THESIS

# USING PASSIVE SENSING TO ISOLATE A BIOSIGNATURE FOR CRAVING AMONG INDIVIDUALS IN EARLY ALCOHOL USE DISORDER RECOVERY

Submitted by
Sara Mei
Department of Psychology

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Master's Committee:

Advisor: Noah N. Emery

Reagan L. Miller-Chagnon
Nathaniel R. Riggs
David Eddie

# ABSTRACT

## USING PASSIVE SENSING TO ISOLATE A BIOSIGNATURE FOR CRAVING AMONG INDIVIDUALS IN EARLY ALCOHOL USE DISORDER RECOVERY

Craving is one of the most robust proximal predictors of both treatment dropout and relapse during early recovery for alcohol use disorder (Andersson et al., 2019; Gossop et al., 2002; Tiffany, 2010). Unsurprisingly, craving management is a central feature of most current AUD treatment models (Hendershot et al., 2011). However, craving can onset rapidly (Epstein et al., 2009) and the ability to accurately predict or modulate cravings varies significantly within- and between-person (Ellis et al., 2022; Joos et al., 2013; Kruschwitz et al., 2019; Preston et al., 2018). These factors make implementation of change strategies in the moment challenging, but creating a measurement and detection of craving through passive biosensor monitoring could offer a crucial opportunity for empirically supported just-in-time interventions. Heart rate variability has been associated with craving and changes in affect (Carter & Tiffany, 2002; Wascher, 2021). This study aims to characterize craving as a biosignature via heart rate variability to best capture the momentary nature of craving and individual differences by pairing wearable technologies with EMA among those in early recovery (*N* = 40, observations = 400). Multilevel regression analyses will be conducted to estimate correlations of craving and heart rate variability. Results from this line of research hold clinical implications for relapse prevention by laying the groundwork for the efficacy of isolating a biosignature for craving, which may inform just-in-time interventions by providing real-time information for recovery goals and enabling personalized interventions during critical recovery moments.

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## Introduction

Substance use disorders (SUDs), including alcohol use disorder (AUD), rank among the most devastating mental disorders both globally and in the United States, killing approximately 165,000 Americans annually (Centers for Disease Control and Prevention [CDC], 2021a; 2021b) and exacting an immense economic toll of around $691 billion each year (Rehm & Shield, 2019; World Health Organization [WHO], 2018). This massive burden is, in part, due to critical treatment gaps as well as the relapsing nature of addiction (Cornelius et al., 2003; Miller et al., 2001). Furthermore, while SUDs are multifaceted, alcohol remains the most prevalent and widely consumed substance, account for 45.6% of all substance use across the nation (U.S. Census Bureau, 2022). Given the striking rates of alcohol use compared to other substances, there needs to be a focus specifically on AUD and AUD treatments. Additionally, insights gained from improving AUD treatment would significantly impact general addiction treatment, given that individuals with AUD often engage in polysubstance use (i.e., consuming other substances) (Crummy et al., 2020; Staines et al., 2001). Empirically supported behavioral treatments for AUDs are initially efficacious in helping persons to stop or reduce alcohol use. However, risk of relapse remains significant, particularly within the first year of recovery (Brandon et al., 2007). This vulnerability during the initial recovery stage underscores the need for a deeper understanding of the factors contributing to relapse risk. Notably, among individuals admitted to addiction treatment, craving emerges as a particularly salient factor associated with the amount of time until post-treatment relapse (Paliwal et al., 2008; Schneekloth et al., 2012; Stohs et al., 2019), even after controlling for pre-treatment use patterns (Rohsenow et al., 2007). The intensity of craving also peaks in the beginning stages of recovery due to a constellation of psychoneurological factors (Seo & Sinha, 2014) and classical conditioning with stress-related cues and stress-induced cravings (Sinha, 2007), rendering the initial stages of recovery arduous. However, individuals who navigate through the early stages of recovery characterized by intensified craving and withdrawal symptoms eventually see a reduction in craving (Shumway et al., 2013) and corresponding reduction in relapse risk (Vafaie & Kober, 2022). Considering that craving exacerbates risk for relapse, particularly during the early phase of recovery, it is crucial that the field develops better interventions for managing craving in this critical stage of recovery. The first step towards this goal is to develop a deeper understanding of craving as well as its correlates in the moment when the effects are most pronounced (i.e., when craving and relapse risk are at their highest).

Often defined as an intense desire or urge to use a substance, craving is a cardinal feature of addiction and has been shown to be linked to the initiation, maintenance, and recurrence of use in SUDs and AUD (American Psychiatric Association [APA], 2013; Hasin et al., 2013; Tiffany, 2010). While complex, craving is considered one of the most robust and proximal predictors of relapse and treatment dropout (Breese et al., 2011; Marlatt, 1978; Sliedrecht et al., 2019). Craving is most prominent during the early recovery when relapse rates and stress-related symptoms are highest (Andersson et al., 2019; Gossop et al., 2002). This is in line with a recent meta-analysis that showed craving is associated with double the odds of future drug use or relapse in a sample of both individuals with and without SUDs (Vafaie & Kober, 2022). Taken together, it is not surprising that craving management is a central feature of most SUD treatment models (Hendershot et al., 2011). However, craving can onset rapidly (Epstein et al., 2009) and the ability to accurately predict or modulate cravings varies significantly within- and between-person (Ellis et al., 2022; Joos et al., 2013; Kruschwitz et al., 2019; Preston et al., 2018). These factors make implementation of change strategies in the moment challenging, particularly due to the acute effects of craving on behavior (Ferguson & Shiffman, 2009). If we could objectively measure and detect craving dynamics passively in real time to alert an individual, this would provide a window of opportunity for empirically supported just-in-time interventions (JIT; Carpenter et al., 2020), which could improve short-term and long-term outcomes. One way to do that is to use passive real time data to best capture the phenomenon of craving as a process with momentary expressions. Any potential candidate for passive observation of craving needs to be both feasible and accessible for those seeking AUD treatment while also showing initial promise as a biomarker of craving.

One such process is heart rate, which is already built into most passive monitoring systems (e.g., smart watches), making them objectively measured and widely accessible to a far-reaching range of populations. Additionally, heart rate variability (HRV), defined as the variation in time between consecutive heartbeats, is considered to be an indicator of autonomic nervous system activity (Taralov et al., 2016) and has proven to be an informative indicator of affective regulation and craving (Eddie et al., 2015). In individuals with SUD, alterations in HRV have been observed compared to individuals without SUD, indicating that consistent disruptions in autonomic regulation may be linked to addictive behaviors and craving (Brody et al., 1998; Ingjaldsson et al., 2003). Furthermore, in human lab cue reactivity paradigms, passively monitored HRV is a robust predictor of craving (Carter & Tiffany, 2002) and changes in affect (Wascher, 2021) in response to substance-related cues. Studies have also shown that craving is associated with changes in heart rate and HRV during withdrawal phases, potentially reflecting the stress and autonomic dysregulation experienced by those in early recovery (Claisse et al., 2017; Ralevski et al., 2019). While HRV data are complex, research suggests high-frequency

HRV (HF-HRV) may be more directly linked to craving regulation due to its role in promoting relaxation and emotional stability (Ralevski et al., 2019). Accordingly, focusing on HF-HRV as a measure of parasympathetic activity seems integral to determining a biomarker for craving.

Moreover, wearable biosensor technologies paired with ecological momentary assessments (EMA; Stone & Shiffman, 2002) afford the opportunity to collect real-time data in natural environments and capture these dynamic, temporal processes as they are lived with high ecological validity. Using EMA allows us to bypass many methodological barriers associated with clinical laboratory research and may illuminate the associations between alcohol use and varying moment-to-moment expressions of craving. Previous research with EMA demonstrates the momentary link between craving and substance use (Emery et al., 2021; Moore et al., 2014; Serre et al., 2015). Despite the strong correlation between craving and substance use assessed by EMA, this combination alone yields limited use for clinical interventions. Automatic physiological processes observed in those with SUD interact with internal affective states and environmental cues to undermine effortful cognitive control and outcompete goals to avoid substance use (Bates et al., 2013; Self, 1998; Tiffany, 1990), which ultimately undermine the potential efficacy of frontline treatments. However, this limitation may be overcome by pairing EMA with biosensors to better understand the momentary contextual predictors and motivators of substance use (e.g., craving, affective states), and specifically using passive HRV data may support individuals with better affect regulation and bolstered cognitive control. Accordingly, HRV appears to be a strong candidate for passively capturing craving by pairing wearable technologies with EMA among those in early recovery. However, almost no research has combined the use of EMA and biosensors to measure the affective and psychophysiological mechanisms facilitating substance use.

