EMOTIONAL REGULATION AND MOTIVATION TO DRINK: GENDER, NEGATIVE EMOTIONALITY, BEHAVIORAL UNDERCONTROL, AND FAMILY HISTORY

By

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ABSTRACT OF THE DISSERTATION

Emotional Regulation and Motivation to Drink: Gender, Negative Emotionality, Behavioral Undercontrol, and Family History

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Despite support for the effectiveness of alcohol use disorders (AUD) treatment programs and the positive impact of policy changes related to alcohol use, AUD remains a major public health concern in the United States. As part of an effort to encourage transdisciplinary research, the integration of objective biological measures for AUD risk and existing psychosocial-based risk measures (e.g., demographic variables, personality characteristics, comorbid psychological disorders) are emerging as important areas of inquiry, with implications for the prevention and treatment of AUD. Theories of alcohol use emphasize the fundamental role of emotional regulation in drinking behaviors, and multiple psychosocial factors have been identified which influence such motivations for alcohol use. Through three separate, laboratory-based experimental investigations, this dissertation aimed to gain an understanding of the physiological mechanisms underlying the relationship between psychosocial factors (gender, personality, family history) and one’s desire to use alcohol for emotional regulation. In particular, this dissertation focused on examining the applicability of heart rate variability (HRV), an established psychophysiological measure of peripheral and central modulation of emotional arousal,
in studying individual differences in emotional regulation. Changes in HRV in response to experimental manipulation of emotion and adaptive responding were linked to gender and personality differences in motivations for alcohol use. Gender differences in emotional reactivity suggest distinctive pathways toward unhealthy use of alcohol in men and women; that is, the pharmacological effects of alcohol appear to directly promote alcohol use in men, whereas cognitive expectancies, such as expectation that alcohol can counteract negative emotions, may underlie alcohol use in women, particularly when they are prone to negative mood states. Further, personality constructs of negative emotionality were associated with physiological dysregulation of emotion, which was linked to tendency to use alcohol for emotional regulation, particularly to suppress negative emotion. As a future direction, identification of malleable biological markers and the translation of these findings into clinical practices may help to better identify individuals at risk and suggest a novel approach for preventing or intervening in the development of AUD, which may in turn contribute to population health.
PREFACE

This dissertation is a culmination of over five years of my work as a graduate assistant in Dr. Marsha E. Bates’ laboratory. The data used in the first study, “Gender Differences in Acute Alcohol Effects on Self-Regulation of Arousal in Response to Emotional and Alcohol-related Picture Cues,” was collected as part of a pilot study for two main projects conducted by Dr. Bates. With collaboration and assistance from senior researchers in the lab, I played a major role in the development of a study protocol and data collection for the pilot study. The results of this pilot study helped us refine the research designs and protocols for both parent studies, during which my contribution included, among many other things, recreating picture stimulus sets based on the subjective ratings of pictures collected during the pilot study, modification and development of additional alcohol-, marijuana-, and polydrug-related picture stimuli, and development of several additional questionnaires.

After completing a Masters degree, my academic training shifted from the Behavioral Neuroscience Program in Psychology Department, Rutgers University, to Health Education and Behavioral Science at University of Medicine and Dentistry of New Jersey (UMDNJ), the School of Public Health (SPH). Meanwhile, I was retained as a research assistant in Dr. Bates’ lab working on two research initiatives simultaneously. In addition to recruiting participants (i.e., conducting initial phone and family history interviews) and assisting with experimental sessions on a daily-basis for both studies, my role in the projects became more centered on data management and project coordination as they both moved forward. Data management involved modification of SAS programs, data cleaning, and manipulation of collected data upon the request of study investigators.
Furthermore, I was integral to the analysis of data in preparation for publications, progress reports, and grant applications. My responsibility as a project coordinator involved training undergraduates and new research assistants, and communicating with other collaborating researchers and staff at the addiction treatment facility.

The main objectives of the two projects were formulated around the connection between memory processes and emotional regulation as measured by psychophysiological response to emotional stimuli. My research interest during my early years of graduate training was on the role of stress in motivating an individual to use alcohol. Accordingly, my master’s research focused on understanding the relationships between alcohol use for coping reasons, stress vulnerability, and the stress dampening response of alcohol. Shortly after starting my education at SPH – UMDNJ, I further refined research projects and objectives that were independent of the research questions of the two parent projects. Based on previous evidence on gender differences in alcohol use behavior and in response to stress, I first became interested in investigating whether alcohol affected emotional arousal response differentially by gender in the initial pilot study. Then, together with independently learning about motivation for alcohol use from the literature and research experience with Dr. Patrick R Clifford at SPH – UMDNJ on psychosocial functioning in AUD treatment outcomes, my research interests gradually expanded toward understanding the underlying mechanisms of how global psychosocial factors might influence an individual’s motivation to use alcohol and alcohol use behaviors. In particular, I became interested in understanding the factors associated with alcohol use to enhance positive emotion and to suppress negative emotion, which became the basis for the research questions posed in the second study, “Emotional Regulation and
Alcohol Use: Behavioral Undercontrol, Negative Emotionality, and Gender,” and the third study, “Latent Class Analysis of Risk for Alcohol Use: Integration of Psychophysiological and Psychosocial Factors.”
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I would like to give special thanks to Dr. Marsha E. Bates for allowing me the opportunity to work for her, especially when I showed up in her office without an appointment over five years ago. Marsha, I can’t express in words how much I have appreciated and enjoyed working with you. I also would like to thank Dr. Patrick R. Clifford for his guidance and support during my years in UMDNJ. Pat, your passion for research and student mentoring have taught me about the importance of critical thinking in science, and showed me an example of enthusiastic mentoring. I will miss having
hours of conversation in your office. I would also like to thank all the members of Dr. Bate’s laboratory. Drs. Bronya and Evgeny Vaschillo, without your warm smiles and incredible talent, this dissertation would not exist. Dr. Paul Lehrer, all of our discussions and debates during the weekly laboratory meetings have given me many hints to develop my research questions. You have also given me incredibly caring and generous feedback on my work. I would also like to give special thanks to Dr. Jennifer Buckman, and Dr. Eun-Young Mun, both at the Center of Alcohol Studies, for their kind support through my graduate school years, ranging from simply listening to me, to reviewing my work, to much needed career advice. You two were another reason I felt very fortunate to work at the center. Finally, I would like to thank Drs. Nancy Fiedler and Shou-En Lu, who were part of my dissertation committee, for their valuable guidance.

I dedicate the work to my wonderful husband, Morgan. Your close-to-infinite patience for my complaining about life helped keep me sane. I hope that I can do the same for you when you go through this process a few years from now. I also dedicate this dissertation to my family in Japan, who bravely sent me off to the U.S. eight years ago, for their support, encouragement, and love throughout all these years. You never stopped believing in me. I miss you always.
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CHAPTER 1
INTRODUCTION TO THE DISSERTATION

Background

Alcohol Use Disorders as a Public Health Problem

Alcohol related problems represent a major public health concern in the United States. *Healthy People 2010* (U.S. Department of Health and Human Services, 2000) identifies substance use, which includes alcohol, as one of the leading health indicators. Research supports the effectiveness of alcohol use disorders (AUD) treatment programs, at least in the short-term (see Fuller & Hiller-Sturmhofel, 1999; Miller, Walters, & Bennett, 2001 for reviews), and the positive effect of policy changes related to alcohol use (e.g., increasing the legal drinking age and lowering the legal definition of blood alcohol concentration for driving while intoxicated) (Fell, Fisher, Voas, Blackman, & Tippetts, 2007; Toomey, Lenk, & Wagenaar, 2007; Voas, Tippetts, & Fell, 2003; Wagenaar, Maldonado-Molina, Ma, Tobler, & Komro, 2007) in reducing alcohol-related problems in the United States. However, the most recent data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) suggest that 17.5 million individuals reported symptoms of AUD during 2001-2002, and that the prevalence of AUD increased over the 10 year study period, from 7.41% to 8.46% (Grant, Dawson, et al., 2004; Grant, Peterson, Dawson, & Chou, 1994). Thus, despite continuing clinical and political effort to reduce AUD, alcohol related problems remain a persistent public health problem in the United States (Grant, Dawson, et al., 2004; Grant, et al., 1994).
AUD reflects a multidimensional disorder that can affect an individual’s physical and psychosocial functioning (Bonin, McCreary, & Sadava, 2000; Colder & Chassin, 1999), and clinical symptoms vary among individuals. Traditionally, risk assessment research emphasized clinical symptoms and sociodemographic factors, such as age of AUD onset, family history, comorbid psychiatric disorders, and gender, in capturing the heterogeneity of AUD (e.g., Babor, et al., 1992; Epstein, Labouvie, McCrady, Jensen, & Hayaki, 2002; Litt, Babor, DelBoca, Kadden, & Cooney, 1992). Attempting to incorporate the heterogeneity of clinical symptoms into clinical practice, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) conducted a large-scale multi-site experiment, Matching Alcoholism Treatments to Client Heterogeneity (Project MATCH) study, to examine whether matching patient characteristics and treatment types improved AUD treatment outcomes (Project MATCH, 1993). Contrary to their prediction, the study resulted in only limited evidence for the interaction between client attributes and treatment modality on drinking outcomes (Project MATCH, 1997). The results of the MATCH study contributed to a shift in focus of AUD treatment research toward an understanding of the purported mechanisms of action (i.e., active ingredients) that underlie AUD interventions (Kazdin & Nock, 2003; Kendler, 2005; Longabaugh, et al., 2005). To reflect the shift in main research questions of the field, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) has began strongly encouraging transdisciplinary research (Huebner & Tonigan, 2007). In this regard, investigations involving the integration of objective biological measures of AUD risks and existing psychosocial-based risk measures (e.g., demographic variables, personality characteristics, comorbid psychological disorders) are emerging as important areas of

**Potential Utility of Heart Rate Variability as Biological Marker of Risks for AUD**

The present dissertation focused on characterizing autonomic regulation of emotion arousal as a potential biological maker for AUD risks. How we regulate emotion has profound effects on our physical and mental well-being (Giardino, Lehrer, & Feldman, 2000; Gross, 1998, 2002). The manner in which individuals regulate their emotions vary significantly and some individuals use alcohol to regulate emotion (Cooper, Frone, Russell, & Mudar, 1995; Cox & Klinger, 1988a; Wills & Shiffman, 1985). Recent theories of emotion regulation emphasize the interplay of peripheral arousal modulation by the autonomic nervous system (ANS) and central modulation by the central autonomic network (CAN) (Appelhans & Luecken, 2006; Thayer & Lane, 2000). When facing environmental challenges, the ANS regulates emotion via a general arousal response, such as increase in heart rate, skin conductance, and respiration rate that prepares an organism for action (Iversen, Kupfermann, & Kandel, 2000). This general arousal response by the ANS is in turn projected to brain stem structures that are part of the central autonomic network, where autonomic, neuroendocrine, and behavioral responses are integrated by sending signals back to peripheral organs and forward to frontal and limbic structures that modulate emotion (Benarroch, 1993). As such, emotion regulation is partly determined by an individual’s ability to modulate their emotional arousal through the ANS and CAN.

The primary output of the CAN influences the sino-atrial node through the sympathetic and parasympathetic nervous systems of the ANS (Appelhans & Luecken,
The interplay of SNS and PNS inputs to the sino-atrial node produces complex changes in heart rate (HR) (Thayer & Lane, 2000), which can be measured by heart rate variability (HRV) (Berntson, et al., 1997). In the field of medicine, indices of HRV have been used to predict health status in areas as diverse as cardiovascular mortality (Chattipakorn, Incharoen, Kanlop, & Chattipakorn, 2007; Schmidt, et al., 2005; Stein, et al., 2006; Thayer & Lane, 2007), infant developmental outcomes and health (DiPietro, Bornstein, Hahn, Costigan, & Achy-Brou, 2007; Griffin, et al., 2005; Rosenstock, Cassuto, & Zmora, 1999), and vulnerability to stress (Giardino, et al., 2000).

Furthermore, given the function of the ANS and CAN, HRV also has been used as an index of emotion regulation (Porges, 1991; Porges, Doussard-Roosevelt, & Maita, 1994), as well as a biological marker of emotion dysregulation in individuals with disorders such as depression (Nahshoni, et al., 2004), anxiety (Friedman & Thayer, 1998; Thayer, Friedman, & Borkovec, 1996), and posttraumatic disorder (Cohen, et al., 2000).

Some studies use resting-state HRV to characterize differences between individuals with and without illness, although HRV also may be assessed dynamically to capture within-individual changes in response to experimental manipulations (Butler, Wilhelm, & Gross, 2006). Although both resting-state and reactivity HRV measures represent one’s ability to regulate emotions, the present study focuses on HRV as a measure of emotion reactivity. This dissertation primarily focused on a 0.1-hertz (Hz) HRV index to describe individual differences in emotional reactivity and adaptability to the environment. We designed the experiment specifically to present experimental stimuli every 10 seconds (i.e., 0.1 Hz frequency), which corresponds with the resonance frequency of the cardiovascular system. Stimulation of the cardiovascular system at its
resonance frequency of 0.1 Hz by an internal stimulus (e.g., breathing) or external stimuli (e.g., picture presentation) has been shown to induce high amplitude HR oscillations (Song & Lehrer, 2003; Vaschillo, Vaschillo, & Lehrer, 2004; Vaschillo, et al., 2008). Strong HR oscillation at 0.1 Hz has suggested reflecting baroreflex activation, which is an important reflexive process that stabilizes blood pressure (Vaschillo, Lehrer, Rishe, & Konstantinov, 2002; Vaschillo, Vaschillo, & Lehrer, 2006a) and controls cortical arousal (Dworkin, et al., 1994; Elbert, Roberts, Lutzenberger, & Birbaumer, 1992; Nyklicek, Wijnen, & Rau, 2005; Rau, Pauli, Brody, Elbert, & Birbaumer, 1993; Yasumasu, Reyes Del Paso, Takahara, & Nakashima, 2006). Thus, the combination of stimulus presentation at 0.1 Hz and assessing the amplitude of HR oscillation at 0.1 Hz allows an assessment of individual differences in (1) moment-to-moment emotional reactivity to various external interventions (Nickel & Nachreiner, 2003), and (2) an adaptive modulation of arousal by baroreflex (Cevese, Gulli, Polati, Gotti, & Grasso, 2001).

This dissertation specifically focused on examining the applicability of the 0.1-Hz HRV index as an indicator of emotional reactivity. We previously demonstrated the utility of the 0.1-Hz HRV index in characterizing emotional reactivity to picture cues, and responses to the pharmacological and cognitive effects of alcohol as measured by placebo response through comparing with other traditional HRV measures (standard deviation of the all normal-to-normal [NN] intervals [SDNN], high-frequency [HF] HRV, mean HR, and pNN50 [percentage derived by the number of interval differences of successive NN intervals greater than 50 milliseconds divided by the total number of NN intervals multiplied by 100]) (Vaschillo, et al., 2008). As will be further demonstrated in each study, this dissertation aimed to extend the use of this unique HRV index as a
biological marker of emotional reactivity that is associated with risk factors for AUD, including gender, personality, and family history. The dissertation further examined how differences in the patterns of emotional reactivity described by these factors may lead to different motivations for drinking and subsequent alcohol use.

**Understanding the Interplay of Multiple Risk Factors for Alcohol Use Disorders**

Theories of addiction have emphasized the fundamental role of the desire to regulate both positive and negative emotion in motivating an individual to use alcohol (Cooper, et al., 1995; Cox & Klinger, 1988a; Koob & Le Moal, 2001; Wills & Shiffman, 1985). Empirical studies have commonly identified three distinctive reasons for drinking among individuals who differ in personal history of alcohol use: negative affect suppression or emotion coping, social enhancement or sociability, and positive affect enhancement/disinhibition (Labouvie & Bates, 2002). An individual’s tendency for drinking to either enhance positive emotion or suppress negative emotion is believed to be partly determined by sensitivity to the specific reinforcing effects of alcohol. Alcohol is found to enhance pleasurable feelings during the ascending limb of the blood alcohol concentration curve (Brunelle, Barrett, & Pihl, 2007; Corbin, Gearhardt, & Fromme, 2008; Newlin & Thomson, 1990b), and heightened sensitivity to such stimulant effects has been linked to greater alcohol use (Holdstock, King, & de Wit, 2000; King, Houle, de Wit, Holdstock, & Schuster, 2002). On the other hand, when combined with stress or negative emotion, alcohol has been shown to suppress the stress response and feelings of anxiety, which have been described as a sedative or anxiolytic effect (e.g., Dai, Thavundayil, Santella, & Gianoulakis, 2007; de Wit, Soderpalm, Nikolayev, & Young, 2003; Sher, Bartholow, Peuser, Erickson, & Wood, 2007; Zimmermann, et al., 2004).
Further, the relationship between sensitivity to the specific reinforcing effects of alcohol and motivation for drinking may be influenced by the interplay of multiple factors, including sociodemographic factors (e.g., age, gender) and psychosocial factors (e.g., personality, mood, cognitive function, family and peer influence).

Gender is one factor that might moderate the relationship between motivation to drink and pattern of alcohol use, such that men may be more likely than women to report using alcohol to cope with stress (Frone, Cooper, & Russell, 1994; San Jose, van Oers, van de Mheen, Garretsen, & Mackenbach, 2000). Despite frequently observed gender differences in patterns of alcohol use and reasons for drinking, underlying mechanisms have not been extensively studied. It is possible that alcohol has differential pharmacological and/or cognitive effects on men and women such that men may be more susceptible to the arousal dampening effects of alcohol than women. Previous studies often have excluded female participants, thus only a few studies have examined gender as a potential moderator of the dampening effects of alcohol within the context of stress response, and study results have been mixed (Croissant, Rist, Demmel, & Olbrich, 2006; Hoaken, Campbell, Stewart, & Pihl, 2003; Levenson, Oyama, & Meek, 1987; Sinha, Robinson, & O'Malley, 1998). Therefore, further investigations of the potential gender specific differential dampening effects regarding the regulation of emotion arousal seems warranted.

Personality traits such as negative emotionality and behavioral undercontrol are also considered important in understanding the etiology of alcohol use (Cooper, et al., 1995; Cox & Klinger, 1988a; Wills & Shiffman, 1985), and for subtyping individuals with AUD (Babor, et al., 1992; Cloninger, 1987; Zucker, 1986). Negative emotionality is
characterized by a tendency to experience a significant level of stress and negative affect irrespective of the situation, including depressed mood, anger, and anxiety (Watson & Clark, 1984). Individuals with high negative emotionality have difficulties with emotion regulation, are sensitive to the stress response dampening effects of alcohol, and thus are more likely to use alcohol to cope with stress (Conger, 1956). On the other hand, behavioral undercontrol is often operationalized by personality constructs such as impulsivity, antisociality, aggressiveness, and sensation seeking (Martin, Lynch, Pollock, & Clark, 2000). Individuals high in behavioral undercontrol are disinhibited, focused on immediate reward goals, and unable to foresee the negative consequences of seeking immediate rewards, such as hangovers from binge drinking (Colder & Chassin, 1997). In addition, gender differences have been found such that women exhibit fewer components of behavioral undercontrol such as sensation seeking traits, antisocial personality, and aggressiveness than men (Martin, et al., 2000; Nolen-Hoeksema, 2004) and greater negative emotionality such as higher levels of depressive symptoms (Alfeld-Liro & Sigelman, 1998; Chaplin, 2006; Hankin, et al., 1998). Therefore, examining whether these personality traits have distinctive influences on emotional reactivity in men and women may be important for understanding gender differences in alcohol use.

Finally, family history has been shown to affect AUD risks. Epidemiological data suggest that, in individuals with a family history of AUD relative to those without a family history of AUD, the likelihood of alcohol dependence is increased 45% among individuals who have a second or third degree relative with a current or past AUD, 68% among individuals with a first degree relative with a current or past AUD, and 167% among those with a multi-generational family history (Dawson, Harford, & Grant, 1992).
A family history of AUD also may influence an individual’s motivation to use alcohol (e.g., greater positive alcohol outcome expectancies relative to those with a negative family history) (Brown, Tate, Vik, Haas, & Aarons, 1999; Pastor & Evans, 2003; Wiers, Hartgers, van den Brink, Gunning, & Sergeant, 2000). Similar to AUD, increased risk of developing AUD also has shown in a positive family history of other drug use disorders (Merikangas, et al., 1998; Nurnberger, et al., 2004). In addition, a positive family history of depression increases risk for a mood disorder (Maes, Silberg, Neale, & Eaves, 2007), and risk for AUD (Merikangas, Leckman, Prusoff, Pauls, & Weissman, 1985; Stallings, et al., 1997). Considering the relationships between personality traits and alcohol use, having a positive history of AUD, depression, or other drug use disorders may strongly influence an individual’s motivation for drinking. However, it is not clear how negative emotionality and behavioral undercontrol interact with a family history of these disorders, to affect motivation for alcohol use, or the ability to regulate emotion and alcohol use behaviors. Thus, this dissertation also investigated the impact of family history on emotion regulation, reasons for drinking, and drinking patterns.

**Primary Goal of the Dissertation**

In summary, these findings suggest the contribution of gender, personality, and family history and their interactions in determining an individual’s motivation to drink and subsequent alcohol use. However, little is known about physiological mechanisms underlying the relationships between psychosocial risks factors and one’s desire to either suppress or enhance emotion despite the conceptual and empirical support for the fundamental role of emotional regulation in alcohol use. Therefore, the primary purpose of this dissertation was to examine the utility of HRV, particularly a 0.1-Hz HRV index,
in understanding how gender, personality, and family history can influence emotional regulation in young adults who vary in risk for AUD, and how these differences in emotional regulation may influence motivations for alcohol use. This dissertation consists of three manuscripts that were or will be submitted for peer-reviewed scientific journals for publication consideration. Briefly, Study 1 examines gender differences in the effects of alcohol on arousal response. Study 1 has been published in *Psychology of Addictive Behaviors* for publication. Study 2 examines how behavioral undercontrol and negative emotionality influence alcohol use in an attempt to further understand how individual differences in emotion regulation affect motivation for alcohol use. Finally, Study 3 examines the involvement of emotional regulatory systems in motivating alcohol use behaviors, using a multivariate, person-centered statistical approach that affords the integration of psychological constructs and familial history of psychopathology.

**Data Source**

All data to be used in this dissertation were collected as part of two on-going research projects supported by the National Institutes of Health (PI: M E. Bates), and conducted at the Center of Alcohol Studies – Rutgers, The State University of New Jersey (see Appendix A for detailed methods of Parent Studies 1 and 2). The data for Study 1 were collected as part of a pilot study specific to Parent Studies 1 and 2. Both parent study protocols and the protocol for Study 1 were approved by the Institutional Review Board (IRB) for the Protection of Human Subjects Involved in Research at Rutgers University. The UMDNJ IRB office stated that because UMDNJ was not a study site for either parent study, UMDNJ-IRB approval was not required for the research involved in this dissertation.
References


CHAPTER 2

STUDY 1

Gender Differences in Acute Alcohol Effects on Self-Regulation of Arousal in Response to Emotional and Alcohol-related Picture Cues

by

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Abstract

Basic mechanisms through which men and women self-regulate arousal have received little attention in human experimental addiction research although stress-response-dampening and craving theories suggest an important role of emotional arousal in motivating alcohol use. This study examined gender differences in the effects of acute alcohol intoxication on psychophysiological and self-reported arousal in response to emotionally negative, positive, and neutral, and alcohol-related, picture cues. Thirty-six social drinkers (16 women) were randomly assigned to an alcohol, placebo, or control beverage group, and exposed to picture cues every 10 s (0.1 Hz presentation frequency). Psychophysiological arousal was assessed via a 0.1-Hz heart rate variability (HRV) index. A statistically significant beverage group-by-gender interaction effect on psychophysiological, but not self-reported, arousal was found. 0.1-Hz HRV responses to picture cues were suppressed by alcohol only in men. This gender-specific suppression pattern did not differ significantly across picture cue types. There were no significant gender differences in the placebo or control group. Greater dampening of arousal by alcohol intoxication in men, compared to women, may contribute to men’s greater tendency to use alcohol to cope with stress.
Introduction

Individual differences in the self-regulation of arousal and attendant emotional experience have profound effects across the lifespan on many aspects of physical and psychological health (Appelhans & Luecken, 2006; Giardino, et al., 2000). Not surprisingly, several fundamental, yet distinct research questions in the addictions literature share a common focus on better understanding mechanisms that support self-regulation of arousal, and individual differences that influence emotional regulatory systems. For example, since Conger (1956) first proposed a stress-response dampening (SRD) theory, the dampening effects of alcohol on negative emotional arousal have been hypothesized to explain drinking behavior motivated by the desire to cope with stressful emotional states. Similarly, theories of craving implicate physiological arousal in response to appetitive environmental cues as playing a role in eliciting drug seeking behaviors and in contributing to relapse (Carter & Tiffany, 1999; Tiffany, 1995). There are multiple systems involved in regulation of emotion. The autonomic nervous system (ANS) components of emotion serve a preparatory function, which involves general arousal that prepares an organism as a whole for action (e.g., increase in heart rate), and specific arousal that prepares the organism for a particular behavior (e.g., fleeing from danger, lighting a cigarette) (Iversen, et al., 2000). Together with endocrine response and cortical processing of salient environmental stimuli, individual differences in ANS arousal and its modulation contribute to the experience of emotional states that are relevant to understanding both SRD and craving. The focus of this study was on a basic psychophysiological mechanism that supports self-regulation of arousal in real-time in response to emotional and alcohol cues in the environment, how this mechanism is
affected by alcohol intoxication, and how alcohol effects on arousal may conceivably play a role in differentially motivating alcohol consumption in men and women.

**Alcohol Intoxication and Dampening of Arousal**

Much research has examined how alcohol modifies emotional experience that is stressful in nature. Alcohol intoxication has been shown to affect psychophysiological indicators of emotional arousal by dampening increases in autonomic nervous system (ANS) reactivity, such as heart rate (HR) and galvanic skin response (GSR), in response to a wide variety of stressors such as negative emotional visual stimuli, pain, and the social discomfort of public speaking or making good impression to the opposite sex (Greeley & Oei, 1999; Stritzke, Patrick, & Lang, 1995). Self-report studies further suggest that men are more likely than women to use alcohol to cope with stress (Frone, et al., 1994; San Jose, et al., 2000).

