HEMODYNAMICS AND SLEEP ARCHITECTURE FOLLOWING ACUTE ALCOHOL CONSUMPTION IN COLLEGE AGE MALES

A Thesis
by
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Abstract

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Hypertension-associated cardiovascular disease (CVD) is the leading cause of morbidity and mortality in the Western world (Kochanek et al., 2011). Hypertension is a progressive disease characterized by elevated blood pressures which can cause damage to arteries and increases afterload leading to myocardial remodeling and a progressively worsening cardiovascular function. This increase in afterload requires an increase in contractility which further results in higher blood pressures. Many factors, including alcohol consumption, can exacerbate these symptoms and have been shown to accelerate the disease process. The effects of alcohol ingestion can range from decreases in arterial compliance to heightened nocturnal blood pressure. When nocturnal blood pressure does not dip (decrease below average resting values), the impact is realized with increases in all-cause morbidity and mortality. The reduction or elimination of a dip in blood pressure has been shown to be strongly correlated with many forms of cardiovascular disease.

Heightened nocturnal blood pressure may be attributed to the disruption of sleep architecture, which is a condition worsened by alcohol ingestion; however, little is known regarding the effects of alcohol ingestion on sleep architecture and nocturnal blood pressure. The purpose of this study was to investigate the effects of acute alcohol ingestion on hemodynamics and sleep architecture in a young, healthy cohort. Seventeen male subjects (N=17) underwent acute alcohol ingestion reaching a breath alcohol content of 0.08. Following alcohol treatment, each subject underwent a battery of hemodynamic tests and had their sleep architecture and nocturnal blood pressure monitored pre- and post-treatment. Aortic systolic blood pressures were found to be significantly increased following acute alcohol ingestion. Nocturnal systolic blood pressure was also found to be increased significantly following acute alcohol ingestion. Nocturnal systolic dip was found not to be significantly decreased. Percentage of time in deep sleep and number of awakenings showed no significant differences between pre- and post measures. This study showed a significant increase in aortic systolic blood pressure and nocturnal systolic blood pressure. The increased workload brought on by these pressure changes may increase the risk of developing cardiovascular disease due to hypertension.

Acknowledgments

At this point, I would like to thank my mentor, Dr. Scott R. Collier, for his guidance and support throughout my studies at Appalachian State University. To my thesis committee members, Dr. Scott R. Collier, Dr. Alan C. Utter, and Dr. Lisa A. Curtin, I express my utmost gratitude for your involvement in the realization of this project as well as the direction and encouragement. Thank you to Michael Landram for your understanding and support and for helping me better comprehend and to appreciate research. Also, thank you to Kelsey Branch for keeping my spirits up when things were tough. I would also like to offer my appreciation to everyone helping in the Vascular Biology and Autonomic Studies Lab; specifically Amanda Kosmata, Katelyn Briggs, and Alex Miller. To my fellow graduate students, I thank you for your unyielding support and friendship, and I anticipate the opportunity when we may again work together in the future. I also would like to thank the Office of Student Research for their financial support of this project by the Graduate School Research Grant.

Table of Contents

List of Tables

List of Figures

Foreword

The research detailed in this thesis will be submitted to *Alcohol and Alcoholism*, the official journal of the Medical Council on Alcohol. The thesis has been prepared according to the guidelines set forth by the Graduate School of Appalachian State University.

Introduction

Many factors affect cardiovascular health. Whether these are results of life choices or intrinsic factors, many of them can result in various forms of disease. These factors include family history of cardiovascular disease, sedentary lifestyle, obesity, alcohol consumption, smoking, and many more (Pajak and Kawalec, 2005). No matter the mechanism, most risk factors lead to hypertension, thus making hypertension-associated cardiovascular disease (CVD) the leading cause of morbidity and mortality in the Western world (Kochanek et al., 2011). Hypertension is a progressive disease characterized by elevated blood pressures which can cause damage to arteries and increase afterload. This increase in afterload requires an increase in contractility which results in higher blood pressures (Sunagawa, 2010).

Young adults are not immune to this disease; and when manifested at an early age, high blood pressures can lead to more extensive forms of target organ damage, further increased blood pressure, and increased likelihood of other CVDs (Urbina et al., 2011). Higher blood pressure in early adulthood is also associated with elevated risk of all-cause mortality as well as CVD several decades later (Gray et al., 2011). In a young cohort, the presence of CVD is often accelerated by an external factor. Because of this, young men are at an increased risk of developing hypertension and other forms of CVD (Higashiyama et al., 2012) due to consumption of alcohol (Le-Ha et al., 2012).