The current study seeks to fill this important gap by combining EMA and HRV biosensors to model the relationship between craving and HRV changes in real-time to determine if HRV can serve as a biomarker of acute increases in craving among those with AUD. Additionally, to our knowledge, no such work has been previously conducted using real-time ambulatory assessment for individuals at highest risk for relapse. As such, the current study is highly innovative and will serve as foundational knowledge for future works on JIT interventions. In summary, the current study seeks to examine if moments of high craving are characterized by acute changes in HRV for individuals in their first year of AUD recovery. Based on previous models that demonstrate the multidimensional and multifaceted nature of craving, we hypothesize that the integration of psychophysiological and self-report data would accurately reflect the complex nature of craving, such that moments of high craving would be significantly associated with acute differences in HRV concurrently. More specifically, consistent with previous research (Claisse et al., 2017), we hypothesize that at the within-person level self-reported craving will be positively associated with HF-HRV, such that moments of increased craving will be associated with higher levels of HF-HRV. We will also explore craving’s association with other indicators of HRV; however, given the literature is currently inconclusive, we do not put forth a formal directional hypothesis on other indicators of HRV, such as LF-HRV. Additionally, based on previous work (Ralevski et al., 2019), we hypothesize that at the between-person level HF-HRV will be inversely associated with craving, such that people with less variability in HF-HRV will exhibit higher craving on average. The literature review below is organized into four main sections. First, it will briefly review AUD treatment. Second, models of craving will be covered. Third, HRV and its role in AUD will be discussed. Finally, research on the advantages of EMA will be reviewed.

## Alcohol Use and Treatment

Substance use and substance use disorders (SUDs), including alcohol use disorder (AUD), are highly prevalent among the United States (US) population. According to national survey data, a staggering 59.8% of individuals aged 12 or older (equivalent to 168.7 million people) used tobacco products, illicit drugs, or alcohol in the past month. Alcohol consumption alone accounted for 48.7% of this population (137.4 million people) while 18.1% (50.9 million people) used tobacco products, 8.3% (23.5 million people) vaped nicotine, and 16.5% (46.6 million people) used an illicit drug. Further emphasizing the scope of the problem, 17.3% of the US population aged 12 or older met criteria for a SUD in the past year, which translates to 48.7 million people. This included 29.5 million with an alcohol use disorder (AUD), 27.2 million with a drug use disorder (DUD), and 8.0 million with both (Substance Abuse and Mental Health Services Administration [SAMHSA], 2023). Taken together, these prevalence rates suggest a pervasive public health problem affecting a significant portion of the US population. Among the various substances consumed, alcohol stands out as particularly prevalent, representing nearly half of all substance use across the nation and underscored by the exceedingly high number of individuals meeting criteria for AUD, equating to the entire population of Texas alone (U.S. Census Bureau, 2022). As such, there is an urgent need for research that can lead to targeted interventions to address SUD and specifically AUD, given the striking rates on alcohol compared to other substances.

Beyond its individual toll, SUDs rank among the most devastating mental disorders globally (WHO, 2018), with alcohol and other substance use contributing to approximately 343,000 deaths annually is the US alone (CDC, 2021a; 2021b). Moreover, the economic burden is substantial, with SUDs imposing an immense cost of around $691 billion each year (Rehm &

Shield, 2019; WHO, 2018). In just the US, the cost of excessive alcohol use reached $249 billion (CDC, 2024). This massive burden is, in part, due to critical treatment gaps as well as the relapsing nature of addiction (Cornelius et al., 2003; Miller et al., 2001). Given the striking rates of alcohol use compared to other substances, there needs to be a focus specifically on AUD and AUD treatments. Additionally, insights gained from improving AUD treatment would significantly impact general addiction treatment, given that individuals with AUD often engage in polysubstance use (i.e., consuming other substances; Crummy et al., 2020; Staines et al., 2001).

Empirically supported behavioral treatments for AUD are initially efficacious in helping persons to stop or reduce alcohol use. The gold standard treatment for AUD is cognitive-behavioral therapy, which targets behavioral and cognitive processes underlying an individual's alcohol use by increasing awareness of proximal factors contributing to one's use and leveraging behavior change principles to reduce use. Numerous studies have consistently highlighted CBT's effectiveness in equipping individuals with the skills to initiate and sustain abstinence-based or harm-reduction-based behavior (McHugh et al., 2010; O'Connor & Stewart, 2010). Randomized control trials have established its efficacy in reducing alcohol use for individuals with AUD within the first six months post-treatment (Magill & Ray, 2009; Morgenstern et al., 2001). Despite these advancements, there is a profound inaccessibility for those in need as 92% of people aged 12 or older with a SUD did not receive any formal treatment (SAMHSA & Center for Behavioral Health Statistics and Quality, 2024). Furthermore, risk of relapse remains high—relapse rates within the first year of recovery have been observed to be as high as 86% (Brandon et al., 2007). This vulnerability during the critical initial stages of recovery underscores the necessity for a deeper understanding of the factors associated with relapse among individuals in the first year of a recovery attempt, such as craving (Sliedrecht et al., 2019).

**Overview of Craving**

Often defined as an intense desire or urge to use a substance, craving is a symptom of AUD and considered a cardinal feature of addiction shown to be linked to the initiation, maintenance, and recurrence of use among those with AUD (APA, 2013; Hasin et al., 2013; Tiffany, 2010). Given its centrality in SUD, researchers and clinicians have put forth several theoretical models of craving (Drummond et al., 2000; Marlatt, 1978; Robinson & Berridge, 2001; M. D. Skinner & Aubin, 2010). Despite the breadth of proposed theories, many have shared features. As such, Skinner and Aubin (2010) have distilled and organized most models of craving into one of four general categories: 1) conditioning-based models, 2) cognitive models, 3) psychobiological models, and 4) motivational models.

Conditioning-based models focus on the role of classical and operant conditioning in the development and maintenance of craving through neural circuits associated with reward and incentive processing. They emphasize the learned associations between alcohol-related cues and the rewarding effects of alcohol use, signaling that craving is produced by processes of reward seeking behavior, whether that be due to conditioned withdrawal or promise of a reward (Solomon, 1980; Stewart et al., 1984; Wikler, 1973). Put simply, conditioning-based models conceptualize craving as an automatic, unconscious reaction to an external stimulus and is used as a positive reinforcement (e.g., receiving a dopamine release and socioemotional reward) or a negative reinforcement (e.g., escaping from aversive states such as withdrawal symptoms or discomfort of non-use).

Cognitive models of craving highlight the cognitive processes and beliefs underlying addictive behaviors. They contend that higher order cognitive functions produce craving through a complex, non-automatic process. Rather than a simple response to physiological cues, craving arises from the interaction of cognitive processes such as attention, memory, and interpretation of alcohol-related cues (Marlatt, 1985). The incorporation of how alcohol-related information and/or cues contribute to the experience of craving through constructs such as expectancies, self-efficacy, and attributions, such that positive outcome expectancies may increase the intensity and duration of craving, whereas increased self-efficacy expectations may mediate this relationship (Witkiewitz & Marlatt, 2004). Additionally, cognitive biases, such as attentional biases towards alcohol-related cues and beliefs about drinking, contribute to the experience of craving and the perpetuation of addictive behaviors (Field & Cox, 2008; Robinson & Berridge, 2001). This means individuals are more likely to notice and focus on cues associated with alcohol, such as media advertisements for drinking or environments where they often consume alcohol.