Many studies of acute alcohol effects on the ANS in response to stressors excluded women, however, and those that did examine gender differences reported inconsistent findings. Some studies found no gender differences in SRD effects of alcohol, primarily using reductions in HR as the indicator of reduced arousal (Hoaken, et al., 2003; Levenson, et al., 1987), while others have found gender differences. Sinha, Robinson, and O’Malley (1998) found significant SRD effects of alcohol on HR in women with a family history of alcohol use and/or anxiety disorders, compared to women without positive family histories and women in a placebo condition. Men did not show SRD effects, regardless of family history. On the other hand, Croissant, Rist, Demmel, and Olbrich (2006) reported that sons of alcoholics, but not daughters, showed strong SRD effects on HR following alcohol consumption, compared with drinking a non-
alcoholic beverage. Neither study examined gender-by-alcohol interaction effects on ANS reactivity. Thus, gender differences in stress-dampening effects of alcohol across various levels of risk for problematic alcohol use remain unclear. The inconsistency in HR findings may also be due in part to differences between studies in methodology, such as the timing of HR measurements following alcohol consumption and baseline levels of HR (see Sayette, 1993, for a review).

Furthermore, it is unclear whether arousal dampening effects of alcohol are limited primarily to stress-inducing stimuli or apply more broadly to arousing stimuli irrespective of emotional valence. Due to the importance of “stress-response” dampening to etiological theories of alcohol use (Cooper, et al., 1995; Cox & Klinger, 1988b; Greeley & Oei, 1999), many previous studies included only stress-inducing stimulus conditions and emotionally neutral conditions for comparison. The study of a broader range of stimulus conditions is desirable, as shown in a study by Stritzke and colleagues (1995) that found alcohol reduced GSR in response to both negative and positive emotional stimuli. It thus appears useful to carefully delineate arousal and valence components of ANS arousal regulatory systems.

Alcohol cue reactivity research has focused on alcohol dependent individuals who typically self-report craving and show increased autonomic arousal, such as increased HR and GSR, in response to both visual and olfactory alcohol cues (see Carter & Tiffany, 1999; Drummond, Cooper, & Glautier, 1990, for reviews). Cue reactivity induced by alcohol-related cues is not limited to alcohol dependent drinkers, however. Increased self-report of urges to drink (Cooney, Gillespie, Baker, & Kaplan, 1987) and increased physiological arousal responses to alcohol-related cues (Walitzer & Sher, 1990) have also
been demonstrated in social drinkers. In cue reactivity studies, alcohol exposure typically does not involve administration of alcohol beyond the level of priming or tasting. Furthermore, the limited empirical evidence is equivocal as to whether alcohol cue reactivity during negative mood states differs for men and women who are alcohol dependent (Rubonis, et al., 1994) or heavy social drinkers (Nesic & Duka, 2006). It is important to understand how alcohol administration may influence alcohol cue reactivity, and whether it influences cue reactivity differentially for men and women in response to emotional and alcohol-related cues. Therefore, the present study included alcohol-related picture cues, in addition to emotionally arousing cues, to examine the effects of alcohol in a broader context of arousal response.

*Real-time Change in Heart Rate Variability as a Measure of Autonomic Arousal*

While HR and GSR are useful indicators of changes in arousal and emotional reactivity, they do not directly characterize dynamic aspects of self-regulation (El-Sheikh, 2001). In line with a focus on modulation of arousal and the use of alcohol to self-regulate emotional response, the current study examined a component of heart rate variability (HRV), derived from cardiac beat-to-beat R-to-R intervals (RRI), to capture continuous, fine-grained adjustments that occur in HR in response to emotional and alcohol-related picture cues. Quantitative parameters of HRV characterize the adaptive capacity of the cardiovascular system, working together with the neural circuitry involved in the central autonomic network (Benarroch, 1997), and thus are well suited to quantify dynamic aspects of emotional self-regulation when stimulated (Porges, 2007; Thayer & Lane, 2000).
Various indices of HRV predict cardiovascular mortality (Schmidt, et al., 2005; Stein, et al., 2006), children’s health, resiliency, and social competence (Doussard-Roosevelt, Porges, Scanlon, Alemi, & Scanlon, 1997; El-Sheikh, Harger, & Whitson, 2001; Katz & Gottman, 1995, 1997), and the use of active coping skills in adults (Fabes & Eisenberg, 1997; O'Connor, Allen, & Kaszniak, 2002). HRV indices have also demonstrated utility in the study of emotional regulation (Appelhans & Luecken, 2006; Berntson, et al., 1997) in disorders such as depression (Nahshoni, et al., 2004), anxiety (Dishman, et al., 2000; Thayer, et al., 1996), panic disorder (Cohen, et al., 2000; Friedman & Thayer, 1998), and chronic heavy alcohol use (Thayer, Hall, Sollers, & Fischer, 2006). HRV has most often been operationalized in terms of characteristic background levels of ANS function (i.e., baseline HRV measured at rest), which are subject to suppression by acute and chronic stressors in healthy adults (Giardino, et al., 2000), and by both acute (Bennett, et al., 2001; Koskinen, Virolainen, & Kupari, 1994; Reed, Porges, & Newlin, 1999; Rossinen, et al., 1997) and chronic (DePetrillo, White, Liu, Hommer, & Goldman, 1999; Ingjaldsson, Laberg, & Thayer, 2003; Murata, et al., 1994; Yokoyama, et al., 1991) alcohol consumption.

These strong predictive links between background levels of HRV and physical and emotional health may reflect the cumulative outcomes of individual differences in arousal and modulation of arousal in response to environmental challenges as they occur in real-time (Appelhans & Luecken, 2006; Berntson, et al., 1997). The only alcohol administration study of which we are aware that actually examined real-time changes in HRV in response to visual cues found that alcohol suppressed reactivity to cocaine cues in nine cocaine abusing men (Reed, et al., 1999).
The Present Study

The current study examined alcohol and placebo effects on real-time changes in HRV in response to provocative visual cues as a method for evaluating how men and women modulate their arousal when they are stimulated with environmental cues. Based on the results of our previous comparative evaluation of multiple HRV indices using a subset of the data from the current study (HRV responses to emotionally valenced cues only, Vaschillo, et al., 2008), a 0.1-Hz HRV index was selected as a sensitive measure of ANS regulation. Resonance effects maximize the amplitude of 0.1-Hz oscillations when the cardiovascular system is stimulated at this frequency (Vaschillo, et al., 2002; Vaschillo, et al., 2006a). In Vaschillo et al. (2008), we introduced a novel methodology of stimulating the cardiovascular system at its resonance frequency (0.1 Hz, i.e., one cue every 10 s), a distinctive feature of a 0.1-Hz HRV index, and quantitatively evaluated the relative sensitivity of the new 0.1-Hz HRV index, compared to several other traditional HRV indices, to negative, positive, and neutral picture cues. While all the evaluated HRV indices were sensitive to alcohol effects, the 0.1-Hz HRV index was found to be sensitive to placebo challenge, while other HRV indices were not, and sensitive to the valence of the emotional picture cues. Convergent evidence suggests that the 0.1-Hz HRV index evaluates both moment-to-moment ANS reaction to various external interventions (Nickel & Nachreiner, 2003), as well as activation of the baroreflex (Cevese, Gulli, Polati, Gottin, & Grasso, 2001), a reflex that modulates level of arousal.

In the present study, we used the 0.1-Hz HRV index to determine whether arousal in response to emotionally positive, negative, and neutral picture cues, and alcohol-related picture cues differ for men and women following alcohol administration, and compared
psychophysiological arousal to subjective self-reports of arousal in response to the four stimulus cue types. We hypothesized that alcohol would reduce the 0.1-Hz HRV index of ANS reactivity to alcohol-related as well as emotionally-valenced cues. Men were predicted to show more dampening in the 0.1-Hz HRV index of autonomic nervous system reactivity to negative emotional stimuli during acute alcohol intoxication than would women, based on the self-report literature (Frone, et al., 1994; San Jose, et al., 2000). Examination of gender differences in response to positive emotional and alcohol-related cues was exploratory. Finally, we expected that the 0.1-Hz HRV index, relative to self-reports of arousal, would better model the relationships between arousal, exposure to alcohol, and stimuli among men and women than would self-report level of arousal, due in part to lower levels of errors in measurement relative to self-report measures.

Method

Participants

Participants were 20 men and 16 women, between 21 to 24 years of age, who were recruited through advertisements for social drinkers posted on bulletin boards and in university and community newspapers. Interested individuals called the lab for details about the study, and if interested, provided oral consent to complete a standardized telephone screening interview (Ray, Bates, & Ely, 2004; Tracy & Bates, 1999) to initially determine study eligibility. Based on the screening questions and a more in-depth laboratory assessment, individuals were excluded if positive for a history of psychiatric or neurological disorder or treatment; alcohol dependence; history of any substance abuse treatment; lifetime diagnosis of any substance use disorder on the part of the prospective participant’s biological mother (to rule out prenatal exposure effects); medical conditions
that preclude alcohol administration or confound interpretation of HRV (e.g., diabetes, heart disease, abnormal HR pattern); 20% over- and under-weight from the ideal for age and gender; and for women, pregnancy determined via urinalysis. In addition, individuals who reported weekly use of other illicit or prescribed drugs were not eligible for the study. Few participants reported use of any drugs other than marijuana \( (n = 10) \) in the past 30 days. Eleven individuals reported use of cigarettes in the past 30 days with four reporting regular use. To avoid exposure of participants to an alcohol dose substantially greater than their routine consumption levels in the natural environment, we also excluded men who didn’t consume at least four standard alcohol drinks per occasion, and women who didn’t consume at least three standard drinks per occasion, at least twice per month in the past year.

The majority of the participants were non-Hispanic White (61%); 22% were Asian, 6% were Hispanic White, and the remaining were African American and other (11%). Although we recruited in the university and surrounding communities, participants meeting the study inclusion criteria were all college students, with 14.6 years of education on average \( (SD = 1.2) \). The mean age was 21.8 years \( (SD = 0.98) \) and majority of the participants (85.7%) reported a family income of more than $41,000.

**Measures and Procedures**

**Stimuli.** The picture cue exposure tasks included four categories of picture cue blocks that are the focus of the present study: negative emotional, positive emotional, neutral, and alcohol-related as well as two exploratory picture cue blocks that were not included in the present study (marijuana and polydrug). There were 15 pictures per each picture cue type. Emotional pictures were selected from the International Affective
Picture System (IAPS, Lang, Bradley, & Cuthbert, 2001); negative and positive pictures were matched on standardized ratings of arousal, but varied in valence. Alcohol-related picture stimuli were from the Normative Appetitive Picture System (NAPS, Stritzke, Breiner, Curtin, & Lang, 2004a), as well as from Tapart et al. (2003), with additional alcohol-related pictures developed in our lab.

**Procedures.** Eligible participants were stratified by gender and then randomly assigned to an alcohol, placebo, or no alcohol control group ($n = 12$ per each group). Participants were asked to eat a light low-fat meal (e.g., cereal, oatmeal) 3 hrs prior to reporting to the lab, and to refrain from drinking alcohol or taking any drugs for 24 hrs before the session (except cigarettes and caffeine to avoid withdrawal symptoms during the experimental session). The session was scheduled during weekdays (i.e., Mondays through Fridays), and began between 10 a.m. and 2 p.m. to minimize biological circadian variations in alcohol metabolism and behavioral effects. All participants provided written informed consent and were compensated $10.00 per hr with a maximum of $50.00 for time spent in the lab, which included the time to return to a BAC of zero for the alcohol group. After providing consent, participants completed a series of questionnaires, including a brief version of the Profile of Mood States (POMS, McNair, Lorr, & Droppleman, 1992), which asked “how they feel right now,” and standardized Alcohol and Drug Use Questionnaires (Rutgers Health and Human Development Project; Pandina, Labouvie, & White, 1984). Then, the participants moved to the testing room. After the sensors for physiological recording were attached, the participant was seated in a comfortable chair located 2.5 m in front of a TV screen in a sound-attenuated, dimly-lit room. Before beverage administration, participants performed a standardized low-
demand task, the “plain vanilla task” (Jennings, Kamarck, Stewart, Eddy, & Johnson, 1992) for 5 min to equate mental load across individuals. During this task, the participants sequentially viewed colored rectangles on a computer screen and silently counted the number of blue rectangles. Physiological reactivity during this period served as a pre-drinking baseline.

Alcohol doses to achieve a target blood alcohol concentration (BAC) of 90 mg/dl were calculated based on weight (0.90 ml/kg for men, 0.75ml/kg for women), and mixed with an orange juice mixer in a ratio of 4 parts mixer to 1 part ethanol. The beverage was divided into 3 equal drinks, and each drink was consumed during a consecutive 5-min interval. All participants consumed 3 volume-controlled drinks that were 100% mixer (told no alcohol and received no alcohol = control), mixer with 100μl ethanol float per each cup and other olfactory cues (told alcohol and received no alcohol = placebo), or mixer plus 95% ethanol dose. When a BAC of ~ 60 mg/dl was reached on the ascending limb of the BAC curve (or after 10 min in placebo and control sessions), participants again performed the plain vanilla task, followed by picture cue presentation. Each participant individually completed one session, including a picture cue exposure phase (the focus of the current study), followed by a picture memory phase, as a part of another study. The entire experimental session lasted approximately 3 1/2 hrs. Participants in the alcohol condition remained in the laboratory until their BAC reached zero.

*Picture presentation and arousal ratings.* Each picture cue type was presented in a blocked manner. The blocks were presented in counterbalanced order following the 24 patterns of block orders generated using SAS Proc Plan (SAS Institute, 2000-2006). In each of the six blocks, a set of 15 pictures per block was presented twice for a total of 30
pictures per block. The order of picture presentation was randomized within each of six sets. Each picture was presented for 5 s with a 5 s inter-picture interval, resulting in a 0.1-Hz frequency of picture presentation. Each block lasted for 5 min with a 30 s inter-block interval. Using the Self-Assessment Manikin (SAM; Lang et al., 2001), participants verbally provided a liking (not used in this study) or an arousal rating during the 5 s picture-off interval, with the order of ratings counterbalanced across sets within blocks. Their verbal responses were coded and averaged across 15 picture cues per each of six picture cue blocks. Participants were instructed to rate each picture on a scale of 1 = calm or relaxed to 9 = excited, jittery, or awake for arousal ratings.

*Physiological record.* Electrocardiogram (ECG) activity was recorded during the pre-drinking baseline and presentation of six picture blocks. The ECG record was collected with a sampling rate of 1,000 per second by a Powerlab Acquisition system (ADInstruments, Colorado Springs, CO). Ag-AgCl ECG electrodes were placed on the right arm (active), left arm (ground), and left leg (active). Recorded data were exported to a WinCPRS software program (Absolute Aliens Oy, Turku, Finland) for analyses. The program measured beat-to-beat RR intervals (RRI) of ECG, segmented succession of RRI into 5-min blocks, and calculated RRI spectra through Fourier analysis (Cooke, et al., 1999; Taylor, Carr, Myers, & Eckberg, 1998). The 0.1-Hz HRV index was calculated as the power of the RRI spectrum at 0.1-Hz for the pre-drinking baseline and each picture block. Prior to analysis, the 0.1-Hz HRV index scores were transformed using the natural logarithm.

*Statistical analysis.* Within-individual change scores were calculated by subtracting baseline (pre-drinking) 0.1-Hz HRV index scores from 0.1-Hz HRV index scores for each
of four stimulus cue types to adjust for individual differences in HRV at baseline. Analysis of variance (ANOVA) and chi-square tests were used to examine whether gender differences existed in potential confounding variables, including age, pre-test POMS score, the 0.1-Hz HRV index at baseline, and alcohol and other drug use. For the main analysis, a repeated measures ANOVA was used to examine two between-subject main effects of group and gender, an interaction effect between group and gender on changes (from baseline) in the 0.1-Hz HRV index in response to four picture cue types (within-subject effects), and three between-subject by within-subject interaction effects (group × picture cue type, gender × picture cue type, and group × gender × picture cue type). Arousal ratings were also analyzed using the same analytic approach. Finally, correspondence between the 0.1-Hz HRV index and subjective self-report ratings of arousal was examined by Pearson’s correlation analysis.

Results

Participant Characteristics across Men and Women

We initially examined whether men and women were equivalent in the 0.1-Hz HRV index at baseline as well as other individual characteristics, including age, alcohol use, and BAC levels (see Table 1.1). There were no significant gender differences in the 0.1-Hz HRV index at baseline. Men reported consuming significantly more standardized drinks per occasion in past 30 days than did women. This was expected due to the different study inclusion criteria for men and women based on typical quantity of alcohol consumed (see also the Participants section). There were no other significant gender differences.

Physiological Response to Emotional and Alcohol-related Stimuli
Repeated measures ANOVA (the sphericity assumption was met, Mauchly’s criterion = .73, Chi-square = 8.88, with \( df = 5 \), ns) results revealed an interaction effect between group and gender on the 0.1 Hz-HRV index, \( F(2, 30) = 5.03, p < .05 \), partial \( \eta^2 = .25 \) (see Figure 1.1). Men showed significantly less increase in the 0.1-Hz HRV index following alcohol challenge than did women. The main effect of gender was not significant, \( F(1, 30) = 2.20, p = .14 \), partial \( \eta^2 = .07 \), and the main effect of group was significant at the level of a trend, \( F(2, 30) = 2.90, p = .07 \), partial \( \eta^2 = .16 \). The alcohol and placebo groups (men and women combined) tended to show lower levels of HRV responses, compared to the control group (\( p = .07 \)). The alcohol and placebo groups did not differ from each other (\( p = .69 \)). Among the within-subject effects, only the main effect of picture cue type was significant, \( F(3, 90) = 6.85, p < .05 \), partial \( \eta^2 = .19 \).

Significantly higher levels of HRV responses were observed for negative and positive picture cues but not alcohol-related cues, compared to those for neutral picture cues. All within-subject by between-subject interaction effects were not significant, including the interaction effect between group, gender, and picture cue type. This indicated that the dampened 0.1-Hz HRV response by men in the alcohol group was consistent across different picture cue types.1

**Subjective Ratings of Arousal**

Participants rated their subjective perceptions of arousal to the different cue types in the same order of magnitude as obtained for their physiological responses. The absolute mean of the 0.1-Hz HRV index, without subtraction of baseline, was greatest in response to negative emotional cues (mean = 10.41, \( SD = 1.08 \)), followed by positive (mean = 10.17, \( SD = 1.06 \)), alcohol (mean = 9.97, \( SD = 1.11 \)), and neutral (mean = 9.72, \( SD = 0.88 \)). In
parallel, participants subjectively rated negative emotional cues as most arousing (mean = 5.59, \(SD = 1.83\)), followed by positive (mean = 5.04, \(SD = 1.59\)), alcohol (mean = 3.91, \(SD = 1.66\)), and neutral (mean = 2.40, \(SD = 1.21\)) cues. To account for potential response biases due to rater (e.g., raters' leniency biases or social desirability biases; Podsakoff, MacKenzie, Lee, & Podsakoff, 2003 for a review), the average self-report rating of arousal in response to the neutral picture cue block (arousal ratings were not assessed during baseline) was subtracted from average negative, positive, and alcohol picture cue block ratings. Repeated measures ANOVA results indicated a statistically significant main effect of picture cue type, \(F(2, 60) = 30.38, p < .05\), partial \(\eta^2 = 0.40\), but no other effects.\(^2\) The negative picture cues were rated significantly greater in arousal than the positive and alcohol picture cues, and the positive picture cues were rated significantly greater than the alcohol picture cues.

Overall the correspondence between subjective ratings and the 0.1-Hz HRV index was rather weak and inconsistent as shown by Pearson’s correlations between the 0.1-Hz HRV change scores and both raw subjective arousal ratings (i.e., without subtracting neutral), and change in subjective rating scores (see Table 1.2). Thus, the link between subjective arousal ratings and physiological responses may be influenced by factors other than stimulus cue properties.

Discussion

The present study had two main findings. First, we found that alcohol intoxication significantly dampened emotional arousal in men, compared with women. To our knowledge, this is the first study to use an index of HRV to demonstrate differential ANS arousal response in men and women following alcohol consumption. Second, this
dampening effect of alcohol on the 0.1-Hz index of arousal modulation in men was not selective to picture cues with negative emotional valence, suggesting that alcohol depressed the arousal rather than the valence component of emotional response. This finding corresponds with Strizke et al. (1995), who found attenuated skin conductance response to both negative and positive picture cues in a combined sample of men and women. The present study further showed the effects of alcohol on general arousal by showing dampened reactivity to alcohol, neutral, and positive cues. Suppressed alcohol cue reactivity by alcohol in men is consistent with Reed and colleagues’ (1999) finding that acute alcohol intoxication suppressed increases in RSA during cocaine cue exposure in male cocaine abusers. Future research is needed to determine the generality of alcohol’s dampening of men’s arousal response to emotional challenges other than picture cues, as well as to other ANS regulatory mechanisms involving sympathetic and parasympathetic components. It may be speculated that, at least with respect to the 0.1-Hz HRV index, alcohol decreased men’s general preparatory arousal, rather than interfering with specific arousal for a particular behavior that would be needed to respond to stressful or unpleasant environmental cues.

Several potential explanations for men’s differential response to alcohol were examined. Differences between men and women were not likely due to differences in mood, as the pre-test POMS scores indicated that across beverage conditions, women and men were not significantly different in mood state. It is also unlikely that the arousal dampening effects of alcohol in men were due to gender differences in overall HRV, as men and women did not differ in the 0.1-Hz HRV index at baseline. Previous studies of young adults’ background levels of HRV have reported equivocal gender differences
across various HRV indices. Some studies reported women exhibit greater vagally-mediated HRV, compared to men (Evans, et al., 2001; Rossy & Thayer, 1998), while others found the opposite (Umetani, Singer, McCraty, & Atkinson, 1998).

Placebo groups are traditionally used to differentiate the cognitive influence of alcohol outcome expectancies from the acute pharmacological effects of alcohol (Martin & Sayette, 1993). Our previous study (Vaschillo et al., 2008) showed that in the combined sample of men and women, the 0.1-Hz HRV responses by the placebo group were not distinguishable from those of the alcohol group, but different from those of the control group. The present study additionally included 0.1-Hz HRV responses to alcohol-related cues and beverage group by gender interaction effects in the model. In this context, the group main effect was at the level of trend. Thus, we speculate that a cognitively mediated reduction of HRV by alcohol likely exists in the combined sample of men and women. Together with the observed gender-specific dampening effects of alcohol, this pattern of cognitively mediated effects suggests that women may expect alcohol to suppress arousal in much the same way as men do, yet they do not appear to experience the same pharmacological effects of alcohol on the ANS reactivity as did men. The 0.1-Hz HRV index captures a fundamental component of ANS reactivity and modulation, yet does not differentiate sympathetic and parasympathetic nervous system activation and other ANS mechanisms involved in differentiated emotional response. Therefore, it is possible that women experience pharmacological dampening effects of alcohol on other aspects of ANS regulation. Disentangling the potential mechanism of differential effects of alcohol and placebo in women is beyond the scope of current study and requires further research with larger samples.
A gender-by-group interaction effect on self-reported levels of arousal to the picture cues was not found, suggesting that self-reports do not provide a sensitive indicant of alcohol’s selective suppression of 0.1-Hz HRV arousal in men. Further, there were weak and inconsistent correlations between the 0.1-Hz HRV index and the subjective ratings. Weak correlations may conceivably be related to the difference in the base values used to calculate change scores between the 0.1-Hz HRV index (pre-drinking baseline) and the subjective ratings of arousal (post-drinking response to neutral pictures). Nonetheless, it is not uncommon to find modest coherence between physiological measures and subjective reports of mood or emotion, perhaps due to factors such as the nature and intensity of the emotional experience (Mauss, Levenson, McCarter, Wilhelm, & Gross, 2005) and individual differences in interoceptive awareness (i.e., sensitivity to visceral activity; Pollatos, Herbert, Matthias, & Schandry, 2007).

Several limitations of this study needed to be considered when interpreting the results. First, the modest sample size limited statistical power for identifying group effects. Second, the current findings may not generalize to populations other than young adult social drinkers. Restrictions in the range of age and alcohol use behaviors may have attenuated the true magnitude of association and limited variability in HRV responses to alcohol-related picture cues. Finally, across human and animal studies involving alcohol administration, females are often excluded due to difficulties with controlling potential confounds. For example, it has been suggested that alcohol pharmacokinetics in women may fluctuate with the menstrual cycle potentially due to changing sex steroid hormone levels, although the literature is equivocal (e.g., Cole-Harding & Wilson, 1987; Jones &
Jones, 1984; Lammers, Mainzer, & Breteler, 1995; Sutker, Goist, & King, 1987). Further study is needed to examine alcohol effects on psychophysiological reactivity of women at different phases of the menstrual cycle, as this was not assessed in the present study.

Despite these limitations, the results point to the likelihood of potentially meaningful gender differences in alcohol effects on the modulation of arousal with men, but not women, experiencing dysregulated emotional preparatory response to stimulus cues during acute intoxication. More broadly, the present study demonstrates that a specific emotional regulatory process involving moment-to-moment ANS reactivity and modulation can be objectively quantified when prefrontal function is intact or compromised by alcohol challenge. This basic behavioral approach to assessing ANS participation in emotional experience in real time presents a new opportunity for treatment research for at least two reasons. First, HRV as a background capacity measure of self-regulation as typically studied may be helpful for identifying those at risk for various physical and emotional health conditions. As a potential screening tool, however, HRV indices taken at rest (without stimulation) cast a very wide net. In contrast, it may be possible to screen those with atypical self-regulation of emotional arousal with respect to salient environmental cues from those with poor general health conditions, using a real-time HRV assessment approach. Second, stimulating the cardiovascular system at its resonance frequency via paced breathing has been used to improve ANS regulation in several clinical groups that share difficulties in modulating arousal (Hassett, et al., 2007; Karavidas, et al., 2007; Lehrer, et al., 2003; Lehrer, et al., 2004). Paced breathing, or perhaps the related HRV approach used in this study, involving resonance frequency stimulation with visual cues, may potentially be useful to improve self-regulation among
those at risk or in treatment for substance use disorders. Unlike stationary HRV measured at rest, the HRV paradigm used here has the potential to be manipulated and adapted as a behavioral method to exercise activation of baroreflex, a reflex involved in maintenance of homeostasis, which in turn improves emotional self-regulation through enhancing autonomic modulatory flexibility.
Footnotes

1 The within-subject by between-subject interaction effects between picture cue type and group, between picture cue type and gender, and between picture cue type, group, and gender were statistically non-significant, $F(6, 90) = 1.22, ns$, partial $\eta^2 = 0.08$; $F(3, 90) = 0.72, ns$, partial $\eta^2 = 0.02$; and $F(6, 90) = 0.57, ns$, partial $\eta^2 = 0.04$, respectively.

