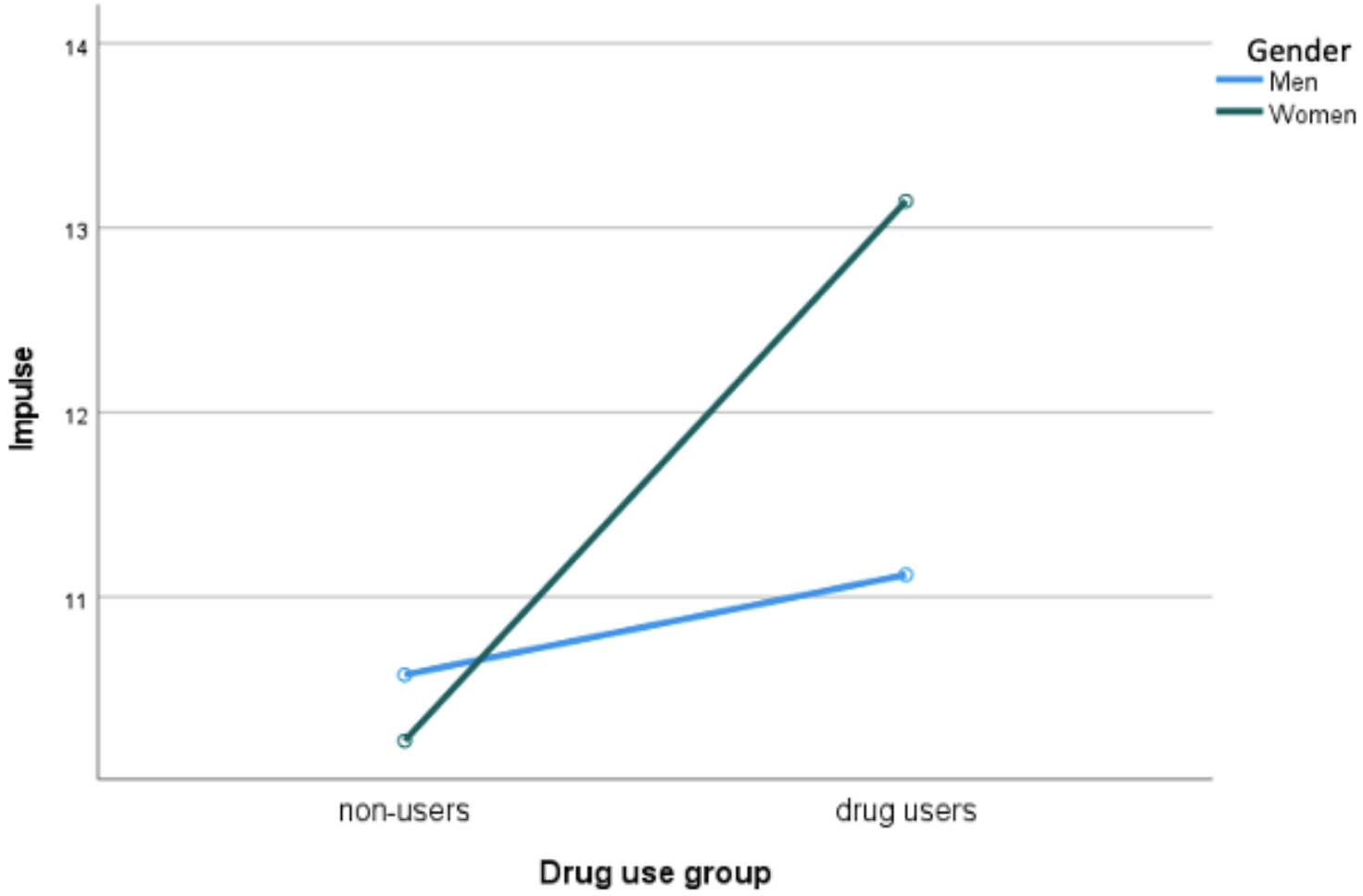

Figure 9. Association between drug use and DERS significantly moderated by gender