Psychobiological models integrate neurobiological and psychological factors to explain craving. These models emphasize the interplay between brain mechanisms, such as neurotransmitter systems and neural circuits implicated in reward processing and emotion regulation, and psychological processes, such as stress and affective states, in driving craving and substance seeking behavior (Koob & Moal, 2008; Robinson & Berridge, 2001). Some models stipulate that the biological processes occur as a learned outcome through conditioning—for instance, the development of interoceptive detection of falling drug blood levels that signal withdrawal (Baker et al., 2004). Central to these models is the recognition that craving is directly shaped by biological neural systems, which is then influenced by individual differences and motivational aspects of drinking behavior (Redish et al., 2008; Verheul et al., 1999). Notably, psychobiological models account for the persistent nature of craving.

Motivational models of craving focus on understanding the underlying motivations that drive individuals to seek and consume alcohol, including the role of both internal and external factors. In Cox and Klinger (1988)'s motivation model, drinking behavior is a choice that an individual makes in order to achieve their desired emotional state. Breiner et al. (1999) update this theory with the addition of two parallel motivational pathways, adding more nuance to an individual's choice (i.e., one cerebral system is sensitive to rewards and induces craving, the other is sensitive to threats and deters craving). The most recent model synthesizes the structure of the motivational system, mindfulness, neural plasticity, self-identity, and the complexity of evaluations in decision-making for alcohol-seeking behavior, in which craving may modulate different mechanisms such as expectancies and emotional arousal (West & Brown, 2013). The motivational paradigm explores how factors such as reward salience, incentive sensitization, and the desire to alleviate negative affect contribute to the experience of craving and the persistence of alcohol use despite negative consequences. In these models, craving is a central component in the larger decision-making framework.

In review, craving has long been incorporated into models of addiction at varying degrees of importance and transience. Conditioning-based models view craving as an automatic, unconscious reaction to a stimulus. Under the cognitive paradigm, craving is conceptualized as the output of information processing systems. Psychobiological models postulate that craving can be partially attributed to biological factors and individual differences. Motivational models operate under the assumption that craving is a central component of a larger decision-making framework. Despite these distinct distillations, evidence suggests that craving is multidimensional with different components that potentially make a whole construct. Further, the obvious overlap throughout the various models signify that the components of craving are not mutually exclusive and thus, leveraging one may allow us to affect another. For instance, increasing one's awareness to their heightened attentional bias around alcohol-related cues may offer an opportunity to offer a biobehavioral intervention that targets the neural system associated with reward, bypassing the automatic conditioning after years of incentive salience—lowering craving will thus lower the risk of relapse.

Additionally, researchers suggest that craving is not a monolithic nor static phenomenon but rather a multi-dimensional and dynamic construct. One significant aspect highlighted by this research is the dual nature of craving (Drummond et al., 2000). Firstly, craving can be viewed as an entity—an identifiable and discrete experience characterized by an intense desire or urge to consume alcohol. In this sense, craving manifests as a distinct psychological state, often accompanied by physiological arousal and cognitive preoccupation with obtaining alcohol and drinking. This definition highlights the immediacy and salience in the subjective experience of individuals with AUD and the significance of craving as a target for intervention and treatment. However, craving is also understood as a process—a dynamic and evolving sequence of events shaped by various biopsychosocial mechanisms over time. This perspective emphasizes the temporal aspect of craving, acknowledging its fluctuating nature and the diverse factors that contribute to its onset, intensity, and duration. Craving can arise in response to internal cues (e.g., stress, negative affect, or physiological withdrawal symptoms) or external cues (e.g., environmental triggers or social contexts associated with alcohol use).

By recognizing craving as both an entity and a process, researchers and clinicians gain a more comprehensive understanding of its complexities and clinical implications. This dual perspective underscores the need for multifaceted approaches to develop effective interventions that target craving at both the individual and systemic levels within the context of AUD by integrating insights to incorporate all the proposed models (e.g., conditionally, cognitively, physiologically, and affectively). Moreover, acknowledging the dynamic nature of craving highlights the importance of personalized and adaptive in-the-moment treatment strategies that can address the evolving experiences of individuals with AUD over time.

***Associations Between Craving and AUD treatment.*** Craving is associated with the amount of time before post-treatment relapse (Paliwal et al., 2008; Schneekloth et al., 2012; Stohs et al., 2019), even after controlling for pre-treatment use amounts (Rohsenow et al., 2007). The intensity of craving also peaks in the initial stages of recovery due to a constellation of psychoneurological factors (Seo & Sinha, 2014) and classical conditioning with stress-related cues and stress-induced cravings (Sinha, 2007), rendering the process arduous; though individuals who navigate through the early stages of intensified craving and withdrawal symptoms eventually see a reduction in craving (Shumway et al., 2013). Considering that craving exacerbates risk for relapse, particularly during the early phase of recovery, it is crucial to leverage our therapeutic understanding of craving within this pivotal intervention timeframe for the amelioration of AUD treatments. One physiological process that appears to be associated with craving that has been studied in the lab is heart rate variability.

## Heart Rate Variability

Heart rate variability (HRV), defined as the variation in time between consecutive heartbeats, is considered to be an indicator of autonomic nervous system activity (Taralov et al., 2016) and has proven to be an informative indicator of affective regulation and craving (Quintana et al., 2013). In individuals with AUD, alterations in HRV have been observed compared to individuals without AUD, indicating that consistent disruptions in autonomic regulation may be linked to addictive behaviors and craving (Brody et al., 1998; Ingjaldsson et al., 2003). Furthermore, in human lab cue reactivity paradigms, passively monitored HRV is a robust predictor of craving (Carter & Tiffany, 2002) and changes in affect (Wascher, 2021) in response to alcohol-related cues. Studies have also shown that craving is associated with changes in heart rate and HRV during withdrawal phases, potentially reflecting the stress and autonomic dysregulation experienced by those in early recovery (Claisse et al., 2017; Ralevski et al., 2019). As such, HRV seems to be a promising biomarker for predicting craving for individuals with SUD.

The interplay between affect, craving, and physiological responses, influenced by emotional states and environmental cues, involves moment-to-moment changes in cardiovascular activity and brain perfusion, mediated by the central autonomic network (CAN; Quintana et al., 2013). This network comprises of various brain regions and the peripheral autonomic nervous system, including both the sympathetic and parasympathetic systems, and serves to regulate physiological arousal to adapt to situational demands (Benarroch, 1993). Importantly, the CAN plays a pivotal role in affect regulation and alcohol craving by flexibly adjusting physiological arousal in accordance with changing situational demands (Eddie et al., 2015; Friedman & Thayer, 1998). In other words, alcohol use induces alterations in the central nervous system, affecting neurotransmitter systems and neural pathways involved in emotion processing and reward, thereby influencing the functioning of the sympathetic and parasympathetic systems and exacerbating physiological responses linked to affect and craving.

Research on the relationship between parasympathetic and sympathetic nervous system activity, as measured through HRV, and craving is still ongoing and evolving. Analyses for HRV characterize both sympathetic and parasympathetic activities. Generally, researchers distinguish very low frequencies (< 0.04 Hz), low frequencies (0.04–0.15 Hz) and high frequencies (0.1–0.4 Hz; Berntson et al., 1997). Reduced HF-HRV has been linked to loss of flexibility in the parasympathetic cardiovascular tone and worse emotional regulation (Simplicio et al., 2012) and higher levels of trait (i.e., between-person) HF-HRV are associated with reduced vulnerability to craving even after long-term abstinence (Claisse et al., 2017). Conversely, low-frequency HRV (LF-HRV) or LF/HF ratio, has been commonly theorized to represent sympathetic activity, though some evidence suggests that it may be indicative of both sympathetic and parasympathetic activity (Reyes del Paso et al., 2013). Consequently, data on LF-HRV and substance use is much less consistent, suggesting that alcohol and potentially other substances have relatively greater effects on the parasympathetic system, which have a more exclusive impact on determining between-person HF-HRV (Ralevski et al., 2019).