2 The within-subject by between-subject interaction effects between picture cue type and group, between picture cue type and gender, and between picture cue type, group, and gender were statistically non-significant, $F(4, 60) = 1.36, ns$, partial $\eta^2 = 0.08$; $F(2, 60) = 2.67, ns$, partial $\eta^2 = 0.08$; and $F(4, 60) = 0.90, ns$, partial $\eta^2 = 0.06$, respectively. All between-subject effects (group, gender, and group $\times$ gender effects) were not statistically significant, $F(2, 30) = 1.37, ns$, partial $\eta^2 = 0.08$; $F(1, 30) = 2.23, ns$, partial $\eta^2 = 0.07$; and $F(2, 30) = 0.12, ns$, partial $\eta^2 = 0.01$, respectively.
References


Gainesville, FL: The Center for Research in Psychophysiology, University of Florida. 


Table 1.1

**Participant Characteristics: Age, Alcohol Use, and Pre-test POMS score**

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
<th>t Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 16)</td>
<td>(n = 20)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>21.6 (.96)</td>
<td>22.0 (1.00)</td>
<td>t (34) = -0.99</td>
</tr>
<tr>
<td>0.1-Hz HRV index</td>
<td>8.87 (1.14)</td>
<td>9.24 (1.08)</td>
<td>t (34) = -1.00</td>
</tr>
<tr>
<td>Alcohol use (past 30 days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quantity (per occasion)</td>
<td>2.4 (1.5)</td>
<td>5.3 (3.1)</td>
<td>t (28.3) = -3.66$^a$</td>
</tr>
<tr>
<td>Frequency (per week)</td>
<td>1.6 (1.6)</td>
<td>2.6 (1.8)</td>
<td>t (34) = -1.73</td>
</tr>
<tr>
<td>POMS (pre-test)</td>
<td>.094 (7.28)</td>
<td>-1.00 (7.33)</td>
<td>t (34) = 0.79</td>
</tr>
<tr>
<td>BAC (alcohol condition – pre-test)</td>
<td>.074 (.013)</td>
<td>.079 (.034)</td>
<td>t (34) = -0.31</td>
</tr>
<tr>
<td>BAC (alcohol condition – post-test)</td>
<td>.064 (.008)</td>
<td>.054 (.011)</td>
<td>t (34) = 1.74</td>
</tr>
</tbody>
</table>

*Notes.* Numbers in parentheses indicate standard deviations. $^1 =$ Average number of standard drinks per occasion; POMS = Profile of Mood States (McNair et al., 1992); BAC = Blood Alcohol Concentration; $^a =$ Statistically significant differences between genders ($p < .05$).
Table 1.2

Zero-Order Correlation between the 0.1-Hz HRV Index and Subjective Ratings of Arousals (N = 36)

<table>
<thead>
<tr>
<th></th>
<th>Negative</th>
<th>Positive</th>
<th>Alcohol</th>
<th>Neutral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>.15</td>
<td>-.24</td>
<td>-.30</td>
<td>.07</td>
</tr>
<tr>
<td>(n = 12)</td>
<td>(.19)</td>
<td>(-.03)</td>
<td>(-.46)</td>
<td>(N/A)</td>
</tr>
<tr>
<td>Control</td>
<td>-.31</td>
<td>-.23</td>
<td>.19</td>
<td>.16</td>
</tr>
<tr>
<td>(n = 12)</td>
<td>(-.34)</td>
<td>(-.29)</td>
<td>(-.18)</td>
<td>(N/A)</td>
</tr>
<tr>
<td>Placebo</td>
<td>-.19</td>
<td>.33</td>
<td>.08</td>
<td>-.01</td>
</tr>
<tr>
<td>(n = 12)</td>
<td>(-.11)</td>
<td>(.35)</td>
<td>(-.07)</td>
<td>(N/A)</td>
</tr>
</tbody>
</table>

Notes. Upper numbers indicate correlations between the 0.1-Hz HRV change scores (baseline 0.1-Hz HRV subtracted) and original scores (i.e., without subtracting average ratings for neutral picture cues) of subjective ratings of arousals. Lower numbers in parentheses indicate correlations between the 0.1-Hz HRV change scores (baseline 0.1-Hz HRV subtracted) and change scores for the subjective ratings of arousal after subtracting ratings for neutral picture cues. All correlations were statistically non-significant at \( p < .05 \).
Figure Caption

Figure 1.1 Means and 95% confidence intervals for 0.1-Hz HRV responses to emotional and alcohol-related picture cues. NG = Emotional Negative, PS = Emotional Positive, NT = Emotional Neutral, AL = Alcohol-related. The horizontal x-axis line at y = 0 indicates the reference line for no within-person change in 0.1 Hz HRV. The 0.1-Hz HRV index response score above y = 0 indicates increased response to the picture cues from baseline. The 0.1-Hz HRV index score below y = 0 indicates decreased response to the picture cues from baseline.
Figure 1.1

Changes in 0.1-Hz HRV Responses (log)

Alcohol | Control | Placebo
--- | --- | ---
Female | Male

NG | PS | NT | AL | NG | PS | NT | AL | NG | PS | NT | AL
CHAPTER 3

STUDY 2

Emotion Regulation and Alcohol Use:
Behavioral Undercontrol, Negative Emotionality, and Gender

Abstract

The constructs of negative emotionality (NE) and behavioral undercontrol (BU) are thought to increase risk for problematic alcohol use through association with motivation to use alcohol for emotion regulation. The interplay of multiple physiological processes, such as the autonomic nervous and baroreflex activities, regulate emotional responding to internal and external challenges, but little is known whether these processes represent underlying physiological mechanisms that link an individual’s susceptibility to negative emotions and their likelihood of engaging in unhealthy drinking behaviors. The present study compared emotional reactivity in men and women who differ in level of BU and NE. Eighty-two young adults (33 women) were classified into four personality groups (NE, BU, NE + BU, comparison) by median splitting the sample based on their Beck Depression Inventory II and Zuckerman’s sensation seeking scores. All participants were exposed to a paced presentation (every 10 s, 0.1 Hz) of emotional (negative, positive, and neutral) and alcohol-related picture cues. The study found a statistically significant personality group effect with the high NE group displaying a significantly greater 0.1-Hz heart rate variability (HRV) response to negative picture cues relative to the other groups. Further, personality group-by-gender analysis revealed that the heightened arousal reactivity in the NE group was attributable to differences among personality groups in women. In addition, higher suppression reasons for drinking were
noted for women compared to men, and for the NE and NE + BU groups compared to the comparison group. These findings suggest a potential link between sensitivity to negative emotions and self-reported drinking to suppress negative emotions, particularly among women.
Introduction

The constructs of negative emotionality and behavioral undercontrol have been useful in understanding the etiology of alcohol use (Cooper, 1994; Cooper, et al., 1995; Cox & Klinger, 1988b; Wills & Shiffman, 1985) and subtyping individuals with alcohol use disorders (AUD) (e.g., Babor, et al., 1992; Cloninger, 1987; Zucker, 1986). Negative emotionality is characterized by an individual’s tendency to experience a significant level of stress and negative affect, including depressed mood, anger, and anxiety, regardless of the situation (Watson & Clark, 1984). It correlates positively with the initiation of alcohol use, the development and maintenance of heavy drinking, and related problems in adolescents and young adults (Colder & Chassin, 1993, 1997; Ferrier-Auerbach, et al., 2009; James & Taylor, 2007; Johnson & Pandina, 1993; Pandina, Johnson, & Labouvie, 1992). On the other hand, individuals with behavioral undercontrol are described as being highly disinhibited, strongly motivated to pursue immediate rewards, and lacking the ability to foresee the negative consequences of reward-seeking behaviors, such as hangovers from binge drinking (Colder & Chassin, 1997). Behavioral undercontrol is often operationalized by personality constructs such as impulsivity, antisocial personality, aggressiveness, and sensation seeking, and has been associated with greater alcohol use (Magid, MacLean, & Colder, 2007) and alcohol use problems, such as more frequent participation in drinking games and experiencing more negative consequences of risky drinking behaviors (Johnson & Cropsey, 2000; MacKillop, Mattson, Anderson Mackillop, Castelda, & Donovick, 2007; Martin, et al., 2000; Sher & Trull, 1994).

Although motivational models of alcohol use posit that both negative emotionality and behavioral undercontrol increase risk for problematic alcohol use (Cooper, 1994;
Cooper, et al., 1995; Cox & Klinger, 1988b), evidence suggests that these two constructs may be linked with differing motivations for alcohol use. Compared to individuals with low levels of these characteristics, individuals with high levels of negative emotionality are more likely to use alcohol to cope with stress and negative emotion (Bolton, Robinson, & Sareen, 2008; Cooper, Russell, Skinner, Frone, & Mudar, 1992; Holahan, Moos, Holahan, Cronkite, & Randall, 2004; Kuntsche, Knibbe, Gmel, & Engels, 2006; Robinson, Sareen, Cox, & Bolton, 2008), whereas individuals who are behaviorally undercontrolled are more likely to use alcohol to enhance positive emotion (Comeau, Stewart, & Loba, 2001; Cooper, et al., 1995; Kuntsche, et al., 2006; Magid, et al., 2007). Despite ample evidence that the desire to regulate positive and negative emotion is an important motivation for alcohol use (Cooper, et al., 1995; Koob, 2003; Labouvie & Bates, 2002; Simons, Gaher, Correia, Hansen, & Christopher, 2005), little attention has been paid to the possibility that distinct underlying regulatory responses to emotional challenge may lead individuals with negative emotionality and/or behavioral undercontrol tendencies to engage in unhealthy drinking behaviors. A psychophysiological approach is a useful to study regulation of emotional response because it provides tools to quantify dynamic, real-time changes in arousal in response to emotional challenge.

Regulation of emotion is achieved through the interplay of peripheral and central arousal modulation by multiple systems. In particular, recent theories of emotion regulation have emphasized the importance of the autonomic nervous system (ANS) (Appelhans & Luecken, 2006). Through coordinated activities by the sympathetic and parasympathetic nervous systems, the ANS modulates a general arousal response that
prepares an organism for action (Iversen, et al., 2000). Peripherally, this is observed as physiological changes, such as an increase in heart rate (HR), skin conductance, and respiration rate (Iversen, et al., 2000). Centrally, autonomic arousal response is projected to brain stem structures that are part of the central autonomic network. This network integrates autonomic, neuroendocrine, and behavioral responses by sending signals back to peripheral organs and forward to frontal and limbic structures that modulate emotion (Benarroch, 1993). Thus, together with the central autonomic network, flexible modulation of arousal by the ANS contributes to an individual’s emotional experience. The present study focused on characterizing the regulation of emotional arousal by the ANS in individuals with different levels of negative emotionality and behavioral undercontrol by assessing heart rate variability (HRV) in response to emotionally-arousing picture cues.

HRV represents complex changes in HR that are induced by sympathetic and parasympathetic influences on the heart (Berntson, et al., 1997). HRV has been suggested as a sensitive index of emotion regulation (Appelhans & Luecken, 2006; Porges, 1991; Porges, et al., 1994). Reduced levels of HRV have been used to index emotion dysregulation in individuals with disorders such as depression (Nahshoni, et al., 2004), anxiety (Friedman & Thayer, 1998; Thayer, et al., 1996), and posttraumatic stress disorder (Cohen, et al., 2000). Indices of HRV can be used to characterize the background state of the ANS or its dynamic reaction to internal or external stimuli. Background HRV is measured at a resting-state to characterize differences between individuals in their ANS arousal modulatory capacity (see, Butler, et al., 2006 for a brief overview). HRV reactivity, on the other hand, characterizes the adaptive response
capacity of the ANS in response to experimental manipulations (Butler, et al., 2006; Rottenberg, Clift, Bolden, & Salomon, 2007). In the present study, we studied HRV reactivity in response to emotionally-arousing and alcohol-related pictures.

In this study, a novel 0.1-Hz HRV index, based on the 0.1 Hz resonance in the HR baroreflex system (see Vaschillo, et al., 2008) was used to understand individual differences in emotional reactivity. The baroreflex is a reflexive control process that stabilizes blood pressure (Cevese, et al., 2001) and controls cortical arousal (Dworkin, et al., 1994; Elbert, et al., 1992; Nyklicek, et al., 2005; Rau, et al., 1993; Yasumasu, et al., 2006). Stimulation of the cardiovascular system at its resonance frequency by an internal stimulus (e.g., breathing) or external stimuli (e.g., picture presentation) has been shown to induce high-amplitude HR oscillation (Song & Lehrer, 2003; Vaschillo, et al., 2004; Vaschillo, et al., 2008). Thus, by assessing the amplitude of HR oscillation at 0.1 Hz, the 0.1-Hz HRV index allows characterization of (1) individual differences in moment-to-moment autonomic arousal reactivity to various external interventions (Nickel & Nachreiner, 2003) and (2) an adaptive modulation of arousal by the baroreflex (Cevese, Gulli, Polati, Gotti, & Grasso, 2001).

This study extends the utility of this psychophysiological index in quantifying individual differences in emotional regulation by using it to examine differences in reactivity to emotionally arousing and alcohol-related picture cues among individuals exhibiting different levels of negative emotionality and behavioral undercontrol. While background level of HRV measured at rest have often been used to predict physical and psychological health, including cardiac mortality (Schmidt, et al., 2005; Stein, et al., 2006) and stress vulnerability (Giardino, et al., 2000), moment-to-moment dynamic
fluctuation in HRV may better capture an individual’s ability to flexibly respond to on-
going environmental challenge, and reflect an aspect of emotional regulation that may be useful to further understand the underlying mechanisms of individual differences in alcohol use motivations.

Although both etiological and clinical studies of subtypes of alcohol use risk have typically conceptualized negative emotionality and behavioral undercontrol as two distinctive personality risks for alcohol use problems (Cloninger, 1987; Zucker, 1986), several studies have indicated that negative emotionality and behavioral undercontrol may not necessarily be mutually exclusive risk typologies. Previous studies with non-clinical samples have shown that individuals who are high in both personality characteristics show greater alcohol use and associated problems than individuals who are either high in one of the traits or low in both traits (Colder & Chassin, 1997; Hussong & Chassin, 1994; Johnson & Pandina, 1993; Pandina, et al., 1992; Weinberger & Schwartz, 1990). Within a clinical sample of individuals with a history of alcohol and drug use problems, a distinct subset of individuals who exhibited both antisocial personality and depression was also identified (Epstein, Ginsburg, Hesselbrock, & Schwarz, 1994). The present study sought to further understand the conjoint operation of negative emotionality and behavioral undercontrol by characterizing autonomic arousal regulation in individuals who exhibited high levels of both constructs relative to those who were high in only one, or neither, and assessed how their emotion regulation related to alcohol use and related problems.

Women, relative to men, are less likely to exhibit personality characteristics of behavioral control, such as sensation seeking traits, antisocial personality, and
aggressiveness (Martin, et al., 2000; Nolen-Hoeksema, 2004) and more likely to exhibit characteristics of negative emotionality, such as depressive mood (Alfeld-Liro & Sigelman, 1998; Chaplin, 2006; Hankin, et al., 1998). However, the moderating role of gender in the relationship between personality characteristics and alcohol use and its related problems has been inconclusive. Some studies suggest that negative emotionality and behavioral control lead to alcohol use in a similar manner for adolescent males and females (Colder & Chassin, 1997; Martin, et al., 2000; McGue, Slutske, Taylor, & Iacono, 1997). On the other hand, others found the associations between behavioral undercontrol, and alcohol use and related problems in young men, but not in women (Caspi, Moffitt, Newman, & Silva, 1996; Windle, 1990; Windle & Barnes, 1988). To further study a potential mechanism that could support gender differences in alcohol use patterns, analyses were conducted to examine whether the relationship between personality traits and emotion regulation is influenced by gender.

In summary, the purpose of the present study was to compare emotional reactivity in men and women who differed in levels of behavioral undercontrol and negative emotionality, using the 0.1-Hz HRV index as a measure of emotional reactivity. To better capture the role of emotional reactivity in problematic alcohol use, the present study focused on men and women who either were at high risk for, or had already developed an alcohol and/or other drug disorder. Based on the association between personality and motivations for drinking, it was hypothesized that when compared with individuals who were low in both personality characteristics (i.e., the reference group), those with higher levels of behavioral undercontrol would show significantly reduced 0.1-Hz HRV responses to emotionally-arousing picture cue presentations, whereas those with high
levels of negative emotionality would show heightened 0.1-Hz HRV response. Given that the greatest alcohol use and associated problems were previously observed in individuals who were high in both negative emotionality and behavioral control (Epstein, et al., 1994), 0.1-Hz HRV response to emotional picture cues in the dually affected individuals was hypothesized to differ from the comparisons, although the directionality of their response is uncertain. Further, based on the gender differences in personality characteristics, heightened HRV reactivity was expected to be prominent in women with negative emotionality whereas the reduced HRV response was expected to be prominent in men with behavioral undercontrol, compared to their opposite sex counterpart.

In addition to investigating the relationship between emotional reactivity and personality, we also examined alcohol use behaviors (i.e., alcohol use, alcohol-related problems) and reasons for alcohol use to confirm the previous findings. It was expected that high behavioral undercontrol and negative emotionality would be associated with greater alcohol use and problems, relative to comparison groups. It was also expected that individuals with high negative emotionality would be more likely to report suppression reasons for drinking, while individuals with high behavioral undercontrol would report more disinhibition reasons for drinking.

Methods

Participants. The study sample ($N = 82$) was predominantly white (67.1%) and male (58.5%). Minority participants were Asian (14.8%) and non-Hispanic African American (6.8%), and 9.1% of the sample was classified as other or more than one race. The mean age of the study sample was 21.1 years ($SD = 2.66$). On average, the sample
completed 14.1 years of education \((SD = 1.3)\), and the majority of participants \((79.8\%)\) reported a family income of more than $41,000.

Participants were recruited from one of three sources. College students \((n = 43, \text{23 women})\) were recruited following participation in a study that compared the effectiveness of a brief motivational interview and written feedback in reducing alcohol use in students who were referred to a mandatory college counseling program for alcohol and other drug use for violating campus alcohol policies \((\text{White, et al., 2006; White, Mun, \& Morgan, 2008; White, Mun, Pugh, \& Morgan, 2007})\). Infractions ranged in severity from being in a dorm room with alcohol present, to alcohol poisoning requiring a hospital emergency room visit. College athletes \((n = 12, \text{5 women})\) were recruited prior to participation in another study examining the resonant frequency HRV on the athletic performance. College athletes are more likely to engage in binge drinking and experience more alcohol related negative consequences than college student non-athletes \((\text{Nelson \& Wechsler, 2001; Yusko, Buckman, White, \& Pandina, 2008})\). Third, similarly aged participants \((n = 27, \text{5 women})\) were recruited from an inpatient addictions treatment facility. Participants in this group met DSM-IV diagnostic criteria for a substance use disorder \((\text{SUD})\). For these participants, the alcohol and substance use disorders sections of the Structured Clinical Interview for the DSM \((\text{SCID, First, Spitzer, Gibbon, \& Williams, 1997})\) were administered to assess AUD and SUD. The prevalence of abuse or dependence diagnoses for specific drugs was: alcohol \((80.8\%)\), cocaine \((73.1\%)\), opioids \((65.4\%)\), marijuana \((92.3\%)\), and other drugs \((53.9\%)\). All participants in this sample met dependence criteria for one or more substances. The average period between admission to the inpatient facility and the laboratory testing session was 40.2 \(\pm\) 30.0 days.
Participants were excluded if they reported a history of learning disabilities (e.g., attention deficit/hyperactive disorders, dyslexia), psychiatric disorder diagnosis within the past 12 months, current psychotropic medication use, any medical conditions or medication use that might interfere with physiological recording (e.g., severe asthma, cardiac conditions), or if they showed any abnormal cardiac activity during baseline recording in the laboratory session. A total of 89 individuals completed the study protocol. Seven were excluded for the following reasons: an atypical heart beat ($n = 1$), procedural problems ($n = 4$), accidental loss of physiological data ($n = 1$), or missing data on alcohol-related measures ($n = 1$).

**Measures and Procedures**

*Indicator of negative emotionality.* The Beck Depression Inventory II (BDI-II, Beck, Steer, & Brown, 1996), a measure of current mood and other symptoms related to depressive disorders, was used to assess the level of NE. The BDI-II contains 21 items that indicate the presence and degree of depressive symptoms within the prior two week period. Each item is rated on a 4-point scale (0 = Not at all to 3 = Severely) and scores can range from 0 to 63, where 0-13 = minimal depression, 14-19 = mild depression, 20-28 = moderate depression, and 29-63 = severe depression. The relation of BDI scores to negative emotionality has been established through confirmatory analysis with other indicators of this construct (Martin, et al., 2000). In addition, positive relationships have been shown between depressive symptoms and alcohol use (Schutte, Hearst, & Moos, 1997), alcohol related problems (Crum, Storr, & Chan, 2005; Schutte, et al., 1997), and using alcohol to cope (Berger & Adesso, 1991; Holahan, et al., 2004).
**Indicator of behavioral inhibition.** The Zuckerman Sensation Seeking Scale-V (Zuckerman, 1994) was used as an indicator of BU. This scale was originally developed to quantify individual differences in optimal level of arousal (Zuckerman, Kolin, Price, & Zoob, 1964). The current version of the scale, Form V (Zuckerman, Eysenck, & Eysenck, 1978), contains 40 pairs of statements concerning personal attitudes and traits (e.g., “I enjoy spending time in the familiar surroundings of home” vs. “I get restless if I stay around home for any length of time”). Participants were asked to choose the paired statements that better described them. A sensation seeker was defined as someone who has a need for arousing stimuli, is willing to take risks to obtain an optimal level of arousal, or has intolerance to repetitive stimulus presentation (Zuckerman, 1979a, 1979b, 1994; Zuckerman, Bone, Neary, Mangelsdorff, & Brustman, 1972). This instrument has been shown to be a sensitive indicator of the construct of behavioral undercontrol (Earleywine & Finn, 1991). Arousal-seeking behavior in sensation seekers has been linked to a number of risk-taking behaviors, including heavy alcohol use (Baker & Yardley, 2002; Hittner & Swickert, 2006).

**Definition of Personality Groups.** Based on their BDI-II and Zuckerman’s sensation seeking scale scores, participants were classified into one of four groups: high behavioral undercontrol + high negative emotionality (BU + NE, n = 23, 7 women), high behavioral undercontrol only (BU, n = 19, 6 women), high negative emotionality only (NE, n = 19, 7 women), and low behavioral undercontrol + low negative emotionality (comparison, n = 22, 14 women). High and low group designations were formed applying a median split to the BDI-II and Zuckerman sensation seeking scale score distributions.
The means and standard deviations associated with the BDI-II and sensation seeking scale scores across classification groups are presented in Table 2.1.

Although the BDI-II and Zuckerman sensation seeking scale both yield a continuous measure, a median split procedure for categorizing individuals was selected to facilitate data interpretability, and is a commonly reported approach for analyzing these data when studying personality (e.g., De Pascalis, Valerio, Santoro, & Cacace, 2007; Gatzke-Kopp, Raine, Loeber, Stouthamer-Loeber, & Steinhauer, 2002; Neely, Lundstrom, & Bjorkvist, 2002; Zuckerman, 1990). As noted by Frarington and Loeber (2000), despite some disadvantages (e.g., loss of information and reduced statistical power), dichotomization simplifies the presentation and interpretation of the study findings, particularly when interactions are included (Farrington & Loeber, 2000). In addition, dichotomization avoids distributional problems such as non-normality, which has been associated with BDI-II scores (Gatzke-Kopp, et al., 2002).

**Alcohol use and Alcohol Related Problems.** Alcohol use during the 30 days prior to the laboratory session was measured by the frequency of alcohol use per week and quantity of alcohol use per occasion, which were obtained using the Alcohol and Drug Use Questionnaire (Rutgers Health and Human Development Project, Pandina, et al., 1984), of which reliability and validity has been demonstrated (Labouvie & McGee, 1986; Pandina, et al., 1984; White, 1987). Alcohol related problems, occurring during the prior 12-month period, were assessed with the Alcohol Dependence Scale (ADS), which was developed to assess the severity of alcohol dependence symptoms (ADS, Skinner & Horn, 1984). The ADS consists of 25 items asking questions related to alcohol withdrawal symptoms, awareness of a compulsion to drink, increased tolerance to
alcohol, impaired control over drinking, and salience of alcohol-seeking behavior (e.g., do you often have hangovers on Sunday and Monday mornings?, do you get physically sick as a result of drinking?). The scale has been used to gauge alcohol-related problems in individuals with an AUD as well as in non-clinical samples (e.g., Connor, Williams, & Ricciardelli, 1999; Connor, Young, Williams, & Ricciardelli, 2000; Kahler, Strong, Stuart, Moore, & Ramsey, 2003; Wood, Sobell, Sobell, Dornheim, & Agrawal, 2003).

Reasons for Drinking. Suppression and disinhibition reasons for alcohol use were assessed using the Reasons for Drinking Questionnaire, which has been shown to be reliable and valid (Labouvie & Bates, 2002). The questionnaire contains 29 reasons for using alcohol. Participants rate each statement using a three-point scale (0 = not at all important, 1 = somewhat important, 2 = very important). Due to the present focus on NE and BU, the disinhibition reasons (8 items, e.g., to help me express certain feelings more freely, to make it easier to lose control over certain feelings or desires), and suppression reasons (13 items, e.g., to help me feel better emotionally, to let me forget all my troubles) were included in this study, but not the social reasons for drinking items (8 items).