High alcohol intake has been shown to lead to increases in arterial blood pressure

(Foerster et al., 2009, Keil et al., 1989) and a higher risk of cardiovascular disease (Steffens et al., 2006). Alcohol consumption is associated with the progression of various forms of CVD (Higashiyama et al., 2012, Ohmori et al., 2002, Sull et al., 2010, Sundell et al., 2008, Yoshita et al., 2005) and prehypertension is observed at a higher frequency in college-aged populations (Gillman et al., 1995). Further alcohol use has been shown to have an effect on young vasculature (Le-Ha et al., 2012). Therefore, the link between alcohol consumption and prehypertension should be examined more closely.

Alcohol has multiple, deleterious effects on human hemodynamics. These effects are shown by increases in arterial stiffness (Kurihara et al., 2004) and decreases in nocturnal blood pressure dipping (Seppa and Sillanaukee, 1999). Nocturnal blood pressure dipping is a physiological method of maintaining health of the heart and the vascularity by decreasing myocardial demand which also provides a mechanism to combat chronic rises in blood pressure (Friedman and Logan, 2009). During nocturnal dipping, baroreceptors reset and arterial turbulence decreases, instigating the relaxation of the vasculature. Those who do not experience nocturnal blood pressure dipping are at an increased risk of hypertension (Cuspidi et al., 2011, Tsioufis et al., 2011), CVD (Mehta and Drawz, 2011, Napan et al., 2011, Vasunta et al., 2012), and other forms of disease or dysfunction (Mehta and Drawz, 2011, Moller et al., 2007, van de Borne et al., 1997). Effects are often widespread and cause a multitude of event series which end in results such as kidney disease or further autonomic dysfunction.

Nocturnal blood pressure dipping is paramount for one's health and is unequivocally tied to sleep architecture. Both are strong factors in determining cardiovascular health

(Arnedt et al., 2011, Sherwood et al., 2011). Blood pressure dipping is seen at a lower frequency and duration when the number of sleep disturbances is increased making sleep interruptions a very strong predictor of cardiovascular events (Crum et al., 2004, Matthews et al., 2008). Sleep architecture has a profound effect on blood pressure regulation both overnight and during daytime hours (Fung et al., 2011, Lanfranchi et al., 2009, Sabanayagam and Shankar, 2010). More specifically, alcohol has been shown to affect sleep quality in a young adult population (Ehlers et al., 2010). Disturbances in the sleep cycle are strongly correlated with impaired nocturnal blood pressure dipping (Suzuki et al., 2011), yet little is known regarding the effects of acute alcohol consumption on blood pressure regulation and sleep architecture in a college age population. Male college students may be at particular risk given that they report greater consumption of alcohol compared to female college students (Dawson and Archer, 1992), and male college students' tend to have decreased hemodynamic function compared to their female counterparts (Evans et al., 2001). The purpose of this study is to examine the effects of acute alcohol consumption on hemodynamics and sleep architecture in a sample of male college students.

It is hypothesized that acute alcohol consumption will result in an increase in central hemodynamics, including an increase in arterial stiffness, which will result in an increase in blood pressure. In regards to sleep architecture, alcohol consumption will disturb sleep architecture, which will instigate a rise in nocturnal blood pressure. The negative impact on sleep architecture will facilitate decreases in REM and deep sleep as well as increases in the frequency of sleep disturbances (Fung et al., 2011).

Cardiovascular diseases such as hypertension and coronary artery disease are leading

causes of mortality in the modern world and require expensive testing, treatments, and medicines. The causes and time of onset can vary greatly and developing bodies of data showing manifestation of alcohol related effects on the human cardiovascular system will help us understand the progression of CVD in young individuals (Dyer et al., 1990), leading to effective prevention and treatment options. These may be in the form of social awareness programming highlighting the acute effects of alcohol ingestion and the progression of CVD as we age. The present study may provide information about the effects of alcohol consumption on the health of the cardiovascular system and regulating mechanisms. Also, information regarding the acute effect of alcohol on sleep architecture and nocturnal blood pressure could further raise the social awareness surrounding these factors. Achievement of dipping blood pressure status reduces the instance for cardiac events and may provide knowledge that could result in longer lifespan. Obtaining information that acute alcohol consumption negatively affects multiple health parameters may provide further information as to the mechanisms behind the hypertension epidemic.