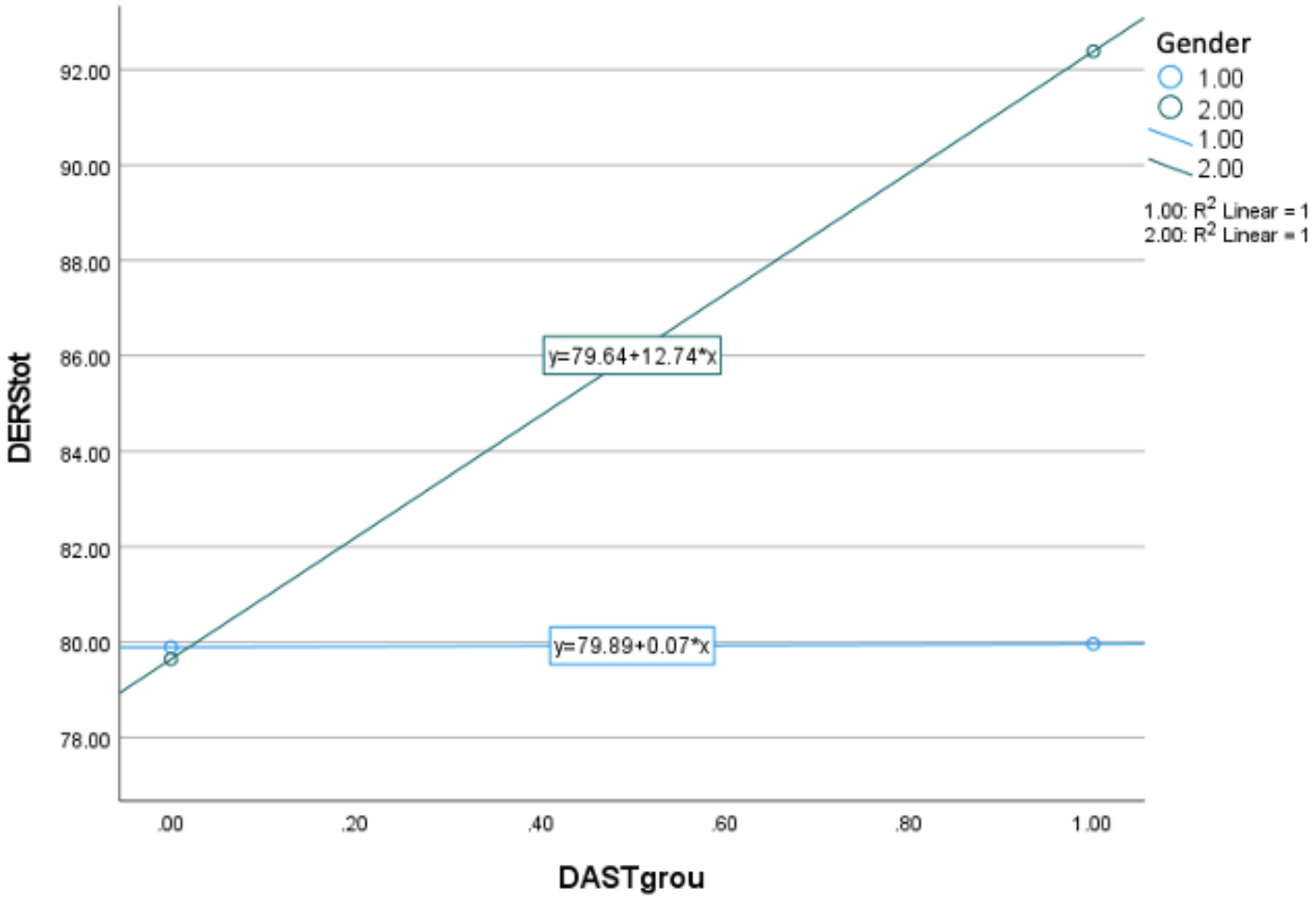

Figure 10. Association between drug use and impulse control significantly moderated by gender