Physiological Assessment. Electrocardiogram (ECG) was continuously recorded during the baseline, stimulus presentation, and paced-breathing procedure. The ECG record was collected at a rate of 1,000 samples per second by a Powerlab Acquisition system (ADInstruments, Colorado Springs, CO). Ag-AgCl ECG electrodes were placed on the right arm (active), left arm (ground), and left leg (active). Recorded data were exported to a WinCPRS software program (Absolute Aliens Oy, Turku, Finland) for analyses. The program measured beat-to-beat RR intervals (RRI) of ECG and segmented
the succession of RRIs into 5-minute blocks. RRI spectra were calculated through Fourier analysis (Cooke, et al., 1999; Taylor, et al., 1998) after cubic interpolation of the non-equidistant waveform of the RRI sequence was completed for artifacts and irregular beats. The 0.1-Hz HRV index was calculated as the power of the RRI spectrum at 0.1 Hz for the baseline and each picture block. After applying a natural logarithm transformation to the 0.1-Hz HRV index, within-individual change scores were calculated by subtracting the baseline 0.1-Hz HRV index scores from 0.1-Hz HRV index scores for each of four stimulus cue types to adjust for individual differences in HRV at baseline.

Stimuli. The picture cue exposure task included six categories of picture blocks: emotionally negative, positive, neutral pictures and alcohol-related pictures. The study also included marijuana-related and polydrug-related (cocaine and ecstasy) pictures, but the results were not the interest of the current study. Emotional pictures were selected from the International Affective Picture System (IAPS, Lang, et al., 2001). Negative and positive pictures were matched on standardized ratings of arousal, but varied in valence while neutral pictures were of moderate valence and low arousal (Bradley, Cuthbert, & Lang, 1990). Alcohol-related picture stimuli were from the Normative Appetitive Picture System (NAPS, Stritzke, et al., 2004a), as well as from Tarpert et al. (2003), with additional alcohol-related pictures developed in our lab. In each block, a set of 15 pictures was presented twice; the order of picture presentation within each block was randomized.

Procedures. Eligible participants individually completed one study session that lasted approximately four hours and consisted of a picture study phase, followed by memory task phase that was part of another study. Laboratory sessions were scheduled to
start between 9:30 a.m. and 3:30 p.m., on Mondays through Fridays. All participants were asked to refrain from alcohol or any other drug use 24 hrs prior to the laboratory session, excluding caffeine and cigarettes to avoid experiencing within-session withdrawal symptoms. Upon arrival, participants provided a breath sample to insure zero blood alcohol concentration. All participants provided written informed consent, and were compensated $50.00 for their time, which was distributed as either a check (for college students) or a gift certificate (for inpatients) at the completion of the session. Participants also completed a series of questionnaires to assess demographic information, health status, alcohol and other drug use, and personality, and the Positive and Negative Affect Schedule (PANAS) (Watson, Clark, & Tellegen, 1988) to assess mood state prior to the experiment. The PANAS consists of 20 adverbs that describe positive (e.g., interested, excited, enthusiastic) and negative (e.g., distressed, upset, nervous) mood states. Participants were asked to rate how they feel right now using a Likert type scale, where 1 = Very slightly or not at all, 2 = A little, 3 = Moderately, 4 = Quite bit, and 5 = Extremely.

After the sensors for physiological recording were attached, participants were seated in a comfortable chair located 2.5 m in front of a TV screen in a sound-attenuated, dimly lit room. To equate their cognitive load before picture presentation, participants performed a standardized low-demand “plain vanilla” task (Jennings, et al., 1992) for 5 minutes, wherein they viewed colored rectangles on a computer screen and silently counted the number of blue rectangles. Physiological reactivity during this period served as a baseline.
**Picture presentation.** Each picture cue type was presented in a blocked manner. The blocks were presented in counterbalanced order across participants. In each block, a set of 15 pictures per category was presented twice for a total of 30 pictures per block. Each picture was presented for 5 seconds with a 5-second inter-picture interval, resulting in a 0.1 Hz frequency of picture presentation. Each block lasted for 5 minutes with a 30-second inter-block interval.\(^1\)

**Analysis.** Preliminary analysis of variance (ANOVA) and chi-square tests were performed to examine personality group differences in age, basal 0.1-Hz HRV, gender, and pre-experiment mood state measured by the PANAS. In addition, to better characterize the potential differences in outcomes by personal history of alcohol and other drug use, the following measures were compared between those who were at high risk for AUD and those who had already developed SUD by chi-square test and ANOVA: their representation in each of four groups, BDI-II scores, sensation seeking scores, alcohol use, alcohol-related problems, and reasons for drinking. Because chronic abuse of alcohol and other drugs may suppress HRV (Ingjaldsson, et al., 2003; Mehta, et al., 2001a; Thayer, et al., 2006; Yokoyama, et al., 1991), an ANOVA was also used to compare the 0.1 Hz HRV index at baseline between those who were at high risk for AUD and those who had already developed SUD. To correct the non-linear distributional properties of alcohol use and related problem measures, a natural logarithm transformation was applied to the frequency and quantity of alcohol use in the past 30 days variables, the ADS score, and the two reasons for drinking subscales, after adding a constant of one.
A repeated measures (0.1-Hz HRV index in response to four picture cue types) analysis of covariance (ANCOVA) was conducted to examine between-subject effects (personality group, gender, and personality group × gender), and within-subject effects (picture cue type, picture cue type × personality group, picture cue type × gender, picture cue type × personality group × gender) on changes in the 0.1-Hz HRV index, with substance dependence diagnosis as a covariate. ANCOVA also was used to examine whether alcohol use (frequency of drinking per week for the past 30 days, quantity of drinking per occasion for the past 30 days), use problems (as indicated by ADS score), and the two reasons for drinking (disinhibition and suppression reasons) varied by personality group or gender. All post-hoc mean comparisons were conducted using the Tukey-Kramer post-hoc mean comparison tests.

Results

Personality Group Differences in Background Characteristics and Affect

The study first examined whether personality groups differed in the 0.1-Hz HRV index at baseline as well as other individual characteristics, such as age, gender, and pre-experiment mood state (see Table 2.1). There were no significant differences among the four personality groups with respect to age, gender, or the 0.1-Hz HRV index at baseline. The NE group reported significantly greater negative mood state, as measured by a greater baseline negative PANAS score than the BU and comparison groups. A negative PANAS score has been shown to be highly associated with negative emotionality (Watson, Clark, & Carey, 1988), thus supporting our operationalization of depressive symptoms as an indicator of NE. Finally, no significant gender or gender by group difference interactions were found in BDI and SSS scores ($p > .05$).
Differences Between Participants With and Without Substance Use Diagnoses

A greater proportion of individuals who met substance dependence criteria were classified within the NE and BU + NE groups relative to the BU and comparison groups. Accordingly, those with substance dependence obtained significantly greater total sensation seeking scores (23.57 ± 5.27 and 20.30 ± 6.58, respectively), $F(1, 80) = 5.07, p = .027$, partial $\eta^2 = .060$, and BDI-II scores than those who were only at high risk for AUD (17.19 ± 9.61 and 6.15 ± 5.76, respectively), $F(1, 80) = 30.03, p < .01$, partial $\eta^2 = .273$. Individuals with substance dependence diagnoses also showed a significantly lower baseline 0.1-Hz HRV (8.47 ± 1.33) than those who were at high risk for AUD (9.12 ± 1.21), $F(1, 80) = 4.92, p = .029$, partial $\eta^2 = .057$, indicating the suppressive effects of heavy substance use on basal HRV. Interestingly, there was no significant differences between participants with and without a substance dependence diagnosis in the quantity or frequency of alcohol use in the past 30 days (for the inpatients, 30 days before entering the treatment facility) ($p > .05$); however, those who met criteria for substance dependence reported significantly greater alcohol-related problems, $F(1, 80) = 4.46, p = .038$, partial $\eta^2 = .053$, disinhibition reasons for drinking, $F(1, 80) = 13.87, p < .01$, partial $\eta^2 = .148$, and suppression reasons for drinking, $F(1, 80) = 40.68, p < .01$, partial $\eta^2 = .337$. Therefore, whether or not a participant met criteria for a substance dependence diagnosis (1 = Yes, 0 = No) was included as a covariate in the analyses of the 0.1-Hz HRV index and of alcohol-related problems and reasons for drinking, in order to account for the potential effects of chronic heavy substance use on emotional reactivity and alcohol problems.

The 0.1-Hz HRV Index and Emotional and Alcohol-related Stimuli
A repeated measures ANCOVA revealed a significant effect of personality group, $F(3, 73) = 3.00, p = .036$, partial $\eta^2 = .110$, and a significant personality group $\times$ gender effect, $F(3, 73) = 2.74, p = .049$, partial $\eta^2 = .101$ on changes in the 0.1-Hz HRV index from baseline in response to four emotionally-arousing picture cues (the sphericity assumption was met, Mauchly’s criterion = .93, Chi-square = 5.27, with $df = 5$, $ns$). There was no significant main effect of gender, $F(1, 73) = 0.00, p = .98$, partial $\eta^2 = .000$. For within-subject effects, there was a significant effect of picture cue type, $F(3, 219) = 6.12, p < .01$, partial $\eta^2 = .077$, and a significant effect of picture cue type $\times$ personality group, $F(9, 219) = 2.36, p = .014$, partial $\eta^2 = .089$. There were no significant effects of picture cue type $\times$ gender, $F(3, 219) = 2.09, p = .102$, partial $\eta^2 = .028$, or picture cue type $\times$ personality group $\times$ gender, $F(9, 219) = 0.61, p = .791$, partial $\eta^2 = .024$. Substance dependence diagnosis was not a significant covariate, $F(1, 73) = 1.55, p = .216$, partial $\eta^2 = .021^2$. The average change in 0.1-Hz HRV index from baseline in response to picture cues were significantly greater for negative cues ($1.67 \pm 1.07$) than for neutral ($1.21 \pm 1.16$) ($p < .01$) or positive cues ($1.31 \pm 1.18$) ($p < .01$), and greater for alcohol cues ($1.46 \pm 1.12$) than for neutral ($p < .01$), or positive cues ($p < .01$).

The Tukey-Kramer post-hoc mean comparison test revealed significantly greater 0.1-Hz HRV response to negative picture cues in the NE group, relative to the BU ($p < .01$), BU + NE group and comparison group, and to neutral picture cues in the NE group, relative to the BU group (all $p < .05$). The NE group also showed a trend for greater response to positive picture cues compared with the BU + NE group ($p = .064$). Probing the group-by-gender interaction revealed that only females in the NE group showed a significantly greater 0.1-Hz HRV response to negative picture cues relative to females in
the BU + NE, BU, and comparison groups (all \( p < .05 \)). In addition, females in the NE group showed a significantly greater 0.1-Hz HRV response to neutral picture cues, compared with females in the BU group (\( p < .05 \)). Among females, the NE group showed a trend for greater response to neutral picture cues than the BU + NE group (\( p = .069 \)). There were no significant differences between personality groups in men’s 0.1-Hz HRV response to each picture cue type. Figure 2.1 shows the results of these post-hoc tests.

**Alcohol Use, Alcohol Dependence Scale, and Reasons for Drinking**

Models were significant for the quantity of drinking in the past 30 days, \( F(7, 74) = 2.95, p = .008, R^2 = .22 \), disinhibition reasons for drinking, \( F(8, 73) = 2.69, p = .012, R^2 = .23 \), and suppression reasons for drinking, \( F(8, 73) = 7.55, p < .01, R^2 = .45 \). As shown in Table 2.2, there were main effects of gender and the interaction of personality group and gender on the typical quantity of alcohol consumed per occasion in the past 30 days. Personality group and gender had significant main effects on suppression reasons for drinking. With regard to disinhibition reasons, although the overall model was significant, neither main nor interaction effects achieved statistical significance, suggesting that the effects accounted for shared variance in drinking for disinhibition.

The overall models for ADS score, \( F(8, 73) = 2.05 p = .052, R^2 = .18 \), and for the frequency of drinking in the past 30 days, \( F(7, 74) = 1.06, p = .396, R^2 = .09 \) did not achieve statistical significance. Based on these omnibus tests of personality group and gender main effects, and personality group-by-gender interactions (see Table 2.2), Tukey-Kramer post-hoc mean comparison tests were conducted for significant effects.

The Tukey-Kramer post-hoc mean comparison test revealed significantly greater quantity of alcohol use by men than women (\( p < .01 \), particularly between men and
women in the BU group ($p < .01$). For suppression reasons for drinking, the NE and BU + NE groups scored significantly higher than the comparison group ($p = .030$ and $p < .01$, respectively), and women scored significantly higher than men ($p = .047$). Table 3 summarizes means and standard deviations of alcohol use in the past 30 days, ADS score, disinhibition reasons for drinking, and suppression reasons for drinking by personality group and by personality group-by-gender.

Discussion

The present study employed a novel 0.1-Hz HRV index as a measure of emotional reactivity to examine how arousal modulation by the ANS may act as a unifying biological mechanism underlying the relationships among personality, gender, and motivations for alcohol use. Consistent with the study hypothesis, significantly greater emotional reactivity to negatively-valenced pictures and greater suppression reasons for drinking were observed in individuals with high negative emotionality compared to individuals with low behavioral undercontrol and negative emotionality (i.e., the comparisons). This finding suggests a possible association between physiological vulnerability to stress and alcohol use to suppress negative emotion. Women in the present study reported higher suppression reasons for drinking than men, which may indicate women are more likely to use alcohol to suppress negative thoughts and emotions; a behavior that is associated with a pattern of escalating alcohol use (Labouvie & Bates, 2002). In addition, heightened 0.1-Hz HRV reaction to negatively-valenced emotional pictures was primarily due to differences between women with high negative emotionality and women in the other three personality groups. Thus, increased physiological reactions to negative stimuli, in conjunction with a strong tendency in
women to use alcohol to suppress reaction to such negative stimuli, may be an underlying mechanism by which negative emotionality in women elevates risk for problematic alcohol use behaviors.

The present study also found significant differences in 0.1-Hz HRV response to neutral picture cues between individuals with high behavioral control and individuals with high negative emotionality. Gender-by-personality group analyses suggested that these differences were primarily related to personality group differences among women. Specifically, women with behavioral undercontrol showed significantly lower HRV responses to neutral cues than women with negative emotionality. In terms of emotionally-valenced pictures, however, both male and female with behavioral undercontrol did not show significantly lower 0.1-Hz HRV responses than the other personality groups. Thus, the hypothesis that behavioral undercontrol would be associated with a general ANS under-reactivity was not supported; rather, only a subtle dampening of HRV reactivity to neutral picture cues was observed in women with behavioral undercontrol tendencies.

One distinctive characteristic of behavioral undercontrol, as indicated by sensation seeking, is the propensity to quickly decrease sensitivity to repetitive presentations of non-arousing stimuli (Eysenck, 1994; Zuckerman, et al., 1972). Faster physiological habituation to visual or auditory stimuli has been observed with skin conductance in boys with conduct problems (Zahn & Kruesi, 1993) and with startle response in young adults with high sensation seeking and impulsivity traits (LaRowe, Patrick, Curtin, & Kline, 2006). The current study presented blocks of picture cues (i.e., 30 pictures over 5 minutes) and averaged physiological reactivity across each block. We
did not analyze reactivity to individual pictures, and thus habituation was not measured. Yet, the subtle HRV hyporeactivity to non-arousing neutral stimuli among females with behavioral undercontrol, in conjunction with the general hyperarousal observed in women with negative emotionality, may be due to their fast habituation to non-arousing neutral stimuli. Habituation could also explain the apparent normal physiological reactivity to emotional and appetitive picture cues observed in the behavioral undercontrol group as the result of averaging declining HRV reactions across time. Future studies may benefit from measuring changes in the amplitude of physiological response to individual stimulus cues in addition to mean response across the entire picture cue block to empirically evaluate this possibility.

In addition to demonstrating similar physiological reactivity to non-arousing and arousing stimuli as the comparison group, individuals with behavioral undercontrol also reported similar levels of alcohol use, alcohol-related problems, and use to enhance disinhibition. Furthermore, the exploratory analyses of individuals who were dually affected by behavioral undercontrol and negative emotionality did not reveal evidence for dysregulation in physiological arousal or for greater frequency of alcohol use or related problems, compared with individuals who were low in both personality characteristics. This latter group (i.e., BU + NE), however, did demonstrate greater use of alcohol to suppress negative thoughts and emotions, similar to that reported in the negative emotionality-only group, which may suggest an association between negative emotionality and suppression reasons for drinking. At the same time, lack of significant findings in behavioral undercontrol may indicate that the manner in which the operationalization of the construct of behavioral undercontrol was not optimal. For
example, the present study used the total score of Zuckerman’s sensation seeking Scale. Although strong associations have been demonstrated between a total score and alcohol-related problems, some have found that the subscales of the sensation seeking scale, especially those from the Disinhibition subscale, may have been more sensitive to detecting risk for alcohol-related problems in sensation seekers (see Hittner & Swickert, 2006 for a review). Moreover, negative emotionality and behavioral undercontrol are conceptualized as complex personality constructs comprised of multiple personality dimensions; however, the present study’s operationalization of each of these constructs was based on a single indicator. Future research may benefit from integrating multiple indicators of negative emotionality and behavioral undercontrol in a large sample to better characterize emotional regulation associated with these personality constructs.

To specifically examine emotional reactivity in those in the upper range of alcohol use and related problems, the present sample included individuals at high risk for problematic use of alcohol (i.e., college student who participated in a college counseling program or college athletes) and those who have already developed alcohol and/or other drug use disorders (i.e., inpatient treatment sample). Consistent with previous studies (Ingjaldsson, et al., 2003; Mehta, et al., 2001a; Thayer, et al., 2006; Yokoyama, et al., 1991), substance dependent individuals showed significantly lower 0.1-Hz HRV index at baseline. Thus, it is possible that the prior heavy substance use patterns in substance dependent individuals could have obscured the influence of behavioral undercontrol and negative emotionality, and gender, on emotional reactivity by limiting the maximum HRV responses in this subset of participants, particularly among men. Further, although there were no significant differences in frequency and quantity of alcohol use, between
those who were at high risk for problematic alcohol use and those who had already
developed a substance use disorder, more substance dependent individuals were
classified in the NE and BU + NE groups, and they reported more depression symptoms,
sensation seeking needs, alcohol-related problems, and reasons for drinking. In the
traditional view of substance use behaviors, such differences by the severity of the
problems may typically be considered as confounders, thus we accounted for differences
in the severity of alcohol and other drug use problems in the main analyses. However,
although this strategy increased the statistical power of the analyses, a dependence
diagnosis was not a significant covariate in the analysis of emotional reactivity. Kazdin
and Nock (2003) proposed that examining a dose-response relation should be an
important research direction in understanding the causal role of proposed mechanisms in
behavioral change. The present study combined individuals who varied in personal
history of severity of alcohol and other drug use problems and who are typically
compared as separate populations. That we found greater personality and motivational
risks for problematic alcohol use in individuals with a history of more severe use
problems suggests that there is a gradient in the impact of risk for AUD on substance use
problems, and supports the need of examining alcohol or other drug use behavior with a
continuous approach rather than a dichotomous approach based on clinical diagnosis.

The present results, while compelling, should be interpreted cautiously because of
these study limitations. Nonetheless, the present results support the utility of HRV in
characterizing risk for problematic alcohol use behaviors in individuals with different
personalities and different reasons for using alcohol. A potential link between sensitivity
to negative emotion and self-reported drinking to suppress negative emotion, particularly
among women, was captured by the 0.1-Hz HRV index. Therefore, accounting for personality factors may be more important for characterizing emotional reactivity among women as opposed to men. In addition, observed differences in autonomic modulation of arousal by personality and gender may have important implications for the development of new prevention and intervention strategies. These data encourage integration of biological markers, such as HRV, as a potential future direction in risk assessment and treatment for AUD. HRV is particularly appealing as an intervention target as it is sensitive to internal and external stimulation and can be positively changed through behavioral training, such as HRV biofeedback. HRV biofeedback has been shown to improve autonomic balance and flexibility (i.e., the ability of the ANS to properly respond to changes in the environment) (Lehrer, et al., 2003; Vaschillo, et al., 2002). Cardiovascular resonance frequency paced-breathing HRV biofeedback has been used in the successful treatment of asthma (Lehrer, et al., 2004), depression (Hassett, et al., 2007; Karavidas, et al., 2007), anxiety and phobia (Chernigovskaia, Vaschillo, Petrash, & Rusanovskiĭ, 1990), and hypertension (McCraty, Atkinson, & Tomasino, 2003), and thus has important clinical implications for the treatment of substance use disorders, which are also associated with emotional dysregulation (Thayer & Lane). In conclusion, the present study offers preliminary evidence for the utility of HRV as a biological marker of emotional dysregulation associated with personality risk in women and a treatment tool that can counteract autonomic dysregulation that may motivate a woman to use alcohol.
Footnotes

1 During the 5-second picture-off interval, participants verbally provided a liking or an arousal rating with the order of ratings counterbalanced across sets within blocks. Using the Self-Assessment Manikin (SAM, Lang et al., 2001), participants also verbally provided a liking or an arousal rating during the 5-second picture-off interval, with the order of ratings counterbalanced between subjects. However, the results are not presented here.

2 Without including substance dependence status, the pattern of the findings was essentially the same, but with less statistical significance due to loss of power.
References


application of power spectrum analysis of heart rate variability at rest and in response to recollection of trauma or panic attacks. *Psychiatry Research, 96*(1), 1-13.


Table 2.1

Participants Characteristics

<table>
<thead>
<tr>
<th></th>
<th>BU + NE (n = 23)</th>
<th>BU (n = 19)</th>
<th>NE (n = 19)</th>
<th>Comparison (n = 21)</th>
<th>F statistics/Chi-Square</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>21.7 (2.77)</td>
<td>20.6 (3.17)</td>
<td>21.8 (2.93)</td>
<td>20.5 (1.78)</td>
<td>$F(3, 78) = 1.34$</td>
</tr>
<tr>
<td>% female</td>
<td>30.4</td>
<td>31.6</td>
<td>36.8</td>
<td>61.9</td>
<td>$\chi^2 (3) = 5.70$</td>
</tr>
<tr>
<td>% inpatient treatment</td>
<td>56.5</td>
<td>15.8</td>
<td>47.4</td>
<td>9.5</td>
<td>$\chi^2 (3) = 15.33^‡$</td>
</tr>
<tr>
<td>sample</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANAS (pre)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>29.4 (6.58)</td>
<td>30.8 (7.25)</td>
<td>31.3 (8.99)</td>
<td>27.8 (7.93)</td>
<td>$F(3, 78) = 0.85$</td>
</tr>
<tr>
<td>Negative</td>
<td>13.6 (3.37)</td>
<td>12.2 (2.19)</td>
<td>16.2 b, d</td>
<td>12.3 (3.13)</td>
<td>$F(3, 78) = 5.35^†$</td>
</tr>
<tr>
<td>BDI-II</td>
<td>17.8 b, d</td>
<td>2.8 b, d</td>
<td>14.8</td>
<td>2.8 b, d</td>
<td>$F(3, 78) = 55.29^‡$</td>
</tr>
<tr>
<td>SSS</td>
<td>26.0 c, d</td>
<td>26.6 c, d</td>
<td>17.0</td>
<td>15.5</td>
<td>$F(3, 78) = 46.33^‡$</td>
</tr>
<tr>
<td>0.1-Hz HRV</td>
<td>8.7</td>
<td>9.3</td>
<td>8.5</td>
<td>9.1</td>
<td>$F(3, 78) = 1.38$</td>
</tr>
<tr>
<td>Index -Baseline</td>
<td>1.34</td>
<td>1.16</td>
<td>1.31</td>
<td>1.26</td>
<td></td>
</tr>
</tbody>
</table>
Notes. Numbers in parentheses indicate standard deviations; PANAS = Positive Affect and Negative Affect Schedule; BDI-II = Beck Depression Inventory II (Beck, et al., 1996). 0-13 = minimal depression and 14-19 = mild depression; SSS = Zuckerman’s sensation seeking scale (Zuckerman, 1994); \(^1\) = Negative Affect score was transformed with natural logarithm for the analysis; \(^2\) = BDI-II score was transformed with natural logarithm for the analysis for comparison of four groups; \(^\dagger\) \(p < .05\); \(^\ddagger\) \(p < .01\); \(^a\) = significantly greater than the BU + NE group \((p < .05)\); \(^b\) = significantly greater than the BU group \((p < .05)\); \(^c\) = significantly greater than the NE group \((p < .05)\); \(^d\) = significantly greater than the comparison group \((p < .05)\).
Table 2.2

ANOVA Table for Personality Group, Gender, Personality Group-by-Gender Differences in Quantity of Drinking, Alcohol Related Problems, and Reasons for Drinking

<table>
<thead>
<tr>
<th></th>
<th>F (df)</th>
<th>p</th>
<th>Effect size (partial $\eta^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantity of drinking (per occasion in the past 30 days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personality Group</td>
<td>0.38 (3, 74)</td>
<td>.771</td>
<td>.015</td>
</tr>
<tr>
<td>Gender</td>
<td>10.13 (1, 74)</td>
<td>.002</td>
<td>.120</td>
</tr>
<tr>
<td>Personality Group × Gender</td>
<td>3.40 (3, 74)</td>
<td>.022</td>
<td>.121</td>
</tr>
<tr>
<td>Disinhibition reasons for drinking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personality Group</td>
<td>2.41 (3, 73)</td>
<td>.074</td>
<td>.090</td>
</tr>
<tr>
<td>Gender</td>
<td>0.06 (1, 73)</td>
<td>.441</td>
<td>.008</td>
</tr>
<tr>
<td>Personality Group × Gender</td>
<td>0.01 (3, 73)</td>
<td>.999</td>
<td>.000</td>
</tr>
<tr>
<td>Suppression reasons for drinking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personality Group</td>
<td>4.27 (3, 73)</td>
<td>.008</td>
<td>.149</td>
</tr>
<tr>
<td>Gender</td>
<td>4.08 (1, 73)</td>
<td>.047</td>
<td>.053</td>
</tr>
<tr>
<td>Personality Group × Gender</td>
<td>0.11 (3, 73)</td>
<td>.952</td>
<td>.005</td>
</tr>
</tbody>
</table>