In sum, some studies suggest that parasympathetic activity (i.e., namely HF-HRV) may be more directly linked to craving regulation due to its role in promoting relaxation and emotional stability. Accordingly, focusing on HF-HRV as a measure of parasympathetic activity seems integral to determining a biomarker for craving. However, the evidence for using one branch of the autonomic nervous system over the other to predict craving is not yet conclusive. Many studies have focused on HRV as a holistic marker of autonomic balance rather than specifically dissecting the contributions of parasympathetic versus sympathetic activity. Moreover, the relationship between HRV and craving can be complex and influenced by various factors such as individual differences and contextual factors. As such, EMA research appears to be the most appropriate method to better understand the momentary associations between craving and HRV, given that data are collected across multiple contexts and observations represent deviation from a person's own mean (i.e., people serve as their own controls). Additionally, HF-HRV appears to exhibit paradoxical patterns of associations across levels of analyses (i.e., positive at the within-level and inverse at the between-level). Accordingly, it is critical to disentangle these effects by modeling associations both at the state- and trait-level. EMA is uniquely equipped to allow us to examine these effects at both within- and between-person levels.

**Ecological Momentary Assessment**

EMA employs repeated real-time assessments based on self-report surveys to capture individuals' emotional, behavioral, or cognitive experiences (i.e., event-level) in their natural environment (i.e., *in vivo*) via smartphones or computers (Stone & Shiffman, 2002). Common types of assessments include: 1) time- or interval-contingent assessments, in which participants receive prompts based on random time intervals within a range pre-determined by the researcher; 2) event-contingent assessments, in which the participant has to initiate the survey after a specified event of interest (e.g., after eating, a trip, a social interaction, etc.), or 3) a prompt after specific psychophysiological measures (e.g., when an accelerometer measured physical activity that surpassed or fell below a predefined activity threshold), or 4) a combination of time- and event-contingent sampling based on physical activity or location (de Vries et al., 2021). Due to the ability to accurately capture the variability in momentary behavior and experiences, this intensive longitudinal approach offers advantages over cross-sectional surveys or multi-wave designs, particularly in modeling dynamic craving and alcohol use associations as outlined by the aforementioned theoretical frameworks (Drummond et al., 2000; M. D. Skinner & Aubin, 2010). Assessing craving as it occurs, rather than retrospectively, is crucial for establishing temporal precedence. Additionally, EMA methodology reduces retrospective recall bias inherent in traditional measures, enhancing the generalizability of findings specifically with patterns in alcohol use (Shiffman, 2009). Further, another advantage includes aggregating data from repeated measures to create reliable trait-like measures of a person's experience (Emery et al., 2023) that also bypass concerns of recall, such as recency bias, mood-congruent memory biases that tend to influence global trait measures (Solhan et al., 2009).

Despite offering advantages over traditional laboratory methodologies, EMA designs possess certain limitations despite the range of assessment types a study can employ. Time- or interval-contingent assessments aim to capture various aspects of a participant's daily life by querying their experiences within a short timeframe prior to survey receipt (e.g., within the last 30 minutes). While this approach can capture specific daily occurrences, the time intervals between surveys, often implemented to alleviate participant burden, restrict the coverage to only a portion of the day. Even with the most exhaustive survey schedules, participants would typically only report experiences for approximately half of their day (i.e., considering a 24-hour day with 8 hours of sleep and surveys querying experiences within the past 30 minutes). Conversely, event-contingent surveys offer the advantage of directly studying the targeted experience of interest, though this hinges upon participants' attention and initiative to trigger the survey. Moreover, previous EMA research indicates that individuals in recovery from AUD seldom report craving (approximately 8% of all possible observations), and when they do, these cravings are often of low intensity ($M$ = 0.55 on a 0-10 Likert scale). This is significantly lower when compared to the laboratory sessions counterpart, in which the urges to drink were reported to be of average intensity ($M$ = 4.48; Litt et al., 1998). Thus, this suggests that people with AUD often experience craving at low intensity throughout their daily experience; they may not identify the need nor the event of interest to fill out event-contingent surveys. Consequently, while EMA is well-suited for investigating the temporal and dynamic nature of craving and its contextual associations and accounting for individual differences, it still appears to be missing time-sensitive information on the experience of craving among a group of people where the opportunity to intervene is often short-lived and the consequences are disproportionately severe.

If we could objectively measure and detect craving passively in real time to alert an individual, this bypasses the limitations of traditional EMA methods and provides a window of opportunity for empirically supported JIT interventions, which could improve short-term and long-term outcomes. One way to do that is to use passive real time data to best capture the phenomenon of craving as a process with momentary expressions. HRV proves to be a promising psychophysiological indicator for craving, and heart rate is already built into most passive monitoring systems (e.g., smart watches), making them widely accessible to a far-reaching range of populations. Moreover, wearable biosensor technologies paired with EMA afford the opportunity to collect real-time data in natural environments and capture these dynamic, temporal processes as they are lived with high ecological validity. Using EMA allows us to bypass many methodological barriers associated with clinical laboratory research and may illuminate the associations between alcohol use and varying moment-to-moment expressions of craving. However, almost no research has combined the use of EMA and biosensors to measure the affective and psychophysiological mechanisms facilitating alcohol use. There is a growing consensus that using mobile technologies, such as EMA and biosensors, provides clear added value to understanding the momentary contextual predictors and motivators of alcohol use (e.g., craving, affective states). Yet, identification of passive ambulatory psychophysiological measures of craving and, by extension, relapse risk that can be incorporated into a JIT intervention with an intuitive user experience are still sorely needed.

## Current Study

The current study aims to combine EMA and HRV biosensors to model the relationship between craving and HRV changes in real-time to determine if HRV can serve as a biomarker of acute increases in craving within a naturalistic setting. That is, can we isolate a heart rate signature of craving in real time when in use or in abstinence. Craving is one of the most robust proximal predictors of both treatment dropout and relapse during early recovery for AUD (Andersson et al., 2019; Gossop et al., 2002; Tiffany, 2010). Correspondingly, craving management is a central feature of most current AUD treatment models (Hendershot et al., 2011), yet current AUD treatments are not effective almost immediately after individuals complete treatment due to high relapse rates (Brandon et al., 2007). This may be due to the nature of craving as it can onset rapidly (Epstein et al., 2009) and the ability to accurately predict or modulate cravings varies significantly within- and between-person (Ellis et al., 2022; Joos et al., 2013; Kruschwitz et al., 2019; Preston et al., 2018). These factors make implementation of change strategies in the moment challenging, but creating a measurement and detection of craving through passive biosensor monitoring could offer a crucial opportunity for empirically supported JIT interventions.

A strong potential candidate for passive observation of craving needs to be both feasible and accessible for those seeking AUD treatment while also showing initial promise as a biomarker of craving. One such process is heart rate variability, which has been associated with craving and changes in affect (Carter & Tiffany, 2002; Wascher, 2021). The combination of EMA and HRV biosensors will also allow us to explore the within-person role of craving-HRV covariance as a proximal predictor of alcohol use, while accounting for between-person differences in craving and HRV. This unique combination of self-report and psychophysiological data has potential to help address critical treatment gaps for AUD by providing the scientific groundwork for aiding individuals with moment-to-moment information for their recovery goals, alerting them when they are more at-risk to salient triggers, and by extension has implications for personalized physiological-based for JIT interventions to help introduce therapeutic skills at critical "teachable" moments for individuals. As such, the current study has two aims: 1) examine if moments of high craving are characterized by acute differences in HRV for individuals in their first year of AUD recovery; and 2) explore other indicators of craving, such as LF-HRV.