Methods

Subjects

For this study, 17 college-aged males (21-25 years old) were recruited. Exclusion criteria included a history of cardiovascular, respiratory, gastrointestinal, renal, or other medical condition that would endanger the subject for this study. Subjects were excluded if they were current smokers or currently taking any prescription or over the counter medications. All participation was voluntary, and subjects were able to withdraw at any time without penalty. Each subject was administered a drinking behaviors questionnaire before arrival to the lab to determine whether each subject fit inclusion criteria. This questionnaire was administered via telephone. Upon completion of this questionnaire and inclusion in the study, each subject was then instructed to arrive at the lab at the appropriate time. Participants were verbally informed of procedures, risks, and benefits of the study before giving their written informed consent for participation. Before participating in the study, subjects completed a health history questionnaire (including demographic information).

Experimental Procedure

Subjects were recruited from the male student body of Appalachian State University via a campus-wide email. Those who replied to the email took part in a drinking behaviors questionnaire via telephone to determine whether they fit inclusion criteria. Potential subjects were instructed to maintain regular diet and forego exercise on testing days. Potential subjects (N = 17) who met inclusion criteria and expressed interest in participation were in-

structed to report to the Vascular Biology and Autonomic Studies Laboratory at Appalachian State University for informed consent, initial testing, and instruction and familiarization with the Zeo™ sleep monitor as well as the Oscar2™ ambulatory blood pressure monitor. Subjects completed a health history questionnaire upon arrival. Baseline testing consisted of height, weight, blood pressure (BP), body composition via Bioelectrical Impedance Analysis (BIA), Pulse Wave Analysis (PWA) (Wassertheurer et al. 2010), and Pulse Wave Velocity (PWV) (Calabia et al., 2011, Ding et al., 2011). BP was taken in accordance with American Heart Association (AHA) standards. Subjects sat quietly for 15 minutes before BP was taken. The first and fourth Korotkoff sounds were utilized for systolic and diastolic blood pressure. Subjects were directed to wear the Zeo™ sleep monitoring system (Shambroom et al., 2012) and Oscar2™ ambulatory blood pressure monitor (Goodwin et al., 2007) for one night in order to achieve a baseline measurement. The subjects were instructed to maintain their regular diet and exclude exercise on testing days.

Upon completion of this baseline period, subjects arrived at the lab one week later to undergo treatment and perform the battery of post treatment hemodynamic testing. Subjects were instructed to eat two hours before reporting to the laboratory. First, breath alcohol concentration (BrAC) was measured and subjects were instructed on alcohol consumption treatment. BrAC was taken via the ASIII before alcohol administration to ensure a 0.0 baseline reading. Following BrAC, urine specific gravity and anthropometric data were collected. Participants were administered a single drink of 100 proof vodka mixed in a solution of 1 part vodka to 4 parts tonic water and lime that was normalized to each subject by bodyweight (2mL/kg of body weight). Participants were instructed to consume this drink within

15 minutes. This combination has reliably been shown to result in an average blood alcohol concentration of .07 to .08 (Poltavski et al., 2011). Upon arriving at a BAC of 0.08, subjects were instructed to wait patiently for 30 minutes. Thirty minutes post consumption; a second round of measurements consisting of BP, PWA, and PWV were taken.

Upon completion of the measurements, each subject was given another Zeo™ sleep monitor as well as Oscar2™ ambulatory blood pressure cuff in order to observe the effects of the treatment on sleep and nocturnal BP dipping. Following testing, subjects were required to remain in the lab under supervision until BAC returns to a baseline range between 0.02 and 0.05. Once this criterion was met, subjects were allowed to leave the lab, released to a sober driver of their choice. All subjects were instructed to maintain their normal routines with the exception of further alcohol consumption and exercise as well as wearing the Zeo™ sleep monitor and Oscar2™ ambulatory blood pressure cuff while they slept.

Each subject returned to the lab the next morning, 12 hours post consumption and returned the Zeo™ sleep monitors and Oscar2™ ambulatory blood pressure cuffs. At this time, they were re-measured for urine specific gravity, body composition, and completed the same hemodynamic measurements as previously performed.

Tanita BIA

Body composition and weight (kg) were assessed using Bioelectrical Impedance Analysis (Tanita body composition analyzer scale TBF 310, Arlington Heights, IL). Subjects removed their shoes and socks before stepping on the scale. Height (cm) was assessed using a stadiometer (Health o Meter Professional Standard Beam Scale with Height Rod 402KL, North Shore Care Supply, Northbrook, IL). Height was measured while the subjects

were standing in the erect position, with shoulders relaxed, arms hanging freely, and heads aligned in the Frankfort plane.