Notes. ADS = Alcohol Dependence Scale; Partial $\eta^2 = .01, .06, and .14, respectively, for small, medium, and large effect sizes for ANOVA (Cohen, 1988). A substance dependence diagnosis (1 = Yes, 0 = No) was a significant covariate for disinhibition reasons for drinking, $F(1, 73) = 6.36, p = .014$, and suppression reasons for drinking, $F(1, 73) = 26.73, p < .001$. 
Table 2.3

*Alcohol Use and ADS Score by Gender and Overall Sample*

<table>
<thead>
<tr>
<th></th>
<th>BU + NE (n = 23)</th>
<th>BU (n = 19)</th>
<th>NE (n = 19)</th>
<th>Comparison (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantity of drinking (per occasion in the past 30 days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>5.18 (4.84)</td>
<td>8.42 (4.43) G</td>
<td>5.79 (4.30)</td>
<td>3.97 (3.71)</td>
</tr>
<tr>
<td>Women</td>
<td>2.63 (3.52)</td>
<td>2.12 (3.33) G</td>
<td>3.94 (3.52)</td>
<td>4.83 (4.43)</td>
</tr>
<tr>
<td>Overall</td>
<td>3.69 (5.71)</td>
<td>4.22 (5.23)</td>
<td>4.78 (5.23)</td>
<td>4.38 (5.41)</td>
</tr>
<tr>
<td>Frequency of drinking (per week in the past 30 days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>2.35 (4.64)</td>
<td>2.90 (4.25)</td>
<td>1.90 (4.12)</td>
<td>2.04 (3.48)</td>
</tr>
<tr>
<td>Women</td>
<td>1.77 (3.31)</td>
<td>1.58 (3.14)</td>
<td>1.96 (3.31)</td>
<td>2.50 (4.25)</td>
</tr>
<tr>
<td>Overall</td>
<td>2.04 (5.47)</td>
<td>2.14 (5.06)</td>
<td>1.93 (5.01)</td>
<td>2.26 (5.22)</td>
</tr>
<tr>
<td>ADS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>10.64 (4.76)</td>
<td>8.91 (4.40)</td>
<td>8.89 (4.23)</td>
<td>4.04 (3.62)</td>
</tr>
<tr>
<td>Women</td>
<td>8.01 (3.44)</td>
<td>7.83 (3.28)</td>
<td>6.86 (3.44)</td>
<td>6.24 (4.43)</td>
</tr>
<tr>
<td>Overall</td>
<td>9.23 (5.61)</td>
<td>8.35 (5.23)</td>
<td>7.81 (5.14)</td>
<td>5.02 (5.41)</td>
</tr>
<tr>
<td>Disinhibition reasons for drinking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>3.99 (4.88)</td>
<td>3.40 (4.51)</td>
<td>3.93 (4.33)</td>
<td>2.19 (3.76)</td>
</tr>
<tr>
<td>Women</td>
<td>4.83 (3.57)</td>
<td>3.88 (3.28)</td>
<td>4.55 (3.57)</td>
<td>2.48 (4.58)</td>
</tr>
<tr>
<td>Overall</td>
<td>4.39 (5.71)</td>
<td>3.63 (5.36)</td>
<td>4.23 (5.27)</td>
<td>2.33 (5.59)</td>
</tr>
<tr>
<td>Suppression reasons for drinking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>6.50 (4.88)</td>
<td>5.65 (4.51)</td>
<td>5.70 (4.33)</td>
<td>2.72 (3.76)</td>
</tr>
<tr>
<td>Women</td>
<td>9.99 (3.57)</td>
<td>6.86 (3.28)</td>
<td>9.12 (3.57)</td>
<td>4.24 (4.58)</td>
</tr>
<tr>
<td>Overall</td>
<td>8.06 (5.71)\textsuperscript{a}</td>
<td>6.23 (5.36)</td>
<td>7.21 (5.27)\textsuperscript{a}</td>
<td>3.40 (5.59)</td>
</tr>
</tbody>
</table>

Notes. Numbers in parentheses indicate standard deviations; Means and standard deviations are raw scores (i.e., non log-transformed) with adjustment for inpatient sample; The personality group and/or gender comparisons were based on log-transformed data; For the individuals who were from the inpatient treatment facility, all questions were asked in the time frame of 30 days before entering the treatment facility; ADS = Alcohol Dependence Scale, A score of 9 or more is highly predictive of DSM diagnosis of alcohol dependence (Skinner & Horn, 1984); Score ranges for disinhibition and suppression reasons were 0-16, and 0-26, respectively; \textsuperscript{G} = significant differences between men and women ($p < .05$); \textsuperscript{a} = significantly different from the comparison group ($p < .05$).
Figure Caption

*Figure 2.1.* Means and 95% confidence intervals for 0.1-Hz HRV responses to emotional picture cues and alcohol- and drug-related picture cues in overall sample (upper figure), in women (middle figure), and in men (lower figure). NG = Negative, PS = Positive, NT = Neutral, AL = Alcohol. The horizontal x-axis line at y = 0 indicates the reference line for no within-person change in 0.1 Hz HRV. The 0.1-Hz HRV index above y = 0 indicates increased response to the picture cues from baseline. The 0.1-Hz HRV index below y = 0 indicates decreased response to the picture cues from baseline. Statistically significant lower 0.1-Hz HRV responses than the DEP group (†p < .01; †p < .05; *p < .10).
Figure 2.1.

Overall ($N = 82$)

Women ($n = 33$)
Changes in the 0.1-Hz HRV Index (log)

Men ($n = 49$)
CHAPTER 4

STUDY 3

Latent Class Analysis of Risk for Problematic Alcohol Use: Integration of Psychophysiological and Psychosocial Factors

Abstract

This study aimed to identify subtypes of risk for problematic alcohol use among 163 college students based on differences in psychological (personality and affective) and familial risk indicators using latent class analysis. Three latent classes were identified: Negative Affect Risk (high negative affect state), Negative Affect and Personality Risk (high negative affect state and personality tendencies for negative emotion and high behavioral control), and Comparison. Following class identification, differences in alcohol use behaviors and in neurophysiological capacity to adapt to environmental challenge were examined across the classes. The two high risk classes demonstrate greater alcohol-related problems and reasons for drinking (social, disinhibition, suppression) relative to the comparison class. During the paced-breathing, the High Negative Affect Risk class displayed suppressed reactivity in the 0.1-Hz HRV index relative to the other two classes. This class also demonstrated increased HF HRV whereas the two other classes showed decreases. Together with elevated alcohol-related problems and motivations for alcohol use to regulate emotion, these results support physiological dysregulation as an important underlying mechanism linking negative emotionality, particularly high negative affect state, and problematic alcohol.
Introduction

The ability to employ healthy strategies to regulate emotion in response to a changing environment has a profound affect on an individual’s physical and psychological well-being (Appelhans & Luecken, 2006; Giardino, et al., 2000). A central motivation for drinking alcohol, interestingly, is the desire to regulate positive and negative emotions (Cooper, et al., 1995; Cox & Klinger, 1988b). This suggests that relative deficits in more adaptive strategies for self-regulating one’s emotional state may contribute to unhealthy alcohol use. Maladaptive use of alcohol to regulate emotions has been linked to constructs such as behavioral undercontrol and negative emotionality, each of which may reflect a distinct psychological predisposition towards an equally ineffective emotional response strategy of increased alcohol use. The present study used self-report measures of the constructs of behavioral undercontrol (e.g., sensation seeking, impulsivity) and negative emotionality (e.g., anxiety sensitivity, depression), and family history of psychopathology, in an effort to identify homogeneous subtypes of persons at risk for problematic alcohol use behaviors. Quantitative psychophysiological indices then were used to characterize subtype differences in underlying physiological mechanisms of emotional self-regulation.

Behavioral undercontrol is a multidimensional construct characterized by highly disinhibited behavioral patterns, strong motivational tendencies to seek immediate reward, and failure to predict negative consequences of immediate reward seeking behaviors (Colder & Chassin, 1997; Sher & Trull, 1994). Dimensions of behavioral undercontrol, such as sensation seeking and impulsivity, are associated with drinking to enhance positive emotion (Comeau, et al., 2001; Simons, et al., 2005), engaging in
greater alcohol use and experiencing greater alcohol-related problems (Johnson & Cropsey, 2000; MacKillop, et al., 2007; Martin, et al., 2000; Sher & Trull, 1994), as well as having an increased sensitivity to the stimulant and pleasurable effects of alcohol (Brunelle, et al., 2004; Erblich & Earleywine, 2003). Negative emotionality, on the other hand, is a construct that has been identified as a psychological vulnerability to experiencing negative emotion regardless of the situation (Watson & Clark, 1984). It is related to personality dimensions such as anxiety sensitivity (Cox, Fuentes, Borger, & Taylor, 2001; Zvolensky & Schmidt, 2007), defined as the fear of experiencing anxiety and anxiety-related bodily sensation (Reiss, 1987), and introversion (Gudleski & Shean, 2000; Roy, 1991; Schrader & Tsourtos, 1996), which is characterized by low levels of positive affect and less optimism and energy (Watson, Clark, McIntyre, & Hamaker, 1992). Symptoms of depression and anxiety have been positively associated with coping reasons for drinking in community samples (Bolton, et al., 2008; Robinson, et al., 2008) as well as in samples of individuals with alcohol use disorders (AUD) (Cooper, et al., 1992; Holahan, Moos, Holahan, Cronkite, & Randall, 2003; Holahan, et al., 2004). Moreover, relative to non-anxious/non-depressed individuals, those with such disorders show a higher prevalence of AUDs (Grant, Stinson, et al., 2004), greater and more frequent use of alcohol, and greater alcohol-related problems (Buckner, Timpano, Zvolensky, Sachs-Ericsson, & Schmidt, 2008). These findings suggest an important relationship between extent of alcohol use, use of alcohol to regulate emotion, and psychological constructs such behavioral undercontrol and negative emotionality.

Family history of psychopathology is a well-studied risk factor that affects alcohol use behaviors through a complex interaction of genes and environment (Newlin
According to one population-based study, a positive family history of AUD increases the odds ratio of developing alcohol dependence by 0.45 among those with a second or third degree relative with a current or past AUD, by 0.68 among those with a first degree relative with a current or past AUD, and by 1.67 among those with a multi-generational family history, relative to those without a family history of AUD (Dawson, et al., 1992). Similarly, a positive family history of other drug use disorders (Merikangas, et al., 1998; Nurnberger, et al., 2004) and family history of depression (Merikangas, et al., 1985; Stallings, et al., 1997) are also associated with an increased risk of developing an AUD. Thus, empirical evidence suggests the contribution of a family history of psychopathology heightens risk of maladaptive alcohol use, although the paths through which heightened risk occurs are not entirely clear.

The potential roles of multiple psychological and familial risk factors in defining motivations for drinking reflect the complexity and heterogeneity of the etiological pathways to AUD. Yet, little is known about how family history interacts with, or promotes, psychological risk factors to affect an individual’s overall risk for problematic alcohol use. One approach to better understanding how the dynamic interplay of multiple risk factors leads to the development of maladaptive alcohol use is to attempt to identify smaller, homogeneous subgroups of individuals based on level or type of risk for problematic alcohol use and using person-centered quantitative approaches such as latent class analysis (LCA). In this study, homogeneous groups were identified among college students with different profiles of affective, personality, and familial risk based on the interdependent action of multiple observed variables at the level of the individual (Bates, 2000). The development of risk profile subtypes may be useful for characterizing
different patterns of alcohol use behaviors, and potentially different etiological pathways to AUD, by identifying underlying psychological and physiological mechanisms that contribute to risky alcohol use (Babor & Caetano, 2006). Accordingly, the present study examined (1) whether individuals could be categorized into different unobservable (latent) classes based on observed levels and types of risk, and (2) whether these classes differed in alcohol use behaviors, alcohol-related problems, reasons for drinking and physiological indices of emotional regulation.

Regulation of emotion is achieved through the coordinated activity of multiple systems, including the central and autonomic nervous systems. These systems play a fundamental role in regulating emotion by modulating peripheral arousal response to environmental demands (Appelhans & Luecken, 2006; Thayer & Lane, 2000). In particular, vagal activity has received substantial attention in studies of emotion regulation because it conveys the inhibitory inputs from the brain to the heart and causes rapid changes in heart rate (HR) in response to internal and external cues (Porges, 1991; Porges, et al., 1994). Suppressed vagal activity has been associated with emotional dysregulation disorders such as depression (Nahshoni, et al., 2004; Rottenberg, et al., 2007), anxiety (Bleil, Gianaros, Jennings, Flory, & Manuck, 2008; Friedman & Thayer, 1998; Thayer, et al., 1996), and panic disorders (Cohen, et al., 2000). A high frequency (HF; RR interval within 0.15-0.4 Hz) heart rate variability (HRV) index accurately captures the complex changes in HR due to vagal activity and may be useful for assessing emotion, attention, and behavioral regulation (e.g., Doussard-Roosevelt, et al., 1997; Porges, 1991; Porges, Doussard-Roosevelt, Portales, & Greenspan, 1996).

In addition, a 0.1-Hz index of HRV (in the low frequency range, RR interval
within 0.04-0.15 Hz) may be useful in examining emotional regulation based on its relationship to the resonance properties of the HR baroreflex system. The baroreflex is a reflexive control process that helps stabilize blood pressure (Cevese, et al., 2001) and control cortical arousal (Dworkin, et al., 1994; Elbert, et al., 1992; Nyklicek, et al., 2005; Rau, et al., 1993; Yasumasu, et al., 2006). The resonance frequency of the HR loop of the baroreflex is the frequency at which maximal HR oscillations, and thus maximal HRV, in response to changes in blood pressure are observed (Angelone & Coulter, 1964; deBoer, Karemaker, & Strackee, 1987; Halamek, et al., 2003; Legramante, et al., 1999).

Stimulating the baroreflex at 0.1 Hz by, for example, breathing at this frequency (one breath per 10 seconds) has been found to induce strong HR oscillations (Song & Lehrer, 2003; Vaschillo, et al., 2004) and allows evaluation of an individual’s maximal regulatory capacity in response to environmental demands (Vaschillo, et al., 2002). The present study characterized individual differences in emotional regulation based on these two indices of HRV in order to capture the activity of two different physiological subsystems that help determine capacity to self-regulate emotional arousal.

In summary, the goal of this study was to examine whether subtypes of alcohol use risk could be identified based on different propensities for emotional dysregulation by classifying unobserved heterogeneity in the integrated operation of multiple psychological (personality and affective) and familial (alcoholism, depression, and other drug use) risk indicators at the level of an individual. Following identification of the best fitting latent class model, the study further examined whether the latent classes differed in alcohol use behaviors and problems, motivations for use, and the flexibility of vagal and baroreflex control, as indicated by HF HRV and 0.1-Hz HRV responses to breathing at a
rate of ~ 0.1 Hz.

Methods

Participants

A total of 163 college students (52.7% women) were included in this study. Participants were from one of two larger on-going studies. One study examined emotional regulation and memory at varying developmental stages of substance use. **Sixty-one** participants (34 women) from this study were college students who were considered at elevated risk for maladaptive alcohol use due to (1) college alcohol policy infractions ($n = 48$) (infractions ranged in severity from being in a dorm room when alcohol was present to emergency room visit for alcohol poisoning, White, et al., 2006); or (2) being a college varsity athlete ($n = 13$) (Nelson & Wechsler, 2001; Yusko, et al., 2008). Participants interested in the larger study were screened through a structured telephone interview (Ray, et al., 2004; Tracy & Bates, 1999) and excluded if they reported a current psychiatric diagnosis (i.e., past 12 months), a history of alcohol and/or other drug use dependence, current use of psychoactive medication, or any medical condition that might interfere with physiological recording (e.g., use of beta blockers, diagnosis with severe asthma or a cardiac condition).

One hundred and two (52 women) 21 to 24 year old social drinkers were selected from a second study that examined the effects of acute alcohol on memory and emotion regulation (see Udo, et al., in press; Vaschillo, et al., 2008 for procedures), which included administration of one of three beverages: alcohol, placebo, and non-alcohol. Participants from this larger study were recruited through university and community bulletin board and newspaper advertisements for social drinkers. Individuals were excluded if they reported a
psychiatric diagnosis and/or treatment for a psychiatric disorder in the past year, a lifetime history of a psychotic disorder, a history of neurological disorder or treatment, a history of alcohol and other drug use dependence, history of any substance abuse treatment, any substance abuse on the part of the prospective participant’s biological mother during pregnancy (to rule out prenatal exposure effects), medical conditions that preclude alcohol administration or confound interpretation of HRV (e.g., diabetes, heart disease, abnormal HR pattern), more than 20% over- or under-weight from the ideal for gender, height, and body frame based on the Metropolitan Life Height-Weight Table (1983), or reported weekly use of illicit or prescribed drug use other than alcohol. In addition, women were excluded, based on a urinalysis, if determined to be pregnant. Participants were selected for the present study only if they received a non-alcoholic beverage; to rule out acute alcohol and placebo effects on HRV (Vaschillo, et al., 2008), individuals in the alcohol and placebo conditions were excluded.

The majority of the participants were non-Hispanic White (62.6%); 22.1% were Asian, 3.1% were non-Hispanic African American, and the remaining identified themselves as “other” (12.2%). Participants had an average of 14.7 years of education ($SD = 1.52$). The mean age was 21.0 years ($SD = 1.32$) and 90.2% of the sample reported a family income of more than $41,000.

**Measures**

*Depression and anxiety symptoms.* The Beck Depression Inventory II (BDI-II, Beck, et al., 1996) and the Beck Anxiety Inventory (BAI, Beck & Steer, 1990) were used to assess depression and anxiety symptoms, respectively, to assess negative affect state. The BDI-II contains 21 items that indicate the presence and degree of depression
symptoms occurring in the past two weeks. The total score ranges from 0 to 63, where scores from 0-13 = minimal depression, 14-19 = mild depression, 20-28 = moderate depression, and 29-63 = severe depression. Various psychometric properties of the BDI-II, including internal consistency, test-retest reliability, content validity, construct validity, and factorial validity, have been established in psychiatric male and female outpatient samples from both suburban and urban areas, as well as male and female college student samples (see, Beck, et al., 1996).

The BAI contains 21 items that measure the severity of self-reported anxiety occurring in the past two weeks. The total score ranges from 0 to 63, where scores from 0-7 = minimal anxiety, 8-15 = mild anxiety, 16-25 = moderate anxiety, and 25-63 = severe anxiety. All items (i.e., both BDI and BAI) were rated on a 4-point Likert type scale (0 = Not at all to 3 = Severely). The psychometric properties of the BAI has been established in both psychiatric clinical sample and non-clinical samples, including internal consistency, test-retest reliability, content validity, concurrent validity, construct validity, discriminant validity, and factorial validity (see, Beck & Steer, 1990).

*Personality.* The Zuckerman Sensation Seeking Scale-V (Zuckerman, 1994) was used to measure sensation seeking. This scale was originally developed to quantify individual differences in optimal level of arousal (Zuckerman, et al., 1964). It has been translated into different languages, and applied in different cultures; reliability, validity, and factorial structure of the scale has been examined by many hundreds of studies with different types of populations (Zuckerman, 1979a, 1994, 2007). This scale has four subscales in addition to the overall sensation seeking score: experience seeking, boredom susceptibility, disinhibition, and thrill and adventure seeking; however the present study
focused on the disinhibition scale (DIS, 10 items) as the DIS is the most strongly associated with alcohol use of the four sensation seeking subscales (see Hittner & Swickert, 2006, for a review). Individuals with high disinhibition are suggested to seek sensation through other people or partying, social drinking, and sex (Zuckerman, 1994; Zuckerman, et al., 1972). Participants choose from paired statements which one better describes him/herself. An example of a subscale item is “I like ‘wild’ uninhibited parties” vs. “I prefer quiet parties with good conversations.”

The Substance Use Risk Profile Scale (SURPS) (Woicik, Conrod, Stewart, & Pihl, 2008) was used to assess personality and motivational risk factors associated with substance use. The SURPS was developed via a factor analysis of a battery of personality and psychopathological symptoms (see Conrod, Pihl, Stewart, & Dongier, 2000, p. for the development of the scale). The SURPS contains 23 items with four subscales: introversion/hopelessness, anxiety sensitivity, impulsivity and sensation seeking. The SURPS has been used to characterize the relationship between personality and substance use behaviors in female substance abusers, and non-clinical college male and female students (Krank, et al., in press; Woicik, Conrod, & Pihl, in press). Psychometric properties have been demonstrated with female substance abusers and non-clinical college male and female students, which include internal consistency of each subscales, test-retest reliability, factor structure, concurrent validity, discriminant validity, predictive validity in past year alcohol and other drug use, and validity of scales to differentiate DSM-III-R and DSM-IV lifetime psychiatric and psychoactive use disorders, predictive validity (Krank, et al., in press; Woicik, et al., in press). Although the sensation seeking scale from the SURPS was developed using all four subscales of Zuckerman’s (1994)
Sensation Seeking Scale, the items correspond primarily with the Thrill and Adventure Seeking subscale, thus suggesting that the inclusion of both measures of sensation may increase our ability to fully capture personality risks related to behavioral undercontrol.

*Family history.* Following the initial screening interview, a semi-structured phone interview was conducted to assess familial history of psychopathology using the Family History Assessment Module (FHAM) (Janca, Bucholz, & Janca, 1992). The FHAM was originally developed for the Collaborative Studies on Genetics of Alcoholism (COGA) Project to assess AUD, other drug use disorders, depression, mania, schizophrenia, and other drug use disorders in relatives of the person being interviewed (Rice, et al., 1995). Through a direct interview of more than 2,500 individuals, Rice et al. (1995) demonstrated the validity of the FHAM in screening for DSM-III-R psychiatric disorders. For each type of psychopathology, a relative with three or more clinical symptoms is considered positive for the disorder.

*Alcohol use and related problems.* Alcohol use for the past 30 days was quantified by multiplying frequency of alcohol use per week and quantity of alcohol use per occasion in the past 30 days, which were obtained through the standardized Alcohol and Drug Use Questionnaire (Rutgers Health and Human Development Project, Pandina, et al., 1984) with demonstrated reliability and validity (Bates & Labouvie, 1997; Labouvie & McGee, 1986; Pandina, et al., 1984). Alcohol-related problems in the past 12 months were assessed using the Alcohol Dependence Scale (ADS), which was developed to assess the severity of the alcohol dependence symptoms (ADS, Skinner & Horn, 1984). The ADS consists of 25 items related to alcohol withdrawal symptoms, awareness of a compulsion to drink, increased tolerance to alcohol, impaired control over drinking, and
salience of alcohol-seeking behavior (e.g., do you often have hangovers on Sunday and
Monday mornings?, Do you get physically sick as a result of drinking?). This scale has
been used to characterize alcohol-related problems in individuals with an AUD as well as
in non-clinical samples (e.g., Connor, et al., 1999; Connor, et al., 2000; Kahler, et al.,

*Reasons for Drinking*. Reasons for alcohol use were assessed using a reliable and
valid Reasons for Drinking Questionnaire (Labouvie & Bates, 2002), which consists of
three subscales: social reasons (e.g., it tastes good, to have some fun and enjoy things
better), disinhibition reasons (e.g., to help me express certain feelings more freely, to make
it easier to lose control over certain feelings or desires), and suppression reasons (e.g., to
help me feel better emotionally, to let me forget all my troubles). The questionnaire
contains 29 items describing reasons for using alcohol. Participants were asked to rate
each statement using a three-point Likert type scale (0 = not at all important, 1 =
somewhat important, 2 = very important).

*Physiological record*

Electrocardiogram (ECG) was continuously recorded during the baseline
assessment and paced-breathing procedure. The ECG record was collected at a rate of
1,000 samples per second by a Powerlab Acquisition system (ADInstruments, Colorado
Springs, CO). Ag-AgCl ECG electrodes were placed on the right arm (active), left arm
(ground), and left leg (active). Recorded data were exported to a WinCPRS software
program (Absolute Aliens Oy, Turku, Finland) for analyses. The program measured beat-
to-beat RR intervals (RRI) of ECG and segmented the succession of RRIs into 5-minute
blocks. Frequency domain analysis was completed by calculating RRI spectra through
Fourier analysis (Cooke, et al., 1999; Taylor, et al., 1998) to derive the HF HRV and the 0.1-Hz HRV indices. HF HRV was calculated as variation in HRV at 0.15-0.4 Hz frequency (i.e., calculating the area under the spectral curve between 0.15 and 0.4 Hz). The 0.1-Hz HRV index was calculated as the power of the RRI spectrum at 0.1 Hz (i.e., calculating the amplitude of the HR oscillation at 0.1 Hz), the resonance frequency of the HR baroreflex, for the baseline and paced-breathing procedure.

**Procedures**

All participants provided written consent and individually completed a laboratory session that lasted approximately 3 to 4 hrs. Laboratory sessions were scheduled to start between 9:30 a.m. and 3:30 p.m., Monday through Friday. Participants were asked to refrain from alcohol or other drug use. However, to avoid experiencing withdraw symptoms during the experimental session, participants were allowed to consume caffeine and cigarettes for the 24 hours prior to the laboratory session. Upon arrival, a breath sample was taken to assure that there was no alcohol in the participant’s system at the time of testing. A series of questionnaires then was completed to assess demographics, health status, alcohol and other drug use, alcohol-related problems, depression and anxiety symptoms, and personality.