Based on previous models that demonstrate the multidimensional and multifaceted nature of craving, we hypothesize that the integration of psychophysiological and self-report data would accurately reflect the complex nature of craving, such that moments of high craving would be significantly associated with acute differences in HRV concurrently. More specifically, consistent with previous research (Claisse et al., 2017), we hypothesize that at the within-person level self-reported craving will be positively associated with HF-HRV, such that moments of increased craving will be associated with higher levels of HF-HRV. We will also explore craving's association with other indicators of HRV; however, given the literature is currently inconclusive, we do not put forth a formal directional hypothesis on other indicators of HRV, such as LF-HRV. Additionally, we hypothesize that at the between-person level HF-HRV will be inversely associated with craving, such that people with less variability in HF-HRV will exhibit higher craving on average consistent with laboratory research (Ralevski et al., 2019).

# Methods

## Participants

The current study analyzed secondary EMA data (*N* = 40, observations = 400) collected as part of a larger National Institutes of Health (NIH) funded parent study examining cognitive and physiological aspects of affect in early recovery from AUD (AA025251; PI: D. Eddie). Inclusion criteria for the parent study were: 1) meeting past-year AUD criteria (based on the DSM-5 criteria; APA, 2013), 2) endorsing a current goal of alcohol abstinence, 3) being in the first year of a current AUD recovery attempt, and 4) participating in outpatient AUD treatment (e.g., outpatient, mutual-help programs, individual therapy) or an AUD mutual-help program (e.g., Alcoholics Anonymous). Given acute alcohol withdrawal could potentially impact HRV measurements, participants were required to have at least 2 weeks of alcohol and other drug abstinence (assessed with baseline timeline follow-back; Sobell & Sobell, 1992) before enrolling in the study to minimize the influence of physiological withdrawal symptoms. Exclusion criteria were: 1) having cardiac arrhythmias or serious medical conditions that may affect HRV (e.g., cardiovascular disease), 2) taking medications that directly influence HRV (e.g., beta blockers), and 3) having an active SUD related to a drug other than alcohol in the past year. Forty participants provided data on the focal variables (e.g., ambulatory HRV, EMA) making for an analytic sample of 40. The analytic sample (*N* = 40) was 60.0% male, aged 22 to 65 (*M* = 42.2, *SD* = 13.0). Participants were 75.0% White/European American, 17.5% Black/African American, 5.0% Asian, and 2.5% Other race/Mixed race.

## Procedure

Procedures were approved by Mass General Brigham's institutional review board (IRB# 2016P001178). Each participant completed an initial phone screening to determine their eligibility for the study based on inclusion and exclusion criteria. Eligible participants completed an intake appointment with baseline measures and were trained to use the EMA application on their personal smartphone. Participants then completed 6 days of EMA monitoring with both random and self- initiated EMA surveys using the MetricWire EMA smartphone application (MetricWire, 2016). The program generated three prompts for participants to complete brief ~2-min assessments about participants' experience at random times within one of three, 3-hr blocks (e.g., 10 a.m. to 1 p.m., 2–5 p.m., and 7–10 p.m.). In addition to random surveys, participants were instructed to self-initiate a survey in moments when they felt high levels of stress, alcohol craving, or felt at risk for alcohol use. To encourage random EMA survey completion, participants were given a $30 bonus for completing ≥90% of the surveys.

## Measures

### Baseline Measures

**Alcohol use.** With the baseline questionnaires, alcohol use was assessed with Alcohol Dependence Scale (H. A. Skinner & Allen, 1982) and timeline follow-back (Sobell & Sobell, 1992). The ADS is a 29-item measure that evaluates the severity of alcohol dependence based on symptoms and behaviors associated with AUD. Items are scored on a dichotomous scale (0, 1), three-choice scale (0, 1, 2), or four-choice scale (0, 1, 2, 3). A total score (ranging from 0 to 47) is obtained by summing across items, with higher scores indicating greater alcohol dependence (i.e., scores of 1-13 indicate low dependence, 14-21 moderate dependence, 22-30 substantial dependence, and 31-47 severe dependence). The TLFB is considered the gold standard for quantitatively assessing alcohol use by asking individuals to provide an estimate of their daily drinking patterns over a specified time period. In the current study, participants were asked to report their alcohol consumption for the 30 days prior to baseline.

**EMA Measures**

**Craving.** During random and self-initiated begin use reports, craving was assessed with a single item of urge to use alcohol on an 11-point scale from 0 (*no craving*) to 10 (*extreme craving*). This measure is widely used in laboratory and EMA research (Emery et al., 2020; Miranda et al., 2008; Ray et al., 2010) and previous EMA work supports the criterion validity (Ramirez & Miranda, 2014).

**HRV.** Ambulatory measures of HRV were measured using a eMotion Faros 180 ambulatory ECG monitor (see Eddie et al., 2023 for review). Sequences of heart beat-to-beat intervals (RRI) were recorded and exported to WinCPRS software (Absolute Aliens Oy, 2012) for analysis and calculation of HRV indices and mean heart rate. After cubic interpolation of the non-equidistant waveform, the RRI sequence was checked for artifacts (i.e., anomaly introduced in the processing or transmission of digital data) and irregular beats and edited manually where necessary.

Heart rate, expressed as beats per minute, was derived by calculating the average number of R-spikes in the ECG signal occurring each minute during the 5-min recording period. HRV was calculated from edited sequential RR intervals derived from the ECG signal. Frequency domain HRV indices were calculated using Fourier analysis (Cooke et al., 1999; Taylor et al., 1998). Frequency domain indices provide information about how power distributed as a function of frequency (Task-Force, 1996). We categorized frequency domain indices into the following: low frequency variability (VLf: 0.005–0.04 Hz), low frequency variability (Lf: 0.04–0.15 Hz), and high frequency variability (Hf: 0.15–0.4 Hz) indices.

Time domain indices included the standard deviation of all normal-to-normal intervals (SDNN) and the root of the mean square of successive normal-to-normal intervals differences (RMSSD), both of which are useful for gauging autonomic activity. In addition, the number of pairs of adjacent normal-to-normal intervals differing by more than 50 ms throughout each 5-min recording (NN50) was used to derive the percentage of NN50 (pNN50), a measure of parasympathetic vagal activity (Task-Force, 1996). Then, to calculate individual participant's mean HRV across the ECG monitoring period, an average score for each HRV index was calculated for each participant.

**Statistical Power and Minimum Detectable Effect Sizes**

To determine the minimum detectable effect sizes from the number of observations in our data, we conducted a computer simulation using the Monte Carlo feature of Mplus 8.5 (Muthén & Muthén, 2017). Consistent with previous research on affect and substance using samples (e.g., (Emery & Simons, 2020; Emery et al., 2021), 50% of the variance in craving and HRV was specified at the within-person level with the remaining variance specified at the between-person level. The focal effects of interest in this study are the effects of momentary HRV indicators on momentary craving. Unfortunately, previous research has not examined these associations using EMA methods. Thus, we conducted multiple Monte Carlo simulations with small effect sizes ranging $\beta = 0.05$ to $\beta = 0.35$ for both within- and between-level associations. Results using 10,000 replications indicated a sample of 40 individuals with 10 observations each would be sufficiently powered to detect within-person effects of $\beta = 0.15$ or higher, and between-person effects of $\beta = 0.33$ or higher based on a power level above 0.80. Importantly, the final models will have a series of covariates, which will account for additional residual variance not estimated here, effectively increasing power above what was seen here. Accordingly, based on these simulations, we appear to be adequately powered to detect any clinically meaningful effects found in these models.

**Planned Analysis**

Preliminary analyses were conducted to determine the ranges and distributions of all variables. Skewed and kurtotic distributions were transformed if appropriate (Tabachnick & Fidell, 2019) or alternative reference distributions were determined and applied. Univariate outliers were identified by box plots and examinations of z scores for all variables. After checking for skew and kurtosis, outlying values ($SD > 3.29$, $p < .001$) were either deleted from the data set or changed to one unit greater than the nearest non-outlying value (Tabachnick & Fidell, 2019). We centered indices of HRV by subtracting person averages from momentary values at the within-level (L1). At the between-level (L2), variables were centered by subtracting the overall sample averages from person-level averages (grand-mean centered). This approach allows for person-centered variables to reflect moment-to-moment deviations from a person's average level, and grand-mean centered variables reflect person deviations from the overall average for the sample. Centering also partially normalizes the distributions, which simulation studies suggests are optimal for within-person effects and superior to global transformations (i.e., logarithmic transformations; Wang et al., 2019).