Urine Specific Gravity

Hydration was measured by asking the subjects to supply a urine sample at the beginning of the second and third lab visits. The specific gravity of these samples was analyzed utilizing a refractometer to assess urine specific gravity both before consumption of alcohol as well as twelve hours following consumption of alcohol in order to assess hydration status. Values exceeding 1.020 were deemed to be dehydrated.

Alco-Sensor III™ (ASIII)

The ASIII™ is a hand-held pocket breath alcohol tester. Participants breathe into disposable mouthpieces while their BrAC is displayed on a large three-digit display. The ASIII is capable of measuring BrAC manually, but also is powerful enough to capture BrAC from an unconscious person or to detect the alcohol content of a solution.

History Questionnaire and Demographics

Demographic information included gender, age, ethnicity, and extracurricular involvement. An alcohol and substance use questionnaire assessed typical patterns of alcohol and drug use via three family history questions and 10 personal use questions. This included one item that assessed the number of days per month the participant drank and one that assessed how much was typically consumed, which was combined multiplicatively to yield the average number of drinks consumed per month.

Sphygmacor Cardiovascular Management System

Arterial Pulse Wave Velocity and Aortic Blood Pressure Waveforms (PWV, ABPW respectively)

All measurements were conducted in accordance with guidelines set forth by the Clinical Application of Arterial Stiffness, Task Force III. The applanation tonometer (Sphygmacor, Sydney, Australia) was used to derive the ascending aortic blood pressure waveform and a range of central arterial indices. The Sphygmacor was used with a tonometer over a radial artery calibrated with a standard cuff blood pressure measurement. In addition, the PWV (measure of arterial distensibility) module of the Sphygmacor was used to obtain indices of arterial stiffness. The Sphygmacor system is used to obtain the pulse wave: (1) between left common carotid artery and the left femoral artery, (2) between the left femoral and the ipsilateral dorsalis pedis pulse, and (3) between the left common carotid artery and the left radial artery. Distance from the carotid sampling site to the mid-point of the manubrium sterni, manubrium sternum to femoral artery, and femoral artery to dorsalis pedis was measured between these points as straight lines with a tape measure. The distance from the carotid artery to the manubrium sterni was subtracted from the manubrium to femoral artery distance. PWV was determined from the foot-to-foot flow wave velocity. The foot of the pressure wave was identified visually as the point of systolic upstroke. The time delay between a minimum of 15 simultaneously recorded flow waves was averaged. PWV was calculated from the distances between measurement points and the measured time delay (Dt) between proximal and distal foot waveforms: PWV = D / Dt (m/s); where D is distance in meters and Dt is the time interval in seconds. Values attained from carotid to femoral ar-

tery were taken as an index of central compliance, while values attained from the carotid and radial artery along with the measurement from the femoral to dorsalis pedis were taken as an index of peripheral compliance. All data was stored and analyzed off-line after completion of testing.

Ambulatory Blood Pressure Measurement (ABPM)

Upon completion of the initial in-lab testing battery, the subjects were outfitted with a SunTech Medical Oscar2™ ambulatory blood pressure device. This device takes oscillatory blood pressure measurements every 20 minutes throughout the sleep period. The data was stored in the device for later uploading to the VBAS computer.

Ambulatory Sleep Stage Measurement

Subjects wore a Zeo™ sleep monitoring headband for one night leading up to testing. This period was used to establish a baseline with which the testing data was compared. The system consists of a soft headband (metallic fibers woven into the material) and a bedside display. The two-piece system utilizes dry sensor EEG technology to transmit brainwave data wirelessly to the bedside display, where it was stored for analysis. During sleep episodes between initial testing and 12 hours post testing, subjects also wore the Zeo™ ambulatory sleep monitoring headband. The device is capable of generating data on distinct sleep phases (e.g., deep sleep, REM, light sleep, sleep disturbances, sleep onset latency, etc.). The Zeo™ system has been validated against an in-laboratory polysomnography and shown to be an accurate and easy way to measure sleep stages.