After completing the questionnaires, the participant was seated in a comfortable chair located 2.5 meters in front of a TV screen that was located in a sound-attenuated, dimly-lit room. Sensors and electrodes were attached to the participant’s arms and legs for recording of physiological responses. First a standardized low-demand task was completed to measure baseline physiological reactivity. This was followed by several stimulus presentation tasks. Briefly, as a condition of the parent studies, participants were
exposed to emotionally-arousing visual stimuli (negative, positively, and emotionally-neutral, and, alcohol-related pictures or words) at a rate of one every 10 seconds while their physiological responses were recorded. They also completed a breathing task, wherein they were asked to breathe (one complete inhalation/exhalation) once every 10 seconds (i.e., ~ 0.1 Hz frequency) for 5 minutes. Response to the breathing task is the focus of the present study. During the 5 minutes, a breathing pacer (E-Z Air, Thought Technology, Ltd., Plattsburgh, NY) was presented on the screen and the participants were instructed to inhale when the pacer went up and exhale when the pacer went down. To avoid hyperventilation, they were told to breathe naturally, not deeply. Thirty nine percent of participants completed the paced-breathing procedure before the visual stimulus presentation tasks; 61% completed the procedure after the visual stimulus presentation tasks. Our preliminary analysis indicated that there was no order effect on HRV response to the paced-breathing procedure. The study protocol was approved by the university institutional review board. All participants were compensated $50.00 for completion of the session.

Analysis

Mplus (Muthén & Muthén, 1998-2007) was used to conduct a Latent Class Analysis to identify unobserved risk classes based on individual responses to the BDI-II (Beck, et al., 1996), BAI (Beck & Steer, 1990), the disinhibition subscale of the Zuckerman’s sensation seeking scale (Zuckerman, 1994), the four subscales of the SURPS (Woicik, et al., 2008), and familial history of AUD, depression, and/or other drug use disorders. LCA requires binary variables, thus participants were categorized into one of two relative risk groups based on their responses to the psychosocial questionnaires:
“1” (higher risk = scored upper 50 percentile) and “0” (lower risk = scored lower 50 percentile). For the family history of each disorder, participants were coded as “1” if they had at least one first or second degree relative with a disorder or “0” if they had no relatives with the disorder.

Latent class models were fitted to two negative affect variables (depression and anxiety symptoms), five personality variables (introversion, anxiety sensitivity, impulsivity, sensation seeking, and disinhibition) and three family history variables (familial AUD, depression, other drug use disorder), using a maximum likelihood approach with missing data assumed to be missing at random (Little & Rubin, 1987). Initially starting with a one class model, classes were added in a stepwise fashion (a maximum of 5 classes), and the goodness of model fit compared. The best-fitting and most stable model was determined based on changes in the Bayesian Information Criteria (BIC), as well as entropy, class size, and the interpretability of classes (Muthén & Muthén, 1998-2007). Gender (1 = female, 0 = male), and race (1 = white non Hispanic, 0 = other) were included in the model as covariates to improve classification accuracy.

After determining the best-fitting model, differences between the latent classes in alcohol use (quantity per occasion × frequency per week for the past 30 days), ADS symptoms, and reasons for drinking (social reasons, disinhibition reasons, suppression reason) were calculated using effect size measurements (calculated as Cohen’s $d$, the mean differences between two latent classes divided by the standard deviation) (Cohen, 1988). In order to examine if HR baroreflex and vagal activation in response to rhythmical stimulation of the cardiovascular system differed across the latent classes, changes from baseline in the 0.1Hz HRV index and HF HRV index during the paced-
breathing procedure were compared. In addition, whether the participant completed the procedure before or after the stimulus presentation was also included as a covariate to control for potential ordering effects.

Results

The mean, standard deviation, and distributional characteristics of each psychosocial variable are presented in Table 3.1. The mean scores of BDI and BAI are consistent with a “minimal symptoms” description of each disorder (Beck, et al., 1996). This is somewhat lower than levels found in previous studies of college samples (Beck, et al., 1996; Creamer, Foran, & Bell, 1995; Osman, Kopper, Barrios, Osman, & Wade, 1997; Whisman, Perez, & Ramel, 2000). The means of the DIS and subscales of SUPER were comparable to available normative data (see Woicik, et al., in press, for SUPER; Zuckerman, 1994, for DIS). This suggests that the sample is representative of the college student population with regard to personality risks associated with alcohol use, but that clinically significant levels of anxiety and depression may be somewhat underrepresented.

With regard to family history, the proportions of participants with positive family history (i.e., at least one first or second relative with the disorder) were 42.4% for AUD, 36.1% for depression, and 13.9% for other drug use disorders. For family history of AUD in college students, Engs (1990) found that 47.0% of undergraduate students reported having a parent or grandparent with possible alcohol abuse. A more recent study reported that 66.4% undergraduate students indicated having problem drinkers in their first, second, or third degree relatives (Capone & Wood, 2008). The prevalence of family history of AUD in the present study is comparable to the findings in Eng (1990). A direct
comparison across studies is difficult as the definition of positive family history, as well as the methods of obtaining information about relatives, differ. In Engs (1990) and Capone and Wood (2008), information about alcohol use behaviors of relatives was obtained through a few questions based on subjective judgment by the proband (e.g., “have any of your blood relatives ever been problem drinkers or alcoholic?”). On the other hand, the present study collected the information on relatives’ alcohol use problems based on DSM-III-R diagnostic criteria, which is a valid, standardized interview for assessing psychiatric disorders among first and second degree relatives. The prevalence of family history of depression and other drug use has not been reported in previous college student samples, to our knowledge.

Results of Latent Class Analysis

Model tests. Fit statistics were compared across models that contained one to five classes (Table 3.2). A three-class solution was determined to be optimal based on changes in BIC, improvements in model fit, and the ability of the three-class solution to identify well-differentiated classes that reflect theoretically meaningful structures of psychosocial risk for AUD. Based on the pattern of probabilities associated with endorsing each psychosocial or familial risk index, the three derived classes were labeled as: (1) Negative Affect Risk including participants with a higher likelihood of depression and anxiety symptoms, but with lower levels of personality and familial risk; (2) Negative Affect and Personality Risk including participants with a high likelihood of negative affect and all dimensions of personality risk, and (3) Comparison including participants with a low probability of all risk indices. Classification accuracies ranged from 0.91 to 0.94 before adding demographic variables, and ranged from 0.93 to 0.96
after adding gender and race as covariates. Classes were not significantly different in the proportion of women (Negative Affect Risk = 46.9%, Negative Affect and Personality Risk = 66.7%, Comparison = 47.0%) or white non-Hispanics (Negative Affect Risk = 57.1%, Negative Affect and Personality Risk = 70.8%, Comparison = 60.6%). The likelihood of family history of AUD, depression, and other drug use was evenly distributed across the three classes.

**Endorsement probabilities.** Figure 3.1 shows the endorsement probabilities for each psychosocial and family history risk factor across latent classes (i.e., the probability that an individual in a given class will exhibit a given psychosocial risk or positive family history). The two high risk classes differed in the endorsement of personality risk variables, particularly in those risks assessed by the SURPS. The Negative Affect and Personality Risk class exhibited high probabilities of endorsing introversion (77.7%), anxiety sensitivity (67.1%), impulsivity (90.0%), and sensation seeking (65.9%) whereas the Negative Affect Risk class exhibited low probability of endorsing those personality risks (20.3%, 9.1%, 0.0%, 13.7%, respectively). The two high risk classes did not differ as much in the probability of endorsing the DIS scale of sensation seeking (Negative Affect Risk = 59.7%, Negative Affect and Personality Risk = 70.3%). The Comparison class exhibited a low probability of endorsing both negative affect and personality risk factors (all below 30%), except for two indices of sensation seeking traits (disinhibition = 47.4% and SURPS sensation seeking = 40.5%). The probabilities of endorsing a positive family history in the Negative Affect Risk Class, the Negative Affect and Personality Risk Class, and the Comparison Class, respectively, were: AUD (40.4%, 49.9%, and
37.6%; depression (39.8%, 43.1%, and 27.7%); and other drug use disorder (12.0%, 27.2%, and 5.1%).

*Latent class differences in alcohol use.* Class differences in alcohol related problems as measured by ADS, and three reasons for drinking scales were assessed using Cohen’s effect size \((d)\) calculation (Table 3.3). The three groups did not differ in alcohol use during the prior 30 days. However, ADS scores were higher in the Negative Affect Risk and the Negative Affect and Personality Risk classes than the Comparison class \((d = 0.49\) and 0.49, respectively) suggesting greater alcohol-related problems in the two high risk classes. Reports of social reasons for drinking were higher in the high risk classes versus the Comparison class \((d = 0.40\) and 0.55, respectively). For the disinhibition reasons for drinking scale, the Negative Affect and Personality Risk class scores, on average, were higher than both the Negative Affect Risks class \((d = 0.50)\) and the Comparison class \((d = 0.98)\). The Negative Affect Risk class scored higher than the Comparison class \((d = 0.48)\). Finally, the Negative Affect and Personality Risks class scored higher in suppression reasons for drinking, compared with either the Negative Affect Risks class \((d = 0.31)\) or the Comparison class \((d = 1.16)\). The Negative Affect class scored higher than the Comparison class \((d = 0.85)\).

*Latent Class Differences in Vagal and Baroreflex.* Differences in physiological reactivity to the paced-breathing procedure were assessed using Cohen’s effect size \((d)\) calculation. At baseline, the Negative Affect Risk class showed a greater level of the 0.1-Hz HRV index than the Negative Affect and Personality Risk class \((d = 0.52)\) and the Comparison class \((d = 0.21)\), and the Comparison class showed greater level of the 0.1-Hz HRV index than the Negative Affect and Personality Risk class \((d = 0.31)\). During the
paced-breathing procedure, the Negative Affect Risk class showed less increase in the 0.1-Hz HRV index than both the Negative Affect and Personality Risk class \((d = 0.50)\) and the Comparison class \((d = 0.28)\). The Comparison class also showed less increase in the 0.1-Hz HRV index when compared to the Negative Affect and Personality Risk class \((d = 0.22)\) (Figure 3.2, upper figure). For HF HRV, there were no differences at the baseline among three classes. While the Negative Affect and Personality Risk and the Comparison classes showed negative changes in HF HRV in response to the paced-breathing procedures from the baseline, the Negative Affect class showed positive changes in HF HRV. Differences in change scores for HF HRV were \(d = 0.46\) between the Negative Affect Risk class and the Negative Affect and Personality Risk class, and \(d = 0.62\) for the Negative Affect Risk class and the Comparison class (Figure 2b, lower figure).

Discussion

Latent Classes Based on Negative Affect, Personality, and Familial Risk Factors

The present study identified subgroups of college students who did not have clinically significant mean levels of alcohol use problems, but differed in their latent risk profile for developing problematic alcohol use behaviors. Three latent classes were identified using a well-fit LCA model that included two high risk classes: one with a high likelihood of exhibiting symptoms related to depression and anxiety disorders and one with a high likelihood of exhibiting depression and anxiety-related symptoms and personality risks related to alcohol use to enhance disinhibition and suppress negative emotion. A comparison class was also identified with a relatively lower likelihood of exhibiting psychosocial risks. The primary differences among the three classes were the
probabilities of endorsing depression and anxiety symptoms in the two high risk classes relative to the comparison class, and the probabilities of higher subscale scores on the SURPS (anxiety sensitivity, introversion, impulsivity, sensation seeking) within combined negative affect and personality risk class relative to the other two class. Family history of psychopathology did not further differentiate the classes.

It is noteworthy that the three latent classes did not greatly differ in disinhibition, as measured by the Zuckerman’s Sensation Seeking scale, despite their differences in the endorsement of impulsivity. This is particularly interesting as dishibition and impulsivity have often been conceptualized in a similar manner, particularly with regard to their relationship with risky alcohol use (Schuckit, 2009; Sher & Trull, 1994). Sensation seeking traits are generally characterized by a need for arousing stimuli, willingness to take risks to obtain an optimal level of arousal, and intolerance to repetitive stimulus presentation (Zuckerman, et al., 1972; Zuckerman, et al., 1964). Individuals with high disinhibition sensation seeking, in particular, are characterized in terms of reduced behavioral constraint and attempts to obtain an optimal level of arousal by social activities, such as parties, social drinking, and sex (Zuckerman, 1994). Impulsivity is a multidimensional construct that has been defined in several different ways. Yet, one commonly described feature is the lack of ability to plan and anticipate long-term outcomes or inhibit risk-taking behaviors in the face of negative consequences (Magid, et al., 2007; Pihl & Peterson, 1995). These features are also represented in the impulsivity subscale items of the SURPS. Although both personality traits are related to a lack of behavioral inhibition, impulsivity seems to reflect decision-making and planning aspects of behavioral disinhibition, whereas the disinhibition sensation seeking reflects
motivational aspects (i.e., the desire to obtain an optimal level of arousal through social activity). Thus, the distinct influences of these seemingly related risk factors on the observed latent class structure suggest that propensity not to plan behavior may influence alcohol use behaviors in college students.

Family history of alcoholism, depression, and other drug use did not contribute to the differentiation of the three classes. This finding was somewhat surprising given that a positive family history is typically a predictor of a proband’s psychiatric problems (Kendler, Davis, & Kessler, 1997; Stallings, et al., 1997) and specifically, increased risk for AUD with symptoms of co-occurring mood disorders and anxiety disorders (Buckner, et al., 2008; Crum, et al., 2008; Grant, Stinson, et al., 2004). Using structural equation modeling, Capone and Wood (2008) also found that a positive family history of AUD was related to alcohol use and related problems through behavioral control. One possible explanation is that our study criteria excluded college students with a personal history of psychopathology or AUD diagnoses; inclusion of these individuals may have thus revealed additional subtypes reflecting both personal and familial risk for problematic alcohol use. Conversely, the present results may suggest that psychological characteristics are more important indicators of risk than familial history of psychopathology in college students. Finally, previous studies have employed variable-centered approaches that focus on the relationships between variables across persons. In contrast, the present person-centered approach seeks to classify subtypes of persons based on the dynamic operation of influences (variables) within the individual. Thus, the proportions of positive family histories in the classes identified here may reflect the natural heterogeneity of paths and outcomes that occur within the population of persons.
with familial histories of psychopathology. Further research is needed to clarify the relationship between psychological risk and family history of psychopathology and problematic alcohol use.

*Latent Classes in Alcohol Use Behaviors and Adaptability to the Environment*

Following the development of the latent risk class model, its validity for characterizing propensity for problematic alcohol use was examined in terms of class differences in alcohol use, alcohol related problems, and reasons for drinking. Although the three classes did not differ in the quantity of alcohol consumed in the past month, the present study revealed greater alcohol use problems in the two high risk classes than in the Comparison class. Both the Negative Affect Risk and Negative Affect and Personality Risk classes reported more social, disinhibition, and negative affect suppression reasons for drinking relative to the Comparison class. Disinhibition and suppression reasons for drinking are two motivations that have been associated consistently with problematic alcohol use (e.g., Cooper, et al., 1995; Kuntsche, Stewart, & Cooper, 2008; Labouvie & Bates, 2002). Combined with greater report of alcohol-related problems, elevated self-report of disinhibition and suppression reasons for drinking may possibly indicate future problematic use of alcohol in individuals classified in the two high risk classes. In particular, that those two classes showed high probability of even low levels of depression and anxiety symptoms suggest a role of negative affect in increasing risk for alcohol-related problems. The report of disinhibition and suppression reasons for drinking was particularly prominent for the Negative Affect and Personality Risk class. Thus negative affect symptoms in the context of personality needs related to alcohol use for emotional regulation, may further increase risk for problematic alcohol
use. The observed differences in alcohol-related risks and reasons for drinking, despite the lack of differences in the amount of alcohol typically drunk, highlights the importance of examining factors other than alcohol use in understanding vulnerability to AUD.

Finally, the present study examined whether the three classes differed with respect to physiological indices that are markers of neurophysiological capacity for adaptation to changes in the environment, specifically, baroreflex sensitivity (0.1-Hz HRV) and vagal activation (HF HRV) during a resonance frequency paced-breathing exercise. The Negative Affect Risk class showed less increase in the 0.1-Hz HRV index from the baseline than the other two classes during the paced-breathing procedure. In addition, the Negative Affect Risk class showed increased vagal activity, as indicated by a greater HF HRV response to paced breathing, while the other two classes showed a decrease in vagal activity. Previously, paced-breathing at ~ 0.1 Hz has been shown to increase in the amplitude of HR oscillation at this frequency, whereas it decreases HF HRV (Hassett, et al., 2007; Karavidas, et al., 2007). By stimulating the baroreflex at its resonance frequency, frequency of HR oscillation may be shifted greatly towards 0.1 Hz, which may have in turn caused reduction in HR oscillation within other frequency bands, including high-frequency band. Therefore, reduced activation of the baroreflex and lack of suppression in vagal activity may indicate weak resonance response by the HR baroreflex system in those with negative affect. Ultimately, this weak resonance response by the HR baroreflex system may suggest that neurophysiological adaptive capacity is somewhat impaired in individuals in the Negative Affect Risk class. Given the role of the baroreflex and vagal activity in emotional regulation (Nyklicek, et al., 2005; Porges, 1991; Porges, et al., 1994; Yasumasu, et al., 2006), such dysregulation may explain the
presence of depression and anxiety symptoms, and report of strong motivations for alcohol use to regulate emotion in individuals in this class. The present study, however, did not find a physiological indication of emotional dysregulation in those who exhibited a high probability of negative affect and personality risk associated with problematic alcohol use behaviors, compared with those who exhibited low risk profiles, although these individuals reported greatest alcohol-related problems, and greatest dishibition and suppression reasons for drinking among three classes. The present findings seem to suggest there is potentially a distinctive etiological pathway for this population to alcohol use to regulate emotion that is unrelated to the physiological mechanisms that were examined.

Limitation and Conclusions

There are several study limitations that should be considered when interpreting these results. First, the sample size was relatively small for LCA. Although there are no guidelines for the optimal sample size to conduct LCA, the stability and accuracy of the information criteria are influenced by sample size (Yang, 2006). Thus, replication of the present results with a larger sample is recommended. Further, due to inclusion and exclusion criteria of the parent studies, the current results generalize most directly to college students without a significant history of psychopathology. The present sample had relatively low average levels of depression and anxiety symptoms that may not be typical of the college student population at large (Beck & Steer, 1990; Beck, et al., 1996). Nevertheless, in the present study, depression and anxiety symptoms differentiated individuals at high and low risk for alcohol-related problems, suggesting that it may be useful to attend to modest levels of depression or anxiety as indicators of increased risk
for alcohol-related problems and the use of alcohol for emotional regulation. Another potential limitation was the transformation of continuous psychosocial variables into dichotomous variables (i.e., high vs. low) as required by the LCA approach. The benefit of using dichotomous variables is its clinical applicability through producing easily understandable results, but a concern is the loss of information on individual variability (Farrington & Loeber, 2000). This may partially compromise the strength of using LCA to capture unobserved subtypes of persons, and the information loss needs to be weighed against the benefits of using this person-centered approach. Future studies that are longitudinal in design may benefit from employing person-centered approaches that utilize continuous data such as latent transition analysis.

Despite these caveats, the present study has useful implications for clinical practice and future research. The results of the LCA support the potential importance of depression and anxiety symptoms, even at the minimal levels reported in this sample, to problematic alcohol use behaviors among college drinkers. Further, the person-centered approach of this study uncovered a dynamic within-person interplay of depression and anxiety symptoms with personality risk (i.e., anxiety sensitivity, introversion, thrill seeking, and impulsive personality traits) that increased the likelihood of reporting alcohol-related problems. Of potentially even greater significance are the results of HRV analyses. The present study suggest that college students with relatively greater levels of depression and anxiety symptoms have dysregulated vagal (and baroreflex) activity in response to the paced-breathing. To our knowledge, this is the first study to link differences in autonomic activity to differences in psychosocial risk factors among subgroups of individuals identified through the person-centered approach. HRV is a
clinically useful biomarker that can be manipulated through behavioral training, such as resonance frequency HRV biofeedback (Lehrer, Vaschillo, & Vaschillo, 2000; Vaschillo, Vaschillo, & Lehrer, 2006b). HRV biofeedback employs a paced breathing exercise to improve baroreflex sensitivity and restore autonomic regulation, which in turn help enhance emotional regulation (Lehrer, et al., 2000). The effectiveness of this biofeedback procedure for increasing HF HRV and improving mood has been demonstrated with individuals experiencing various mental and physical health problems, including those with depression (Hassett, et al., 2007; Karavidas, et al., 2007). The present results support the potential use of this procedure as a preventive intervention tool for youth who are at risk of developing alcohol related problems that result from their use of alcohol in an attempt to regulate mood states.
References


Company, M. L. I. (1983). The Metropolitan Life Height-Weight Table


Table 3.1. *Descriptive Statistics Pertaining to Psychosocial Variables*

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>Skewness</th>
<th>Kurtosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BDI-II</strong></td>
<td>5.58 (5.29)</td>
<td>1.23</td>
<td>1.55</td>
</tr>
<tr>
<td><strong>BAI</strong></td>
<td>4.65 (4.63)</td>
<td>1.24</td>
<td>0.81</td>
</tr>
<tr>
<td>Disinhibition (SSS)</td>
<td>4.97 (2.29)</td>
<td>-0.16</td>
<td>-0.62</td>
</tr>
<tr>
<td>Introversion (SURPS)</td>
<td>11.26 (3.22)</td>
<td>0.99</td>
<td>2.61</td>
</tr>
<tr>
<td>Impulsivity (SURPS)</td>
<td>9.93 (2.70)</td>
<td>0.26</td>
<td>-0.36</td>
</tr>
<tr>
<td>Sensation seeking (SURPS)</td>
<td>16.37 (3.80)</td>
<td>-0.17</td>
<td>-0.57</td>
</tr>
<tr>
<td>Anxiety Sensitivity (SURPS)</td>
<td>12.50 (0.74)</td>
<td>-0.20</td>
<td>-0.47</td>
</tr>
</tbody>
</table>

*Notes.* BDI-II = Beck Depression Inventory II (Beck, et al., 1996). The total score ranges from 0 to 63 with indication of 0-13 = minimal depression, 14-19 = mild depression; BAI = Beck Anxiety Inventory (Beck & Steer, 1990). The total score ranges from 0 to 63 with indication of 0-7 = minimal anxiety, 8-15 = mild anxiety; SSS = Zuckerman’s Sensation Seeking Scale (Zuckerman, 1994); SURPS = Substance Use Risk Profile Scale (Woicik, et al., in press).
Table 3.2. *Latent class analysis fitness statistics*

<table>
<thead>
<tr>
<th>Models</th>
<th>Free parameters</th>
<th>BIC</th>
<th>Differences in BIC between models</th>
<th>Entropy</th>
<th>Estimated group sizes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 class</td>
<td>10</td>
<td>2150.99</td>
<td>---</td>
<td>1.00</td>
<td>163</td>
</tr>
<tr>
<td>2 class</td>
<td>23</td>
<td>2108.90</td>
<td>-42.09</td>
<td>0.77</td>
<td>105, 58</td>
</tr>
<tr>
<td><strong>3 class</strong></td>
<td><strong>36</strong></td>
<td><strong>2096.76</strong></td>
<td><strong>-12.14</strong></td>
<td><strong>0.87</strong></td>
<td><strong>48, 49, 66</strong></td>
</tr>
<tr>
<td>4 class</td>
<td>49</td>
<td>2110.69</td>
<td>19.93</td>
<td>0.87</td>
<td>49, 42, 17, 55</td>
</tr>
<tr>
<td>5 class</td>
<td>62</td>
<td>2145.65</td>
<td>34.96</td>
<td>0.88</td>
<td>36, 17, 44, 22, 44</td>
</tr>
</tbody>
</table>

*Notes. Bold* = optimal model. BIC = Bayesian Information Criteria.
Table 3.3. *Means and Standard Errors Pertaining to Alcohol Use, AlcoholRelated Problems, and Reasons for Drinking by the three derived Latent Classes*

<table>
<thead>
<tr>
<th></th>
<th>Negative Affect and Personality</th>
<th>Negative Affect Risk (n = 48)</th>
<th>Negative Affect Risks (n = 49)</th>
<th>Comparison (n = 66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use ^1</td>
<td>6.22 (1.14)</td>
<td>6.67 (1.13)</td>
<td>6.59 (1.12)</td>
<td></td>
</tr>
<tr>
<td>ADS score</td>
<td>6.51 (1.10) c*</td>
<td>6.54 (1.11) c*</td>
<td>4.70 (1.09)</td>
<td></td>
</tr>
<tr>
<td>Reasons for drinking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social reasons</td>
<td>8.26 (1.04) c*</td>
<td>8.73 (1.04) c†</td>
<td>7.36 (1.06)</td>
<td></td>
</tr>
<tr>
<td>Disinhibition reasons</td>
<td>2.56 (1.11) c*</td>
<td>3.64 (1.12) a* c‡</td>
<td>1.78 (1.12)</td>
<td></td>
</tr>
<tr>
<td>Suppression reasons</td>
<td>3.65 (1.13) c‡</td>
<td>4.64 (1.12) a* c‡</td>
<td>1.89 (1.11)</td>
<td></td>
</tr>
</tbody>
</table>

*Notes:* Numbers in parentheses indicate standard errors. ADS = Alcohol Dependence Scale. Nine or more is highly predictive of DSM diagnosis of alcohol dependence (Skinner & Horn, 1984); ^1 = quantity of drinking × frequency of drinking in the past 30 days; Score ranges for social, disinhibition and suppression reasons were 0-16, 0-16, and 0-26, respectively; a = greater than Negative Affect Risks class; b = greater than Negative Affect and Personality Risks class; c = greater than Comparison class; * = small effect size (0.2 ≤ d < 0.5); † = medium effect size (0.5 ≤ d < 0.8); ‡ = large effect size (0.8 ≤ d).
Figure Captions

*Figure 3.1.* The latent class analysis probability of a given individual endorsing each of the ten psychosocial and family history binary variables. Three unique (statistically independent) classes of endorsement probabilities for psychosocial risks were identified: two with high psychosocial risks (Negative Affect Risk and Negative Affect and Personality Risk) and one with low psychosocial risks (Comparison). FH = Family History.