To test the hypothesized associations between momentary HRV indices and momentary craving in real-time, we examined concurrent associations (i.e., measured at the same time) between EMA self-reported cravings and ambulatory HRV indices at each signal, we estimated a multilevel model (MLM) with random intercepts and with an unstructured variance-covariance matrix using Stata 18. The data had a two-level structure in which moments (Level 1 [L1]; within-person) were nested within persons (Level 2 [L2]; between-persons). The models contained within-person momentary indices of HRV (i.e., SDNN, RMSSD, pNN50, HF-HRV, and LF-HRV) predicting craving at the same moment (L1) and person-level averages of HRV indices predicting average craving over the sampling period (L2). L1 covariates included day-of-the-week and day-in-the-study to control for daily variation in substance use and mood as well as potential practice effects and time-dependent change in variable frequency (Mohr et al., 2006; Room et al., 2012). L2 covariates included sex and age to account for sex and age differences in patterns of substance use (Agabio et al., 2017; Lancaster & Spiegel, 1992; Leigh & Stacy, 2004; Nicolai et al., 2012) and HRV (Geovanini et al., 2020).

L1 focal variables were centered within-person by subtracting person averages from momentary values (i.e., person-mean centered). L2 variables were centered by subtracting the overall sample averages from person-level averages (i.e., grand-mean centered). In this context, person-mean centered variables reflect moment-to-moment deviations from a person's average level, and grand-mean centered variables reflect person deviations from the overall average for the sample. Craving and HRV indices are expected to vary not only within each person over time (L1; within-person) but also on average from person to person (L2; between-persons). The inclusion of momentary and average indicators allowed for isolation of the within-person associations of state fluctuations in the association between craving and HRV from between-person associations.

Distinctions between person-average craving and HRV from momentary states (e.g., a moment of high craving or HRV) capitalized on the full complement of the EMA data by distinguishing dynamic, within-person changes in momentary craving or HRV from between-person, individual differences in typical (i.e., dispositional) craving or HRV level. Craving and HRV were expected to vary not only within each person over time (L1; within person) but also on average from person to person (L2; between persons). The inclusion of momentary and average indicators allowed for isolation of the within-person associations of craving and HRV fluctuations with emotion differentiation from between-person associations. An intercept-only model (without any predictors) estimated intraclass correlations (i.e., variability in predictors attributed to between-person effects relative to within-person influences).

To test the hypothesized positive association between self-reported craving and HF-HRV at the within-person level, indices of HRV (i.e., HF-HRV, LF-HRV, VLF-HRV) were regressed on self-reported craving scores obtained during the random and self-initiated EMA surveys. The hypothesis will be supported if this analysis produces a significant ($p < 0.05$) positive regression coefficient. This analysis also allowed us to test the exploratory hypothesis of craving's association with other indicators of HRV (i.e., LF-HRV, VLF-HRV). To test the hypothesized inverse association between craving and HF-HRV at the between-level person, indices of HRV (i.e., HF-HRV, LF-HRV, VLF-HRV) were regressed on self-reported craving scores obtained during the random and self-initiated EMA surveys. The hypothesis will be supported if this analysis produces a significant negative regression coefficient.

## Results

**Descriptive statistics.** Compliance with random surveys was calculated by dividing the total number of random surveys completed by all participants by the total number completed plus missed random surveys. With 400 completed random surveys and 480 combined completed and missed random surveys, the overall compliance was 83.3%. Over the 4-day EMA plus HRV monitoring period, participants completed 313 random surveys ($M$ = 7.8, $SD$ = 2.8) and 87 self-initiated surveys over the sampling period. Out of 40 participants, 25 completed self-initiated surveys ($M$ = 11.4, $SD$ = 4.1), with the number of surveys ranging from 3 to 21 surveys over the 4-day period. Participants reported an average of 12% drinking days ($SD$ = 18.9) over the 30 days immediately preceding study enrollment. Participants' mean ADS was 23.8 ($SD$ = 8.5) indicating a "substantial level" of AUD severity (H. A. Skinner & Allen, 1982). Descriptive statistics for Level 1 and Level 2 variables are outlined in Table 1.

The intraclass correlations (ICCs) for the study variables revealed the proportion of total variance attributable to within-person fluctuations versus between-person differences. The ICCs were 0.385 for craving, 0.529 for RMSSD, 0.514 for pNN50, 0.346 for HF-HRV, 0.497 for PNS index, and 0.529 for SD1. This suggests that 38.5% of the total variance explained by craving was due to stable between-person differences, while 61.5% was attributable to within-person fluctuations over time. HF-HRV demonstrated the lowest ICC, indicating substantial within-person variability, consistent with its role as a physiological marker that responds dynamically to momentary changes in autonomic regulation. In contrast, HRV-related indices such as RMSSD, pNN50, PNS index, and SD1 exhibited higher ICCs, suggesting a relatively greater proportion of variance attributable to stable individual differences.

**Multilevel model analysis.** A multilevel model was estimated to test the hypothesized momentary associations of HRV with craving. It was hypothesized that within-person (L1) HF-HRV will be positively associated with self-reported craving, such that moments of greater craving would be characterized by higher-than-average levels of HF-HRV. Additionally, we hypothesized that at the between-person (L2) HF-HRV will be inversely associated with craving, such that people with less variability in HF-HRV will exhibit higher craving on average. We did not put forth a formal directional hypothesis on other indicators of HRV due to the dearth in current literature.

At the within-person level (L1), consistent with our hypothesis, moments of increased craving were characterized by higher-than-average levels of HF-HRV ($b$ = 0.001, $p$ = .038, 95% CI = 0.001, 0.002). However, other momentary indicators of HRV (i.e., RMSSD, pNN50, PNS index, SD1) were not significantly associated with craving ($p$s > .553; see Table 2). At the between-person level (L2), person-average HF-HRV was not significantly associated with person-average levels of craving during the sampling period ($b$ = –0.003, $p$ = .133, 95% CI = –.007, .001) as hypothesized; however, it was in the expected inverse direction. Interestingly, person-average PNS index was inversely associated with craving, such that lower levels of parasympathetic cardiac activity were associated with higher levels of person-average craving during the sampling period ($b$ = –2.230, $p$ = .024, 95% CI = -4.172, -.288). No other significant effects for person-level indicators of HRV were found ($p$s > .205). Full model estimates for Level 1 and Level 2 variables are outlined in Table 2.

**Table 1.** ***Descriptive Statistics for Level 1 and Level 2 Variables***

| | *M* | *SD* |
|---|---|---|
| Craving | 2.22 | 2.60 |
| RMSDD | 24.56 | 18.34 |
| pNN50 | 7.24 | 11.71 |
| HF-HRV | 275.13 | 469.33 |
| PNS Index | -1.61 | 1.00 |
| SD1 | 17.39 | 12.99 |

*Note.* *N* = 40 individuals, observations = 400. *M* = mean, *SD* = standard deviation. RMSDD = the root mean square of successive differences; pNN50 = percentage of successive normal cardiac interbeat intervals greater than 50 msec; HF-HRV = power of high-frequency waves produced by the parasympathetic nervous system, PNS index = parasympathetic cardiac activity, SD1 = short-term HRV in ms and correlates with baroreflex sensitivity.

**Table 2.** ***Multilevel Model Analysis for HRV Indicators on Craving***

| | *b* | *SE* | *z* | *p* |
|---|---|---|---|---|
| Within person (Level 1; L1) | | | | |
| RMSDD | -9.09 | 15.59 | -0.58 | .560 |
| pNN50 | 0.02 | 0.03 | 0.59 | .553 |
| **HF-HRV** | **0.01** | **0.01** | **2.08** | **.038** |
| PNS Index | -0.17 | 0.31 | -0.55 | .584 |
| SD1 | 12.79 | 22.03 | 0.58 | .561 |
| Monday | -0.05 | 0.51 | -0.11 | .916 |
| Tuesday | 0.46 | 0.53 | 0.86 | .390 |
| Wednesday | 0.27 | 0.55 | 0.49 | .621 |
| Thursday | 0.10 | 0.44 | 0.24 | .813 |
| **Friday** | **0.86** | **0.39** | **2.18** | **.029** |
| **Saturday** | **1.12** | **0.37** | **2.98** | **.003** |
| Day-in-the-study | 0.20 | 0.11 | 1.82 | .068 |
| Between persons (Level 2; L2) | | | | |
| RMSDD | -22.90 | 93.52 | -0.24 | .806 |
| pNN50 | -0.17 | 0.14 | -1.27 | .205 |
| HF-HRV | -0.01 | 0.01 | -1.50 | .133 |
| **PNS Index** | **-2.23** | **0.99** | **-2.25** | **.024** |
| SD1 | 32.74 | 132.12 | 0.25 | .804 |
| Sex | 0.74 | 0.54 | 1.38 | .166 |

*Note.* $N$ = 40 individuals, observations = 400. *b* = unstandardized coefficient, *SE* = standard errors**.** RMSDD = the root mean square of successive differences; pNN50 = percentage of successive normal cardiac interbeat intervals greater than 50 msec; HF-HRV = power of high-frequency waves produced by the parasympathetic nervous system, PNS index = parasympathetic cardiac activity, SD1 = short-term HRV in ms and correlates with baroreflex sensitivity. Orthogonal day-of-the-week indicators represent that day's effect compared with the reference day, Sunday. Sex = sex assigned at birth (1 = *male*, 2 = *female*).

## Discussion

Contemporary models of addiction and AUD treatment conceptualize craving as a central, yet multifaceted mechanism encompassing conditional, cognitive, physiological, and affective dimensions operating as both an entity and process (Drummond et al., 2000; Hendershot et al., 2011; M. D. Skinner & Aubin, 2010). Despite its clear clinical significance, accurately detecting and predicting craving in real time remains a challenge, particularly given its highly individualized and dynamic nature (Ellis et al., 2022; Joos et al., 2013; Kruschwitz et al., 2019; Preston et al., 2018). Building on previous lab-based research, passive monitoring of HRV through biosensors offers a promising avenue for craving detection, though the real-world applicability has yet been explored. By integrating wearable technology with EMA, the current study aimed to establish a feasible method for monitoring craving through HRV in a naturalistic setting, which could ultimately inform the development of JIT interventions to enhance addiction treatment outcomes. Multilevel modeling was used to test hypothesized associations of within- and between-person indicators of HRV and craving among those in the first year of an AUD recovery attempt. The results suggested that momentary craving was associated with acute changes in HF-HRV and that it is potentially feasible to use ambulatory methods to detect craving passively in the natural environment. Below the findings are discussed with respect to the theoretical rationale and empirical research that formed the hypotheses.

Consistent with our hypotheses, higher-than-average levels of HF-HRV were positively associated with greater craving in the same moment. This finding aligns with previous laboratory research, in which craving was found to be positively associated with increased HF-HRV for both individuals with AUD in short-term abstinence (less than one month post-treatment either from hospitalization or outpatient) and long-term abstinence (6 months to 15 years post-treatment) from alcohol (Claisse et al., 2017). In this and similar lab-based studies, craving and emotion regulation have been examined using emotionally evocative stimuli within emotion induction procedures—however, most of these have been limited to stress- and/or craving-related cues (Bresin et al., 2018; Claisse et al., 2017; Fox et al., 2007). The pattern of effects found in the present study extends this previous work to following those in early AUD recovery after treatment and to an ambulatory measurement approach, capturing complex affective processes that may influence craving beyond lab induction procedures. HF-HRV is considered a marker of parasympathetic activity (Bertsch et al., 2012) which is linked to heightened attention and improved cognitive performance, potentially leading to increased focus and concentration that underlies self-regulation (Barber et al., 2020). This would align with contemporary models of craving that suggest that craving is not merely a conditioned response but involves higher-order cognitive and emotional processes, consistent with the operationalization of craving as a multidimensional construct that engages both automatic and controlled processes (Marlatt, 1985; M. D. Skinner & Aubin, 2010; West & Brown, 2013). Further, research on the central autonomic network (CAN) suggests that HRV is a dynamic marker of interactions between physiological arousal and self-regulatory processes (Shaffer & Ginsberg, 2017; Wascher, 2021). The increase in HF-HRV observed during craving moments may reflect attempts to regulate affective and physiological responses in response to urges or stimuli that invoke cravings. Relatedly, emerging research has found that HF-HRV is associated with increased self-reported affiliation feelings toward an in-group, suggesting that parasympathetic activity may facilitate social adaptability and a drive toward connection. Given that craving is inherently linked to a motivational state of seeking, it is possible that the observed HF-HRV increases reflect an underlying mechanism tied to affiliation-related processes (Sahdra et al., 2015). This aligns with cue-reactivity research, which has demonstrated that HRV increases when individuals exert effort to suppress or manage craving-related thoughts and emotions (Carter & Tiffany, 2002; Eddie et al., 2015). Taken together, there is growing evidence to substantiate the theory suggesting that craving involves not only physiological and affective elements but also broader social and cognitive dimensions.

Despite finding significant associations between craving and HF-HRV, other indicators of HRV (i.e., RMSSD, pNN50, PNS index, and SD1) did not exhibit significant same moment associations with craving. This is consistent with the current literature, where these HRV metrics show inconsistent relationships with craving across different samples and methodological approaches (Claisse et al., 2017; Eddie et al., 2023; Quintana et al., 2013; Ralevski et al., 2019) and in some cases (e.g., PNS index, SD1) are not included in the analyses (Claisse et al., 2017; Ralevski et al., 2019). Null or mixed findings from HRV indices may be due to numerous factors such as individual variability in autonomic reactivity (Ottaviani et al., 2008), the transient nature of craving (Drummond et al., 2000), and complexities surrounding HRV measurement that are magnified in biobehavioral research by influence of extraneous factors such as respiratory patterns and circadian rhythms (Quintana & Heathers, 2014). Notably, research has suggested that withdrawal-related autonomic dysregulation may alter HRV-craving associations over time. For instance, reductions in parasympathetic activity during early withdrawal have been linked to increased craving severity (Claisse et al., 2017; Ralevski et al., 2019). These findings suggest that HRV-craving relationships may shift dynamically across different stages of recovery. Importantly, the models presented here did not test if this varies by time in recovery which might have contributed to the null findings. Future research might benefit from a more homogeneous sample in terms of time in recovery to control for these differences or test if these associations vary as a function of recovery time. Given that craving is influenced by both state- and trait-level factors, disentangling these effects using EMA and multilevel modeling is critical to advancing our understanding of real-time craving regulation.

At the between-person level, person-average HF-HRV was not significantly associated with person-average levels of craving during the sampling period, though the relationship was in the hypothesized inverse direction. This finding aligns with research emphasizing craving as a dynamic construct influenced by individual differences in autonomic regulation (Verheul et al., 1999). Additionally, prior research has indicated that higher trait HF-HRV is linked to better emotional regulation and reduced vulnerability to substance-related cues (Claisse et al., 2017; Simplicio et al., 2012). This may be due to individuals with greater trait-level parasympathetic tone exhibiting more adaptive coping strategies, which would reduce the impact of craving on behavior. Conversely, those with chronically lower HF-HRV may experience greater difficulty in modulating physiological and emotional responses, heightening susceptibility to craving-related distress. Coupled with the momentary association between HF-HRV and craving, these findings suggest that while momentary increases in HF-HRV may reflect active regulatory efforts during craving episodes, lower overall parasympathetic activity may contribute to a heightened baseline risk of craving, which may render current gold standard treatment for AUD (i.e., cognitive-behavior therapy) not as effective for certain individuals. Furthermore, motivational models highlight that craving is shaped by both approach and avoidance motivational pathways (M. D. Skinner & Aubin, 2010). Individuals with lower trait-level parasympathetic activity may have greater difficulty engaging in self-regulatory efforts to mitigate craving, making them more susceptible to persistent or intense urges. These findings underscore the importance of considering multiple physiological markers when evaluating craving-related autonomic processes. Given that HF-HRV is particularly linked to parasympathetic function, this study provides further support for its role in craving regulation, reinforcing its potential as a biomarker for real-time craving detection.