*Figure 3.2.* Means and 95% confidence intervals for 0.1-Hz HRV responses (upper figure) and HF HRV response (lower figure) to the paced-breathing procedure. The 0.1-Hz HRV index and HF HRV above $y = 0$ indicates increased response to the picture cues from baseline. The 0.1-Hz HRV index and HF HRV below $y = 0$ indicates decreased response to the picture cues from baseline. $a =$ greater than High Negative Affect Risk class; $b =$ greater than High Negative Affect and Personality Risk class; $c =$ greater than Comparison class; $* =$ small effect size ($0.2 \leq d < 0.5$); † = medium effect size ($0.5 \leq d < 0.8$).
Figure 3.1.
Figure 3.2.

Changes in the 0.1-Hz HRV index (log)

-0.6
-0.5
-0.4
-0.3
-0.2
-0.1
0
0.1
0.2
0.3

Changes in HF HRV (log)

-0.6
-0.5
-0.4
-0.3
-0.2
-0.1
0
0.1
0.2

CHAPTER 5
SYNTHESIS AND DISCUSSION

Integration of the Findings from the Three Studies

Through three separate experimental investigations, this dissertation aims to understand underlying physiological processes that may lead an individual to unhealthy alcohol use behaviors, such as the use of alcohol to regulate emotion. The role of emotion dysregulation in increasing risk for problematic alcohol use is well established (e.g., Cooper, et al., 1995; Cox & Klinger, 1988b; Labouvie & Bates, 2002), yet little is known about the mechanisms by which the desire to regulate emotion leads an individual to use alcohol. The primary goal of this dissertation was to utilize an established objective measure of psychophysiology – heart rate variability (HRV), a measure of autonomic activity – to study physiological processes that underlie vulnerability to emotional dysregulation and the use of alcohol to offset it.

In the field of psychophysiology, HRV is an established measure of physical and psychological health, stress vulnerability, and emotional regulation (Appelhans & Luecken, 2006; Berntson, et al., 1997; Giardino, et al., 2000). Although indices of HRV have been used to characterize autonomic dysregulation in individuals with chronic heavy alcohol use (Ingjaldsson, et al., 2003; Thayer, et al., 2006; Weise, Muller, Krell, Kielstein, & Koch, 1986), to the author’s knowledge, no study has explored HRV as a means for understanding the interrelationships of autonomic dysfunction, emotional dysregulation, and alcohol use behaviors. Accordingly, this dissertation was designed to examine HRV as a physiological indicator of emotional regulation in individuals with
different levels and types of psychosocial risk factors for AUD, and assess its utility as a biological marker of risk for problematic alcohol use.

Gender is an influential psychosocial risk factor for alcohol use disorders (AUD). Men are consistently reported to consume greater amounts of alcohol, have more heavy drinking episodes, have more alcohol-related problems, and are more likely to use alcohol to cope with stress or suppress negative emotion than women (see Nolen-Hoeksema & Hilt, 2006 for a review). However, when gender differences in the use of alcohol to suppress negative emotion are considered in conjunction with sensitivity to negative emotion, such as high anxiety sensitivity, the association between drinking to cope with negative emotion and alcohol use was stronger for women than men (Ham & Hope, 2003; Stewart & Zeitlin, 1995; Stewart, Zvolensky, & Eifert, 2001). This suggests that alcohol use behaviors by women may be more tightly linked to emotional state and influenced by the capacity to adaptively regulate emotion than men. Accordingly, both Study 1 ("Gender Differences in Acute Alcohol Effects on Self-Regulation of Arousal in Response to Emotional and Alcohol-related Picture Cues") and Study 2 ("Emotional Regulation and Alcohol Use: Behavioral Undercontrol, Negative Emotionality, and Gender") explored 0.1 Hz HRV as a physiological indicator of gender differences in alcohol use to regulate emotion.

In Study 1, alcohol dampened emotional arousal response only in men, yet both men and women showed a dampened response to a placebo challenge. This may indicate women expect alcohol to suppress arousal in much the same way as men do, yet do not experience the dampening pharmacological effects of alcohol on autonomic nervous system (ANS) reactivity. However, it is not clear why a dampening of arousal was not
observed among women in the alcohol condition, who presumably had a cognitive expectancy for alcohol similar to women in the placebo condition. In Study 2, women with negative emotionality showed a heightened 0.1-Hz HRV response to negatively-valenced picture cues compared to women with behavioral undercontrol, with both negative emotionality and behavioral control, and women without either personality characteristic, whereas negative emotionality did not moderate HRV reactivity to emotional cues among men. Further, women, relative to men, reported greater motivation to use alcohol to suppress negative emotion. Thus, a distinctive physiological profile of emotional regulation for women with different levels of negative emotionality was detected, and they also viewed alcohol as an effective buffer against such negative emotion.

Together, the results of these two studies (Study 1 and Study 2) provide evidence for gender-specific pathways by which individuals may come to use alcohol. Specifically, cognitive processes, such as the expectation that alcohol will dampen negative emotional states, combined with an elevated sensitivity to negative emotion, may be the driving forces for unhealthy alcohol use in women. On the other hand, it may be direct sensitivity to the pharmacological effects of alcohol, rather than sensitivity to negative emotion or cognitive expectancies, that drive alcohol use behaviors in men. Taken together, these gender-specific findings on autonomic reactivity to alcohol administration or differential emotional arousal response by personality characteristics may help explain why men are more likely to report alcohol use in response to stress, while women are more likely to report alcohol use to cope with negative emotion, particularly when they are susceptible to negative emotion. Furthermore, although speculative, such gender-specific pathway to
alcohol use may also reflect gender differences in emotional awareness and complexity. Some studies have demonstrated that women are more interconnected with their own feelings and feelings of others than men, thus women may be more emotionally complex than men (Barrett, Lane, Sechrest, & Schwartz, 2000; Ciarrochi, Hynes, & Crittenden, 2005; Hall & Matsumoto, 2004). Thus, the findings that individual differences in emotional regulation was an important factor influencing alcohol use in women but not in men may be attributed to gender differences in emotional complexity and differentiation.

Another important psychosocial factor examined in the present dissertation is personality risk. In particular, the dissertation focused on personality constructs of negative emotionality (i.e., a tendency to experience negative emotion) and behavioral control (i.e., having disinhibited, sensation seeking, and impulsive traits) as both constructs consistently have been associated with increased risk for problematic use of alcohol (e.g., Ferrier-Auerbach, et al., 2009; James & Taylor, 2007; Johnson & Cropsey, 2000; MacKillop, et al., 2007) and motivation to use alcohol to regulate emotion (e.g., Bolton, et al., 2008; Comeau, et al., 2001; Holahan, et al., 2004; Magid, et al., 2007; Robinson, et al., 2008). Study 2 and Study 3 (“Latent Class Analysis of Risk for Alcohol Use: Integration of Psychophysiological and Psychosocial Factors”) used different analytic approaches and different indices of personality to examine whether subgroups that vary in behavioral undercontrol and/or negative affect also demonstrate differences in their alcohol use, alcohol use-related problems, reasons for drinking, and emotional regulation.

Study 2 used a variable-centered approach by which individuals were classified into four groups based on their level of negative emotionality, as indexed by scores on the
Beck Depression Inventory II, and behavioral undercontrol, as indexed by scores on the Zuckerman’s Sensation Seeking Scale. In this study, individuals who were identified as having high levels of negative emotionality reported the greatest suppression reasons for drinking. Study 3 used a person-centered approach and homogeneous latent classes were identified based on the probability of a given individual to endorse an expanded list of indicators for negative emotionality (i.e., the Beck Depression and Anxiety Inventories as measures of negative affect state, and the Introversion and Anxiety Sensitivity subscales of the Substance Use Risk Profile Scale [SURPS] and behavioral undercontrol (i.e., the Sensation Seeking and the Impulsivity scales of the SURPS and Disinhibition subscale of the Zuckerman’s Sensation Seeking Scale). Three latent classes were identified based on the likelihood of a given individual to report scores in the upper 50 percentile or lower 50 percentile for each of these indicators of negative emotionality and behavioral undercontrol, and on their likelihood of having a positive family history of alcohol or drug use disorders or depression for a given individual. Two high risk classes were identified; one had a high probability of endorsing the negative emotionality state indicators, the other had a high probability of endorsing both negative emotionality state and all personality risk indicators. Both high risk classes reported greater alcohol-related problems and greater disinhibition and suppression reasons for drinking, suggesting that factors associated with negative emotionality may be a robust influence on alcohol-related problems and the use of alcohol for emotional regulatory reasons. Thus, Study 3 provided an integrated picture of how multiple indicators of emotional state and personality risk for problematic alcohol use may increase risk for problematic alcohol use.
To specifically address the physiological processes that may underlie this relationship, Studies 2 and 3 both assessed the physiological reactivity of individuals with differing levels of negative emotionality and behavioral undercontrol. Study 2 assessed reactivity to emotional picture cues and found that individuals with high negative emotionality demonstrated an elevated 0.1-Hz HRV response to negatively-valenced emotional stimuli. Taken together with the stronger motivations to use alcohol for suppression reasons reported by this group, these data offer preliminary support for the hypothesis that physiological dysregulation underlies the association of negative emotionality and alcohol use to suppress negative emotion.

Study 3 assessed reactivity to a paced-breathing procedure that measured optimum neurophysiological capacity to adapt to changes in the environment (Vaschillo, et al., 2002). Characterization of an individual’s adaptive capacity using measures of arousal modulation by the baroreflex system (i.e., the 0.1 Hz HRV index), and inhibitory control by vagal activity (i.e., HF HRV) can enhance our understanding of how people flexibly respond to internal and external challenges. Previous studies demonstrated increases in the amplitude of HR oscillation at ~ 0.1 (Vaschillo, et al., 2006b) and decreases in HF HRV indices in response to paced-breathing (Hassett, et al., 2007; Karavidas, et al., 2007), suggesting that the flexibility to modulate arousal is increased and vagal inhibition is suppressed, respectively. This strong HR oscillation at ~ 0.1 Hz is caused by resonance property of the HR baroreflex system. By recruiting this resonance property, frequency of HR oscillation is shifted towards 0.1 Hz, which may cause reduction in HR oscillation within other frequency bands.
During the paced-breathing procedure, those with a high likelihood of endorsing negative emotional affect state items (indicated by depression and anxiety symptoms), but not other personality risk items, demonstrated underreactivity of the baroreflex and diminished responsiveness of the vagal system, as indicated by smaller increase in 0.1-Hz HRV index and lack of suppression in HF HRV measure, respectively, to paced-breathing, compared with those with a high likelihood of endorsing negative emotional state items and personality risk items, or those with a low likelihood of endorsing negative emotional state items and personality risk items. This may indicate weak resonance property of the HR baroreflex system in those individuals. Together with the crucial roles of both baroreflex and vagal systems in emotional regulation (e.g., Nyklicek, et al., 2005; Porges, 1991; Porges, et al., 1994; Yasumasu, et al., 2006), these findings provide new evidence that physiological dysregulation may be an important underlying mechanism linking negative emotionality and problematic alcohol use.

It is also noteworthy that in both Studies 2 and 3, individuals classified as showing tendencies of negative emotionality and behavioral undercontrol did not show evidence of physiological dysregulation. In Study 2, those who showed high levels of both negative emotionality and behavioral undercontrol did not differ from the low-risk comparison group in 0.1-Hz HRV response to emotionally-arousing picture cues. Similarly, in Study 3, those who had a high likelihood of endorsing all items associated with negative emotionality and behavioral undercontrol did not differ from the low-risk comparison class in the 0.1 Hz or HF HRV response to the paced-breathing procedure. Given that individuals who only reported negative emotionality showed emotional dysregulation measured by HRV in both Study 2 and Study 3, it is possible to speculate
that having behavioral undercontrol tendencies may counteract impaired emotional regulation modulated by the ANS. Meanwhile, both studies clearly showed that these individuals were at elevated risk for problematic use of alcohol, including greater suppression and disinhibition reasons for drinking and greater alcohol-related problems, as has been reported by others (Colder & Chassin, 1997; Epstein, et al., 1994; Hussong & Chassin, 1994; Johnson & Pandina, 1993; Pandina, et al., 1992). The meaning of the apparent dissociation between non-specific, globally elevated personality risk and physiological dysregulation in these individuals is not immediately clear. Future studies that assess other biological processes, such as biochemistry, neurophysiology, and neuroendocrine system function, may uncover other mechanisms that link generalized psychological risk and problematic alcohol use.

Finally, the findings of the three studies on sensitivity of HRV in distinguishing individuals with and without psychosocial risk for problematic alcohol use during the presentation of emotional stimuli and the paced-breathing procedure highlight the importance of multiple approaches to understanding the physiological mechanisms that may underlie the etiology of AUD. Assessing changes in HRV in response to emotionally-arousing stimuli allows quantifying dynamic, moment-to-moment arousal modulatory response by the ANS. This HRV response induced by emotional challenge is useful in studying the underlying physiological processes specific to emotional regulation. On the other hand, given that HRV response to the paced-breathing procedure represents an individual’s neurophysiological adaptability to environmental demands, changes in HRV in response to this procedure seem to have broader implications than moment-to-moment emotion regulatory response. The paced-breathing procedure allows
assessment of one’s global capacity to cope with an environmental challenge. As such, the results of this dissertation suggest that combining information obtained through two procedures may be important in capturing different aspects of vulnerability to use alcohol for emotion regulation. In summary, by linking physiological response to experimental manipulations and psychosocial risks for AUD, all three studies demonstrated that dysregulation in the systems involved in emotional regulation, such as the ANS and baroreflex system, were interrelated with emotional states and the functional utility of alcohol use (e.g., enhancement of dishibition, suppression of negative emotion), and may increase risk for problematic alcohol use. Ultimately, the results of this dissertation support assessing risk for AUD at multiple levels as well as the integration of both objective, physiological measures and psychosocial factors.

A Potential Theoretical Model of Alcohol-Related Problems

The research questions posed in this dissertation may be useful for elaborating a theoretical model of motivation specific to using alcohol to regulate emotion. In particular, the dissertation may have contributed to refining the motivational models of alcohol use proposed by Cox and Klinger (1988b) and Cooper and colleagues (1995), which postulate that the desire to regulate emotion is a strong motivator for alcohol use. More specifically, these motivational theories of alcohol use postulate that motivation to regulate both negative and positive affective states is a common pathway to alcohol use and subsequent alcohol-related problems. They further suggest that various individual characteristics, such as personality factors, current affective state, alcohol expectancies, and reactivity to the specific reinforcing effects of alcohol, act as antecedents of motivation to alcohol use (Cooper, Agocha, & Sheldon, 2000; Cooper, et al., 1995; Read,
Wood, Kahler, Maddock, & Palfai, 2003; Simons, et al., 2005). The personality construct of behavioral undercontrol, reactivity to the stimulant effects of alcohol, and enhancement expectancy are posited to be positively associated with disinhibition reasons for drinking, whereas negative emotionality (including negative affect state and personality tendencies to experience negative emotion), reactivity to the anxiolytic effects of alcohol, and tension reduction expectancy are expected to be positively associated with suppression reasons for drinking (Figure 4.1). In addition, these models suggest a direct pathway from suppression reasons for drinking to alcohol-related problems.

The research questions of this dissertation included anxiolytic effects of alcohol and personality characteristics (negative emotionality and behavioral undercontrol), thus the dissertation partially examined the determinants of alcohol use with the motivational models of alcohol use by Cooper et al. (1995) and Cox and Klinger (1987). The results of this dissertation, and especially those from Study 2 and Study 3, provide empirical support for the associations among negative emotionality, suppression reasons for drinking, and alcohol-related problems. Specifically, the findings from Studies 2 and 3 demonstrated that those with negative emotionality self-reported emotional suppression reasons for drinking (Studies 2 and 3) and greater alcohol-related problems (Study 3). Interestingly, however, no significant association was found between negative emotionality and quantity and frequency of alcohol use in the past 30 days. Thus, the dissertation only supported the direct pathway from suppression reasons to alcohol related problems, but not the indirect pathway that involves alcohol use.

The most unique and important contribution of this dissertation to further understanding motivational components of alcohol use was through incorporating an
assessment of psychophysiological reactivity to an environmental challenge, and linking individual differences in physiological reactivity to personality characteristics. This approach was useful as novel methods to quantitatively examine these selected components of the motivational model. The support for associations among negative emotionality, suppression reasons for drinking, and heightened HRV response to negatively-valenced stimuli (Study 2) suggests (1) an interrelationship between over-reactive physiological response to an environmental challenge and negative emotionality, and (2) a positive influence of over-reactive physiological response to alcohol use to suppress negative emotion. These findings imply that one’s physiological reactivity to the environment, in addition to psychological factors, may motivate an individual to use alcohol. Considering recent shifts in the focus of AUD research toward the integration of biological markers in risk assessment, inclusion of physiological constructs in existing models may help to refine conceptualizations of the etiological pathways leading to problematic alcohol use.

Meanwhile, neither Study 2 nor Study 3 supported a direct relationship between behavioral undercontrol and disinhibition reasons for drinking. Behavioral undercontrol also was not associated with greater alcohol use or alcohol-related problems. This is inconsistent with previous findings on the positive association between behavioral undercontrol and alcohol use to enhance positive emotion (Comeau, et al., 2001; Kuntsche, et al., 2006; Magid, et al., 2007), or behavioral undercontrol and increased alcohol-related problems (Martin, et al., 2000; Simons, et al., 2005). Furthermore, the results of this dissertation provided weak support for the interrelationship between behavioral undercontrol and underreactive physiological response. The only significant
finding for underreactive physiological reactivity in behavioral undercontrol was reduced
HRV response in those with behavioral undercontrol to the neutral stimuli, relative to
those with negative emotionality in Study 2.

Findings pertaining to the potential moderating role of gender are another
important contribution of this dissertation to the motivational models proposed by Cox
and Klinger (1988) and Cooper et al. (1995). The observed male-specific physiological
arousal dampening by alcohol (Study 1) indicates a moderating effects of gender on the
anxiolytic effects of alcohol, at least on the 0.1 Hz HRV index of autonomic nervous
system regulation that was studied. Alternatively, the female-specific finding of
heightened physiological reactivity to negatively-valenced stimuli with negative
emotionality suggests a moderating effect of gender on the relationship between negative
emotionality and physiological reactivity to an environmental challenge. A moderating
effect of gender on the motivational determinants of alcohol use has important theoretical
and practical implications. For example, such gender differences indicate differential
pathways to alcohol use and related problems among men and women that could
potentially lead to gender specific models of alcohol use. At the same time, the present
results were generated from three pilot studies and thus should be interpreted cautiously.

Based on the alcohol use motivational models of Cox and Klinger (1988) and
Cooper et al. (1995) and the results of this dissertation, a revised theoretical model of
alcohol use is proposed in Figure 4.2. Given that the studies comprising this dissertation
examined some components of the Cox and Klinger (1988) and Cooper et al. (1995)
models and the fact that not all tested model components were supported, Figure 4.2
reflects those aspects of the models that were tested and supported via solid lines, while
those aspects of the model that were either not supported or not tested are reflected via
dashed lines and lines with two dots, respectively. First, this model suggests that
motivation for alcohol use to regulate emotion positively influence alcohol use and
alcohol-related problems. Second, motivation to use alcohol to suppress negative emotion
is influenced by reactivity to the anxiolytic effects of alcohol, having negative
emotionality tendencies, and over-reactive physiological response to environmental
challenges, whereas motivation for alcohol use to disinhibit positive emotion is
determined by sensitivity to the stimulant effects of alcohol, having behavioral
undercontrol tendencies, and underreactive physiological response to an environmental
challenge. Third, gender plays a moderating role in alcohol use such that male gender
was associated with enhanced reactivity to the anxiolytic effects of alcohol, whereas
female gender was associated with a heightened reactivity to an environmental challenge
and negative emotionality, and a tendency to use alcohol to suppress negative emotions.

Together, the results of this dissertation’s three studies contribute to the
development of a more nuanced motivational model of alcohol use that extends to
psychophysiological reactivity and modulation of arousal, and identifies gender as a
significant moderator of the motivational paths to maladaptive alcohol use. While the
findings provided positive support for a revised motivational model of alcohol use, this
full motivational model of alcohol use was not comprehensively examined, and some of
the relationships between the components were not supported. For example, inconsistent
with previous studies, the association between behavioral undercontrol and disinhibition
reasons for drinking was not significant in this dissertation. In addition, the relationships
between physiological reactivity to an environmental challenge and behavioral
undercontrol with disinhibition reasons for drinking were not clear, and reactivity to the stimulant effects of alcohol was not examined. This dissertation addressed a novel motivational constructs implicated in the development of AUD and that all three studies served as pilot studies. The three studies were also cross-sectional, thus the studies were not sufficient to examine the proposed directionality of the relationships among the components. Therefore, future research is needed to clarify the meaning of these constructs and their relationships, as well as to deepen our understanding of the associations between motivations to regulate emotion and alcohol use and related problems.

Clinical Application of Heart Rate Variability

A key rationale for studying HRV as a mechanistic biomarker in each of these three studies was its potential utility in the clinical setting. HRV is a precise, quantitative and non-invasive index of the efficiency of a homeostatic reflex that controls blood pressure and modulates emotional responsiveness (i.e., the heart rate baroreflex). It captures an individual’s autonomic adaptability and emotional regulatory capacity through basic electrocardiogram (ECG) recordings in episodes as brief as 5 minutes (Berntson, et al., 1997). The relative simplicity of the assessment procedure suggests an advantage for the potential application of HRV assessment in clinical practice. Furthermore, the ability to easily detect atypical HRV in a person, including heightened reactivity to emotional challenge or suppressed HRV during the paced-breathing procedure, is important as it may suggest a potential means of intervention during any stage of AUD (e.g., development of problematic use of alcohol, relapse into problematic alcohol use after a period of abstinence). Such an intervention is possible because HRV
can be positively modified through skill training, such as resonance frequency HRV biofeedback. In brief, resonance frequency HRV biofeedback involves (1) training an individual to breath his/her resonance frequency by following the pacer and (2) providing biofeedback about changes in HRV, so that the person can learn to increase the amplitude of HR oscillation through controlling his/her breathing (see Lehrer, et al., 2000 for the detailed rationale and training manual). Lehrer and colleagues have shown acute and chronic increase of HRV by resonance frequency HRV biofeedback in conditions such as asthma (Lehrer, et al., 2004) and depression (Hassett, et al., 2007; Karavidas, et al., 2007). Furthermore, improvement in depression symptoms has been reported as a result of HRV biofeedback, which suggests a possible link between improvement of HRV and mood state via this intervention technique. This procedure is both non-invasive and non-pharmacological; it is easily taught and easily learned; and, most importantly, it is adaptable for the home setting and thus can serve to counteract physiological dysregulation on an ongoing basis. Thus, this technique seems to have the potential to become an intervention tool for those who are at risk or have developed problematic alcohol use behaviors resulting, at least in part, from their neurophysiological adaptability, or lack thereof, to environmental demands.

Models and theories of addictive behaviors have long suggested the fundamental role of emotional regulation, both positive and negative, in motivating an individual to drug use (Koob, et al., 1999; Simons, et al., 2005; Sinha, 2008; Wills & Shiffman, 1985). Similar to AUD, vulnerability to specific drug use disorders are purportedly determined by an individual’s tendency to experience specific drug-reinforcement effects (Conrod, et al., 2000). Suppressed HRV has been linked to autonomic dysregulation caused by
chronic abuse of alcohol and other drugs (Brody, Krause, Veit, & Rau, 1998; Ingjaldsson, et al., 2003; Mehta, et al., 2001b; Thayer, et al., 2006; Vongpatanasin, Taylor, & Victor, 2004); however, to the best of my knowledge, no attempt has been made to focus on physiological dysregulation as a part of an intervention for addictive behaviors. In Study 2 and Study 3, physiological dysregulation response was observed in those who reported suppression reasons for drinking. Given a potential link between positive change in HRV and improvement in mood state (Hassett, et al., 2007; Karavidas, et al., 2007), manipulation of HRV may be useful in prevention and intervention for those who have developed, or are at risk for, AUD and/or other drug use disorders due to a strong motivation to use alcohol and/or other drugs to cope with negative emotions.

Prior to incorporating HRV as part of a risk assessment in clinical settings, however, further research will be required to address several issues. For example, for objective detection of atypical autonomic activity through HRV, the development of normative HRV data across various populations and the selection of physiological measures with good sensitivity and specificity are necessary. The costs of the equipment needed to collect and analyze ECG, and personnel training time requirements need to be considered, particularly in non-hospital settings where resources are limited and the majority of the workforce is unfamiliar with HRV. With regards to the requisite equipment necessary for HRV assessment, there are commercially available devices for ECG recording with relatively low costs and HRV analysis software is distributed at no cost (e.g., Kubios HRV Analysis Software by the Biosignal Analaysis and Medical Imaging Group, Kupio, Finland), thus the financial burden is not overwhelming. Training personnel to assess HRV and deliver HRV biofeedback, on the other hand, will require
time and effort. Despite these challenges, the advantages of HRV, including the relative simplicity of HRV assessment and its potential effectiveness of positive HRV manipulation related to improved emotional regulation, should encourage integration of HRV indices in AUD risk assessment and intervention, although small-scale clinical trials to examine the feasibility and effectiveness of HRV biofeedback with respect to AUD is warranted and likely to prove beneficial.

**Limitations of the Dissertation**

The results of these dissertation studies offer preliminary evidence for the utility of HRV research for furthering our understanding of emotional regulatory processes and their involvement in risk for future problematic alcohol use behaviors. Nonetheless, this evidence must be considered in light of the limitations of each individual study, as well as those of the overall dissertation. First, the age range of the sample is limited to young adults between 18 and 30 years, which may affect the generalizability of the findings. The optimum developmental period during which to intervene in alcohol use behaviors appears to vary in relation to multiple psychosocial and sociodemographic factors. For example, gender differences in AUD onset age have been consistently reported, with later AUD onset in women relative to men (Diehl, et al., 2007). Family history of alcohol use disorders appears to be related to early onset (Dawson, 2000; Volicer, Volicer, & D'Angelo, 1983). These and other considerations suggest that to further understand the role of emotion dysregulation in increasing risk for AUD across the lifespan, it would be beneficial to examine samples with a broader age range. Nonetheless, the hazardous range for AUD onset is suggested to be during an individual’s late teens and early twenties (Hasin, Stinson, Ogburn, & Grant, 2007), suggesting that the present sample was
tested within a critical developmental time frame for which novel prevention tools are needed (Enoch, 2006).

The generalizability of the results also is limited by the participant recruitment strategies employed. As a result of ethical concerns related to administering alcohol to individuals with psychiatric disorders, individuals who met diagnostic criteria for a psychiatric disorder were excluded from all three studies. This limited the range of reported psychological problems in the present samples, as seen in Study 3. In addition, excluding individuals with a psychiatric diagnosis was necessary because disorders associated with emotional dysregulation, such as major depression or generalized anxiety disorder, can have a negative impact on psychophysiology (Gorman & Sloan, 2000; Nahshoni, et al., 2004). Population-based studies, however, indicate that individuals with psychiatric disorders such as mood, anxiety, and personality disorders are at increased risk for AUD (e.g., Compton, Conway, Stinson, Colliver, & Grant, 2005; Grant, et al., 2005; Stinson, et al., 2005).

In addition, while individual differences in physiological reactivity to experimental manipulations were consistently found for psychological characteristics (i.e., negative affect and personality characteristics) across the three studies, supporting findings for differences in alcohol use related variables (i.e., quantity and frequency of alcohol use, alcohol-related problems, and reasons for drinking) were limited in this dissertation. This may be attributed to differences in data collection methods through which assessment errors may have been greater for self-reported alcohol use related variables relative to the more objectively quantified psychophysiological measures. It also is possible that restricted variable range specific to alcohol consumption, depression,
and/or anxiety symptoms resulting from study inclusion/exclusion criteria may have reduced statistical power to detect differences in alcohol use related variables among individuals with different psychological characteristics. Therefore, future studies should include individuals with a greater range of psychiatric disorders to further understand the interrelationships among psychosocial risk factors, psychiatric disorder, alcohol use, and emotional regulation.

Due to the small number of individuals meeting AUD criteria, this research was not able to examine differences in emotional regulation between those who have developed AUD and those who have not. Rather, the dissertation emphasized the relationship of individual differences in emotional regulation to risk for problematic use of alcohol. In understanding the etiology of AUD, however, it is important to discover the factors that distinguish emotional regulation in those with and without the disorder, as well as the factors that distinguish those who are at high and low risk for AUD. It also would be informative to identify psychosocial and biological markers of emotional regulatory responding that distinguish those with AUD and those at high risk for AUD from those at low risk.

Significance of the Dissertation in Prevention Research: Contribution to the Future Direction of Addiction Research

A salient characteristic of this dissertation is that all three studies were laboratory-based basic science Type I research projects. In Type I research, the focus is on discovering mechanisms of unhealthy behaviors or disease, developing measures or biological markers of maladaptive behaviors and disease, and discovering potential health applications (Khoury, Gwinn, Yoon, et al., 2007; Woolf, 2008). In recent years, leading
health organizations such as the World Health Organization (WHO), Institute of Medicine (IOM), and National Institutes of Health (NIH) have placed great emphasis on multidisciplinary approaches toward advancing evidence-based prevention/intervention efforts across various health problems (e.g., Kessel & Rosenfield, 2008; Mabry, Olster, Morgan, & Abrams, 2008; Mrazek & Haggerty, 1994). However, despite increasing recognition of basic science research as a fundamental initiating component in the sequence of stages for advancement in evidence-based preventive interventions, bridging the gaps between basic science and clinical practice has been a challenging task in prevention research and practice – and addictions research is no exception.

Rapid advances in human disease genomics and the integration of genomics into public health research, policy, and practice has stimulated a growing expectation for individualized primary prevention efforts and early detection of diseases, including psychiatric disorders (Brand, Brand, & Schulte in den Baumen, 2008; Khoury, Gwinn, Burke, Bowen, & Zimmern, 2007). Nevertheless, despite evidence supporting the inheritability of psychiatric disorders, psychiatric genetics research has proven particularly difficult and has struggled with contradictory findings and problems of low statistical power (Riley & McGuffin, 2000). These challenges may be due to the fact that an individual’s risk for a psychiatric disorder is likely to be polygenic and determined by gene-gene and gene-environment interactions (Hardy & Singleton, 2009; Risch, 1990). Therefore, the etiological pathways of psychiatric disorders are multi-level and multi-componential, which contributes to the heterogeneity of clinical symptoms among affected individuals (Kendler, 2005, 2008). Thus, the complexity of the etiological
pathways and heterogeneity of overt behavioral symptoms have slowed progress in identifying genes underlying disorders like AUD (Gottesman & Gould, 2003).

One possible solution to the apparent disconnect between genotype and phenotype is to develop more homogeneous subtypes of AUD using narrowly defined risk classification schemes that are based on both objective biological risk measures and overt behavioral symptoms (Burmeister, McInnis, & Zollner, 2008; Gottesman & Gould, 2003). This approach requires the identification of intermediate phenotypes, which are “mechanism-related manifestation(s) of a complex phenotype” (Goldman & Ducci, 2007) that reflect stable biological, psychological, and/or behavioral traits that are manifested in an individual and independent of active disease status. Importantly, because intermediate phenotypes are mechanistic by definition, they are not necessarily heritable nor do they necessarily share a genetic basis with the larger more complex phenotypes (Goldman & Ducci, 2007). Intermediate phenotypes not only serve as objective biological markers for vulnerability to AUD, they can also aid in understanding the processes of change related to alcohol use behaviors. Intermediate phenotypes are expected to play a crucial role in advancing subtype research by providing narrowly defined, homogeneous groups of phenotypes that ultimately help identify genes involved in the development of AUD (Hines, Ray, Hutchison, & Tabakoff, 2005).

The results of the present dissertation support the utility of HRV as a biological marker in identifying individual differences in emotional regulation and adaptive response by the ANS and homeostatic reflexes. The heritability of indices of HRV has been projected within a range of estimation that varies between 11% and 48% (Kupper, et al., 2004; Singh, Larson, O'Donnell, & Levy, 2001; Singh, et al., 1999; Sinnreich,
Friedlander, Luria, Sapoznikov, & Kark, 1999; Sinnreich, Friedlander, Sapoznikov, & Kark, 1998; Snieder, van Doornen, Boomsma, & Thayer, 2007; Wang, et al., 2009). In addition, several studies reported that reduced HRV at rest was a significant predictor of developing medical conditions, such as hypertension, cardiac events, and mortality in elderly at 4 to 12 years follow-up (Singh, et al., 2004; Singh, et al., 1998; Tsuji, et al., 1996; Tsuji, et al., 1994). These findings suggest that individual differences in the background state of HRV may be a relatively stable trait and may be useful in predicting future disease development regardless of current active disease status.

Given that intermediate phenotypes are mechanism-related, it raises the question, “are indices of HRV mechanistically linked to changes in alcohol use behavior?” To answer this question, it will be necessary to conduct longitudinal studies that examine whether changes in HRV are related to changes in alcohol use by assessing both HRV and alcohol use behaviors at multiple time points (Kazdin & Nock, 2003). Another question of interest is whether HRV can distinguish individuals suffering AUD who have a positive family history of AUD from those with negative family history, which in turn may help to identify genes that may increase vulnerability for an AUD. Furthermore, it will be important to determine whether there are common profiles of HRV response among disorders that share behavioral characteristics, such as impulsivity in subtypes of AUD and ASPD, or sensitivity to negative emotion in AUD, depression, and anxiety disorders. Examination of these features may promote the discovery of genes underlying vulnerability to these disorders.

AUD can significantly affect an individual’s the quality of life as well as that of those who surround him/her (Bell, Harford, Fuchs, McCarroll, & Schwartz, 2006;
Dawson, Grant, Chou, & Stinson, 2007; Ramisetty-Mikler & Caetano, 2005). The cost of care for AUD, and the physical health problems that occur as a consequence of chronic alcohol abuse, place an enormous burden on society (Harwood, 2000). Advancement of knowledge regarding the etiology of AUD and the early detection of those at risk for AUD can contribute to improved prevention/intervention efforts. Since first proposed by Gottesman and Shields (1973), the necessity to identify “intervening variables” between genes and a vast range of behavioral phenotypes for psychiatric disorders has been recognized. Given the growing interests in the possible role of human genetics in improving population health, it seems likely that the public health will benefit from incorporating intermediate phenotypes into preventive research and practice efforts that involve complex psychiatric disorders, such as AUD.
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Figure Captions

Figure 4.1. A motivational model of alcohol use based on the models proposed by Cox and Klinger (1988b) and Cooper et al. (1995).

Figure 4.2. A revised motivational model of alcohol use based on the combined results of the three studies. A negative sign ("-"”) indicates a negative association between constructs. A solid arrow indicates that the relationship suggested by a theoretical model was supported by the results of this dissertation. A dash arrow indicates that the relationship suggested by a theoretical model was not supported by this dissertation. An arrow with a long line and two dots indicates that the relationship suggested by a theoretical model was not tested in this dissertation.
Figure 4.1

- Reactivity to Anxiolytic effects of Alcohol
- Tension Reduction Expectancy
- Reactivity to Stimulant effects of Alcohol
- Behavioral Undercontrol
- Emotional Enhancement Expectancy

- Drink to Suppress Negative Emotion
- Alcohol Use
- Drink to Disinhibit Positive Emotion

- Alcohol-related Problems

- Negative Emotionality
Figure 4.2

- Reactivity to Anxiolytic Effects of Alcohol
  - Negative Emotionality
  - Alcohol Use
  - Alcohol-related Problems

- Reactivity to Stimulant Effects of Alcohol
  - Drink to Disinhibit Positive Emotion
  - Drink to Suppress Negative Emotion

- Physiological Reactivity to Environmental Challenge
  - Behavioral Undercontrol
  - Gender
APPENDIX A: Detailed Procedures of Parent Studies 1 and 2

**Parent Study 1: Acute and Familial Effects on Memory and Stress Reactivity**

The goal of Parent Study 1 was to examine how individuals who differed in vulnerability to alcohol use disorders (AUD), characterized by differences in family histories (FH) of AUD (i.e., no relative with AUD, at least one first degree relative with AUD, or at least one first degree relative and one second degree relative with AUD), and differences implicit and explicit memory for, and psychophysiological reactivity to emotionally-arousing stimuli, following administration of alcohol. The main research questions of Parent Study 1 included: 1) whether the alcohol impacted implicit and explicit memory processing of emotionally-arousing and emotionally-neutral stimuli differently for FH negative and positive groups, 2) whether the effects of alcohol on heart rate and skin conductance response during the exposure to emotionally-arousing and emotionally-neutral stimuli were associated with implicit and explicit memory processing of these stimuli differently for FH negative and positive groups, and 3) whether the effects of alcohol on heart rate variability (HRV) as an index of autonomic balance and adaptability to the environment differed between FH negative and positive groups.

**Participants.** Healthy social drinkers were recruited via advertisements posted on bulletin boards and in university and community newspapers. A standardized telephone interview (Ray, et al., 2004; Tracy & Bates, 1999) was used to initially screen for participant eligibility. Study inclusion criteria were age between 21 and 24 years, English as a first language, near 20/20 vision (corrected), and consumption of at least 4 standard drinks (3 for women) per occasion at least twice per month in the past year. Exclusion criteria included a history of lost consciousness lasting longer than 30 seconds, medical
conditions that preclude alcohol administration or confound interpretation of HRV (e.g., diabetes, heart disease), use of alcohol or any illicit substances by the participant’s biological mother during pregnancy (to rule out prenatal exposure effects), a history of psychiatric disorders and treatment (including counseling and pharmacological treatment), weight 20% more or less than ideal for their gender, height, and body frame (small, medium, and large) based on the Metropolitan Life Height-Weight Table (1983), report of childhood learning disability or special education, current treatment for a substance use disorder (except tobacco and caffeine), alcohol dependence, history of any substance abuse treatment, self-report of regular illicit or prescription drug use (at once a week), and, for women, pregnancy, planning to become pregnant, or lactating.

**Family History.** After eligibility was confirmed, familial history of psychopathology was assessed via a semi-structured interview, the Family History Assessment Module (FHAM) (Jança, et al., 1992). The FHAM was originally developed for the Collaborative Studies on Genetics of Alcoholism (COGA) to assess AUD, other drug use disorders, depression, mania, schizophrenia, and antisocial personality disorders (ASPD) in relatives of the person being interviewed (Rice, et al., 1995). Through a direct interview of more than 2,500 individuals, Rice et al. (1995) demonstrated the validity of the FHAM in screening for DSM-III-R psychiatric disorders. In both of Parent Study 1, “Acute and Familial Effects on Memory and Stress Reactivity,” and Parent Study 2, “Memory Processes, Emotional Regulation, and Developmental Stage of Drug Exposure,” the FHAM was administered via telephone interviews. Previous studies have reported the validity and reliability of diagnosis through telephone administration of the FHAM, and that it may potentially reduce false negatives when gathering sensitive
information about the participant’s family members (Kendler, Neale, Kessler, Heath, & Eaves, 1992; Paulsen, Crowe, Noyes, & Pfohl, 1988; Slutske, et al., 1996)

The assessment took, on average, from 15 minutes to one hour to complete, depending on the size of family and the number of relatives with potential psychopathology. Irrespective of type of disorder, a relative with three or more clinical symptoms was considered positive for the disorder. There were three categorizations based on family history of AUD: FH - (i.e., no family member with alcohol or drug use disorders), FH +1 (i.e., at least one first degree relative with AUD), FH +2, (i.e., at least one first degree relative and one second degree relatives with AUD = multi-generational family history). Participants were excluded if they reported one or more second degree relatives but no first degree relative who meets the criteria for AUD. Participants were also excluded if they reported any relative with other drug use disorders and no AUD. Family history of depression, mania, schizophrenia, and ASPD was not taken into account for inclusion/exclusion criteria or the definition of family history groups.

Procedures. Two separate studies were conducted that involved either picture or word stimuli. Participants in the picture cue study completed two sessions in which they were randomly assigned to two of three beverage conditions: alcohol and placebo, alcohol and non-alcohol, placebo and non-alcohol. The assignment of beverage conditions was stratified by gender and family history with the order of conditions counterbalanced. Two sessions were scheduled seven to ten days apart. Participants in the word cue study completed a single session, and were randomly assigned to one of three of these beverage conditions (alcohol, placebo, non-alcohol). In both the picture and word studies, each session lasted approximately 3 to 3 ½ hours, and consisted of picture/word presentations
Laboratory sessions were scheduled Monday through Friday between 10 a.m. and 2 p.m. to minimize biological circadian variations in alcohol metabolism and behavioral effects. Participants were compensated $50.00 per session for their time at the completion of the study (i.e., a $100.00 check for the picture study). Except for types of stimuli and number of sessions, the picture and word cue studies do not differ with respect to methods or procedures.

Upon arrival, participants provided written informed consent. The experimental session was rescheduled if participants reported: they had not eaten a light non-fatty meal (e.g., fruit, cereal with non-fat milk, non-fat yogurt) three hours prior to the session (to ensure that participants were not completely starved but had empty stomach at the time of beverage administration), alcohol in their system as measured through a breath sample, use of alcohol or any other drug (except for caffeine and cigarettes to avoid experiencing withdrawal symptoms during the experimental session) 24 hours prior to the session, signs of physical sickness (e.g., fever), and abnormal blood pressure. In addition, participants were excluded if they scored five or more on the brief version of Michigan Alcoholism Screening Test (Brief MAST, Pokorny, Miller, & Kaplan, 1972). The Brief MAST assesses possible alcohol dependence, and has been shown to be highly reliable with regard to the detection of alcohol-related problems in both inpatient and outpatient AUD samples as well as the general population (Chan, Pristach, & Welte, 1994). After above criteria were ensured, participants were weighted for the calculation of alcohol dose, and asked to complete a series of questionnaires.

1 The memory portion of the Parent studies was not described because as it was not relevant to the proposed dissertation. In addition, the memory tasks were conducted after the picture presentations and do not affect the interpretability of findings associated with this dissertation.
Then, the participants moved to the experimental room, where they were seated in a comfortable chair located 2.5 meters in front of a flat-panel TV screen in a sound-attenuated, dimly-lit room. After the electrodes and sensors for physiology recording were attached, participants completed a standardized low-demand, “plain vanilla task” (Jennings, et al., 1992). In the plain vanilla task, they sequentially viewed colored rectangles on a computer screen and silently counted the number of blue or green rectangles. This task provided a baseline (i.e., pre-alcohol ingestion) measure of performance.

The baseline assessment was followed by the beverage administration. Alcohol dosing to achieve a target blood alcohol concentration (BAC) of 90 mg/dl was calculated based on subject weight (0.90 ml/kg for men, 0.75 ml/kg for women). The weight-calculated ethanol was mixed with an orange juice mixer in a ratio of 4 parts mixer (i.e., 45% orange juice, 45% cranberry juice, 10% lemon juice) to 1 part ethanol. All participants consumed 3 volume-controlled drinks that contained one of three beverages: 100% mixer (told no alcohol = control condition), mixer with 100 μl ethanol float per each cup and smear of alcohol around the rim of each cup to provide olfactory cues (placebo condition), or mixer plus 95% ethanol dose (alcohol condition).

When a BAC of ~ 60 mg/dl was reached on the ascending limb of the BAC curve (or after 10 minutes for the placebo condition and no waiting time for the control condition), participants again performed the “plain vanilla task”, followed by picture cue presentations. The second vanilla task served as a post-beverage administration measure, and was followed by picture/word presentations.
Emotionally-valenced picture stimuli were taken from the International Affective Picture System (IAPS, Lang, et al., 2001), a normative picture stimulus set. Positive and negative emotional cues were matched on standardized arousal ratings, but varied systematically in valence. Neutral pictures were of moderate valence and low arousal (Bradley et al., 1990). Alcohol cues were from the Normative Appetitive Picture Set (NAPS, Stritzke, Breiner, Curtin, & Lang, 2004b), with additional stimuli developed by our laboratory through obtaining suitable pictures from the Internet with permission from the website, or pictures taken by the project staff. Our pilot study with 100 undergraduate students (unpublished and not presented here) found that all alcohol-related pictures were matched on valence and arousal ratings.

Picture Presentation. Participants viewed 120 picture cues in 4 categories: emotionally positive, emotionally negative, emotionally neutral, and alcohol-related. In each block, a set of 15 cues per category were presented twice in random order. The order of presenting four picture blocks was also counterbalanced by generating random 24 orders with SAS PROC PLAN (SAS Institute, 2002-2006). Picture presentation was programmed through the E-Prime software (Psychology Software Tool, Inc., Pittsburgh, PA). Each cue appeared for 5 seconds then disappeared for 5 seconds (white screen). Physiological data were collected during cue exposure. Additionally, during the white screen, participants gave either a liking or arousal rating (order counterbalanced). Using the Self-Assessment Manikin (SAM; Lang, et al., 2001), participants gave a rating on how much they like or dislike each picture on a 9-point scale (1 = dislike it very much to 9 = like it very much), and how much they felt aroused when they saw each picture on a

2 Physiological reactivity to the word stimuli data are not relevant to the present dissertation and therefore are not discussed.
9-point scale (1 = calm or relaxed to 9 = excited, jittery, or awake). Participants were asked not to speak or move at all during stimulus presentation except when giving an arousal or liking rating on each picture.

Paced-breathing procedure. In addition to picture/word presentations, all participants completed a task requiring that they breathe one complete inhalation/exhalation approximately every 10 seconds (i.e., ~ 0.1 Hz frequency) for 5 minutes; during this 5-min. period, a breathing pacer (the E-Z Air, Thought Technology, Ltd., Plattsburgh, PA) was presented on a flat-panel TV screen, and participants were instructed to inhale when the pacer goes up and to exhale when the pacer goes down. To avoid hyperventilation, participants were told to breathe naturally. In addition, participants were asked not to speak or move during the procedure.

Measures. The three manuscripts included in the present dissertation used the following instrumentation from Parent Study 1.

Demographic information included age, marital status, years of education, family income, occupation, country of origin, ethnic affiliation, and ethnicity (i.e., Hispanic). Alcohol and other drug use behaviors were measured with the Rutgers Health and Human Development Project (RHHDP) Alcohol and Drug Use Questionnaires. Sensation seeking personality was assessed by the Sensation Seeking Scale V (SSS) (Zuckerman, 1979b, 1994). Depressive symptoms were assessed by the Beck Depression Inventory II (BDI-II, Beck, et al., 1996) and anxiety symptoms were assessed by the Beck Anxiety Inventory (BAI, Beck & Steer, 1990). Alcohol use problems were assessed using the Alcohol Dependence Scale (ADS) (Skinner & Horn, 1984). The Substance Use Risk Profile Scale (SURPS) (Woicik, et al., 2008) was used to assess risk factors associated with substance
use, including introversion, impulsivity, sensation seeking, and anxiety sensitivity (Conrod, et al., 2000; Woicik, et al., in press). Mood states before and after the experiment were assessed by the Positive and Negative Affect Schedule (PANAS) (Watson, Clark, & Tellegen, 1988). Motivations for alcohol use were measured by the Reasons for Drinking Questionnaire (Bates, Labouvie, & Voelbel, 2002).

**Parent Study 2: Memory Processes, Emotional Regulation, and Developmental Stage of Drug Exposure**

The goal of Parent Study 2 was to better understand how emotion regulatory systems and memory processes contributed to substance use behavior across individuals with different substance use histories. The research questions of Parent Study 2 included: 1) whether self-report and physiological measure of arousal emotionally-arousing, emotionally-neutral, alcohol-related, and drug-related picture presentation was associated with personal history of alcohol and drug use, 2) whether implicit and explicit memory processing of emotionally-arousing, emotionally-neutral, alcohol-related, and drug-related picture cues were associated with personal history of alcohol and drug use, and 3) whether arousal response to the picture stimuli was associated with explicit and implicit memory processing.

**Participants.** In order to examine individuals who differ in their personal history of alcohol and drug use, participants were recruited from three sources. The college mandated sample consisted of Rutgers University students who were mandated to the Rutgers University Alcohol and Other Drug Assistance Program for Students (ADAPS) for violating university policies about on-campus substance use. These students were recruited following participation in a study that examined the effectiveness of two types of
prevention approaches (a brief motivational interview or only written feedback of their drinking behaviors) offered as part of a mandatory substance abuse counseling program (White, et al., 2006; White, et al., 2008; White, et al., 2007). Due to ethical concerns, individuals diagnosed as having a more severe alcohol and/or drug use problem (e.g., substance use dependence, multiple DUI offense) were excluded from the original study and provided more intensive treatment. The recruitment of this sample was initiated by asking ADAPS counselors to inform their clients about our study. If their clients indicated interest in participating in the study, the counselors forwarded their clients’ information to the project staff upon agreement from their clients. In turn, our project staff contacted the clients via phone for initial screening interview.

College varsity athletes formed another sample of interest. The participants in this sample were initially recruited for a pilot study to examine feasibility and effects of resonant frequency HRV biofeedback to improve athletic performance and stress management skills in athletes. Our experimental session was completed before the first biofeedback session. For recruitment, the project staff of the HRV biofeedback first provided information about the study to the athletes, and our project staff contacted them via phone if they indicated interests in our study. Student athletes were relevant to this study because they are generally considered at high risk for problematic alcohol use based on their unique patterns of alcohol use, including greater frequency of engaging in heavy, episodic drinking and experiencing greater negative consequence from drinking (Nelson & Wechsler, 2001; Yusko, et al., 2008).

We recruited the third sample from consecutive admissions to an inpatient addictions treatment facility. We provided our inclusion/exclusion criteria to staff members
at the treatment facility, who in turn provided information about our study to potential participants. If they indicated that they were interested in participating in our study, the project staff contacted those participants by phone to conduct initial screening interview. Participants in this group met DSM-IV diagnostic criteria for a substance use disorders (SUD). Their SUD diagnosis was confirmed by performing the AUD and SUD sections of the Structured Clinical Interview for the DSM (SCID) (First, et al., 1997), independent of the diagnosis given by the treatment facility. We obtained the results of urinary drug tests administered at the facility to ensure absence of any drugs in their system at the time of testing.

Participants were excluded from Parent Study 2 if they reported English as not their first language, current use of any psychoactive medication or medication that can cause abnormal recording of ECG signals (e.g., severe asthma, a history of cardiac problems), current diagnosis with psychiatric disorder(s) other than substance use (for the clinical group only), and any medical condition that may interfere with recording of ECG signals.

Family History. The FAHM (Janca, et al., 1992) was also used in Parent Study 2 to assess family history of psychopathology. Unlike Parent Study 1, participants were not excluded based on their family history of alcohol or drug use problems. Irrespective of type of disorder, a relative with three or more clinical symptoms was considered positive for the disorder.

Procedures. Eligible participants completed a single laboratory session, which lasted approximately four hours. The laboratory session was scheduled to start between 9:30 a.m. and 3:30 p.m. Monday through Friday. The experimental session was rescheduled if participants reported: alcohol in their system as measured through a breath
sample, use of alcohol or any other drug (except for caffeine and cigarettes to avoid experiencing withdrawal symptoms during the experimental session) 24 hours prior to the session, signs of physical sickness (e.g., fever), and abnormal blood pressure. Participants were compensated for their time with rate of a $50.00 check per session at the completion of the study (a gift card for the clinical group).

After providing written consent, participants completed a series of questionnaires, and then move to the experimental room. The rest of experimental procedures were the same as Parent Study 1, thus no further descriptions are provided here. Just as a note, for the clinical participants, to ensure that they did not leave the laboratory under the excitatory state due to exposure to drug-related cues, the paced-breathing procedure and the second “plain vanilla task” were completed after the memory phase of the study.

**Picture Stimuli.** In addition to three emotional picture categories and alcohol-related picture category, participants viewed two additional picture categories – marijuana- and polydrug-related picture cues. Thus, there were six cue types with a total of 180 pictures. Emotional pictures and alcohol-related picture cues were identical to Parent Study 1. Since this dissertation focused on emotional and alcohol-related pictures, thus marijuana- and poly-drug related pictures are not described here. Again, the order of presenting sixpicture blocks was counterbalanced by generating random 24 orders with SAS PROC PLAN (SAS Institute, 2002-2006).

**Measures.** Refer to Parent Study 1 as the same measures were used across both studies.
References


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