Interestingly, the person-average PNS index was inversely associated with craving, indicating that lower levels of parasympathetic cardiac activity were linked to higher average craving levels throughout the sampling period. PNS index reflects the degree of parasympathetic influence on cardiac function and autonomic regulation (Shaffer & Ginsberg, 2017). In other words, a lower PNS index suggests reduced parasympathetic influence, which may indicate autonomic dysregulation, heightened stress sensitivity, or difficulties in emotional and behavioral regulation—factors that could contribute to increased craving in individuals with AUD. Furthermore, lower parasympathetic cardiac control has been associated with greater impulsivity (Allen et al., 2000), which may explain why individuals with diminished HF-HRV exhibit greater vulnerability to craving and relapse (Claisse et al., 2017). Moreover, research has demonstrated that individuals with SUDs, including AUD, often exhibit dysregulated autonomic functioning, characterized by lower resting HF-HRV and PNS activity compared to healthy controls (Ingjaldsson et al., 2003; Quintana et al., 2013). While LF-HRV and HF-HRV have been widely used as primary indicators of autonomic function, concerns have emerged regarding their validity as distinct measures of sympathetic and parasympathetic activity, with evidence suggesting that both branches of the autonomic nervous system contribute to LF and HF components of HRV (Billman, 2013; Montano et al., 1994; Pagani et al., 1997). Despite these critiques, LF-HRV and HF-HRV remain the de facto measures in stress research, often excluding more direct assessments of PNS function. However, the current study incorporates the PNS index as a more targeted measure of parasympathetic activity, offering a novel approach that may help clarify inconsistencies in previous HRV-craving research. By directly assessing parasympathetic function, this study provides additional evidence that lower parasympathetic regulation is linked to heightened craving experiences in AUD, reinforcing the role of autonomic regulation in substance use behaviors. Furthermore, though many HRV indices are derived from overlapping metrics that assess autonomic function through different mathematical models (Shaffer & Ginsberg, 2017), it is important to note that, as evidenced by the differences in the effects in the regression model, HF-HRV only exhibited a significant association when controlling for the other indicators. This may suggest that although these indices are similar, there is still a need to include them in prediction models, as they may provide distinct effects, whereas previous research has often neglected to account for this (e.g., Claisse et al., 2017; Ingjaldsson et al., 2003; Quintana et al., 2013; Ralevski et al., 2019). Future research should build upon this approach by integrating comprehensive autonomic assessments, including the PNS index, to further elucidate the physiological mechanisms underlying craving and self-regulation in addiction.

Moreover, the observed discordance between within- and between-person effects on HRV mirrors patterns commonly found in affect research, where associations at one level of analysis do not necessarily generalize to another, a phenomenon more commonly known as Simpson's paradox (Kievit et al., 2013). This similarity reinforces the conceptualization of craving as an affective state (M. D. Skinner & Aubin, 2010), influenced by dynamic regulatory processes that operate differently across within- and between-person levels. The fact that momentary increases in HF-HRV are linked to craving at the within-person level, while lower trait-like parasympathetic activity is associated with higher craving at the between-person level, underscores the importance of distinguishing between state- and trait-level influences on autonomic regulation in addiction. Future research should continue to integrate multilevel modeling approaches to disentangle these effects, ensuring that findings are accurately interpreted within their respective levels of analysis.

This study provides valuable insights into the role of ambulatory HRV monitoring in real-time craving detection, highlighting its potential for integration into addiction treatment frameworks. A key strength of the study is its use of ambulatory assessment, which enhances ecological validity by capturing craving experiences as they occur in naturalistic settings. This approach reduces participant burden with common retrospective self-reports, as craving dynamics are difficult to continuously monitor and report in an ambulatory context (Sayette et al., 2000). Additionally, the integration of physiological measures with EMA bridges the gap between subjective craving experiences and objective biomarkers, and potentially lead to the development of early warning systems that can detect heightened craving states and trigger timely interventions. The use of multilevel modeling allows for a more nuanced understanding of HRV-craving associations by accounting for within- and between-person variability, providing deeper insights into the complex relationship between these constructs. Lastly, this study is one of few to incorporate numerous indices of HRV, such as PNS index and SD1, which have not been incorporated in previous research. Based on our finding that the PNS index may contribute distinct variance to craving at the between-level, it would be remiss to exclude this index (and potentially others) of HRV in future studies.

However, several limitations must be considered. First, although the EMA methods allow for examining both within- and between-person effects to test our hypotheses, some effects might not have been detectable with the current sample. According to our power analyses, we are powered to detect small effects at both levels (i.e., $\beta$ = 0.05-0.30; (Cohen, 1992). Successful replication of these findings across multiple samples would strengthen the generalizability of our results, indicating that the identified HRV-craving relationship holds across different populations and contexts. This would pave the way for larger-scale studies and cross-validation efforts, further solidifying the role of HRV in craving detection. Second, some researchers have suggested that using absolute (e.g., "extremely") versus relative (e.g., "the strongest urge I have ever experienced") anchor-point labels for craving items may lead to differences in self-reports of craving depending on individual interpretation (Sayette et al., 2000). Third, having a single-item craving measure may inadequately capture the various semantic dimensions of craving that individuals may use to describe their anecdotal experiences (Tiffany & Drobes, 1991). Despite these criticisms, previous research shows a single item with absolute anchors exhibits strong criterion validity (Ramirez & Miranda, 2014). Lastly, while the temporal patterning is a significant strength compared to cross-sectional research, it should not be construed as causal as there is not an experimental manipulation. However, as with all research, there is a tradeoff between experimenter control and external validity.

Looking ahead, subsequent research could focus on refining the algorithms used for detecting cravings, integrating them into mobile health applications or wearable devices, and exploring the potential of combining HRV data with other physiological or behavioral markers to enhance detection accuracy. Our findings suggest that previously overlooked HRV indices may play a more significant role than initially thought—coupled with ongoing debates about traditional HRV metrics, alternative approaches like the Classification Angle (ClassA) framework may offer a more precise method for capturing autonomic dynamics without relying on contested assumptions of LF/HF balance (Adjei et al., 2019). This multidimensional approach has demonstrated greater sensitivity in distinguishing stress states by using a finite-difference plot of HRV, which displays successive rates of change in HRV. This method holds important implications for stress analysis and, by transitive property, may enhance real-time craving detection, though further research is needed to substantiate this claim. Given emerging evidence that HRV can predict subsequent alcohol use in individuals in early recovery (Eddie et al., 2023), further research should explore its potential as a marker not only for craving detection but also for identifying those at heightened risk for relapse. Additionally, investigating lagged effects, such as whether HRV at one timepoint can predict craving at the next, could explore the temporal relationship between HRV and craving. With more frequent experience sampling surveys, future studies could better determine the prospective effects. Ultimately, if our findings are consistently replicated, there may be a paradigm shift in how cravings are managed in current treatment models. Specifically, advancing our ability to precisely and promptly address craving through real-time, personalized interventions could become a cornerstone of effective addiction treatment and mental health support, potentially reduce the staggering rates of relapse and associated consequences for those in early recovery.

This study is a meaningful step toward establishing HRV as a viable biosignature for craving detection in individuals undergoing early recovery from AUD. Based on the results, there are complexities in HRV-craving relationships across different levels of analysis, such that the within-person and between-person associations between various HRV indices and craving exhibit paradoxical relationships. Furthermore, this study established the feasibility of wearable and affordable biosensors for ambulatory HRV monitoring of craving, underscoring the potential integration of passive sensing into addiction treatment. Ultimately, advancing our ability to detect and intervene upon craving states in real-time could improve addiction treatment by enhancing precision and personalization in recovery support strategies.

## References


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