Statistical Analysis

Repeated measure analysis of variance (ANOVA) was used to determine differences between baseline, post-consumption, and 12 hours post-consumption measurements. Statistical significance was set at $p \leq 0.05$. Statistical analysis was performed using statistical analysis software (SPSS, Version 19.0; IBM Corp., Armonk, NY). Following a significant F-ratio, appropriate post-hoc analysis was performed.

Results

Subjects each completed their non-alcohol control session to be compared with their individual alcohol data. All subjects served as their own controls following a baseline assessment. Subject descriptive characteristics are presented in Table 1. Alcohol had various marked effects on the areas of hemodynamics ambulatory blood pressure, and sleep architecture. These findings show baseline measures compared to the post alcohol measures.

Urine Specific Gravity

Twelve hours post-alcohol urine specific gravity and pre-consumption urine specific gravity were analyzed and determined to not be statistically different ($p > 0.05$; Figure 1).

Hemodynamic Variables

Aortic systolic BP values were significantly altered by alcohol. Compared to baseline (104.765 mmHg ±1.905), measures taken 30 minutes post consumption (108.294 mmHg ± 1.886) showed a significant increase ($p < 0.05$; Figure 2). When measures taken 12 hours post alcohol consumption (109.824 mmHg ± 1.898) were compared to baseline, a significant increase was determined ($p < 0.05$; Figure 2). No significant differences ($p > 0.05$; Figure 3) were determined through augmentation index measurements, though an increase was observed following alcohol consumption. No significant differences were determined by aortic pulse pressures. Central pulse wave velocity and peripheral pulse wave velocity also showed no significant differences when comparing baseline, 30 minutes post, and 12 hours post consumption measures (all p's > 0.05).

Nocturnal Blood Pressure Variables

Nocturnal systolic BP increased between pre- and post- consumption of alcohol as demonstrated in Figure 4. Baseline nocturnal systolic BP values (120.847 mmHg ± 3.579) were significantly different when compared to nocturnal systolic BP following alcohol consumption (134.194 mmHg ± 6.949) ($p < 0.05$; Figure 4). Alcohol consumption revealed an increase in nocturnal diastolic pressure from baseline (58.354 mmHg ± 2.006) to post consumption measures (61.994 mmHg ± 2.551), but these findings were not significant ($p > 0.05$; Figure 5).

Diurnal Blood Pressure Variables

There were no significant diurnal blood pressure findings ($p > 0.05$; Figures 4 and 5). Diurnal systolic blood pressure ($p > 0.05$; Figure 4) was non-significantly decreased following alcohol consumption (136.118 mmHg ± 3.912) when compared to baseline data (141.941 mmHg ± 5.105). Diurnal diastolic blood pressure showed a non-significant pressure decrease following alcohol consumption (70.706 mmHg ± 2.479) when compared to baseline (72.706 mmHg ± 3.119) time point ($p > 0.05$; Figure 5).

Nocturnal blood pressure dipping

Though there was a decrease in systolic blood pressure dip as well as diastolic blood pressure dip, findings were not significant. The percent dip for systolic pressure was not significantly altered between baseline (11.437 % ± 2.014) and the post alcohol (5.136 % ± 4.102) measures ($p > 0.05$; Figure 6). There was also no significant difference in diastolic blood pressure dip between baseline (18.522 % ± 2.473) and the post alcohol (11.818 % ± 2.756 %) measures ($p > 0.05$).

Sleep Architecture

Total sleep time was found to be statistically significant ($p < 0.05$; Figure 7). Baseline data (333.882 minutes ± 14.681) was significantly less than post alcohol data (394.882 minutes ± 18.626). Time to sleep between pre- and post-alcohol consumption was also statistically significant. Post alcohol data (16.059 minutes ± 3.185) showed a significant ($p < 0.05$; Figure 8) decrease compared to baseline data (32.529 minutes ± 6.805). Time in wake showed no significant difference when comparing baseline (20.235 minutes ± 6.337) and post alcohol (20.412 minutes ± 4.882). Number of awakenings was also not statistically significant. The baseline awakenings (4.235 ± 0.076) data compared to post alcohol (4.353 ± 0.653) showed no significant difference (Figure 9). There were no significant differences between baseline deep sleep (59.647 minutes ± 0.0143) and post alcohol deep sleep (64.941 minutes ± 0.028). There were no significant differences between baseline sleep stage percentages and post alcohol sleep stage percentages ($p > 0.05$; Figure 10).

Table 1: Descriptive Statistics (n = 17)

	Mean	Std. Error
Height	178.6	2.0
Weight	78.9	3.8
BodyFat	17.2	2.3

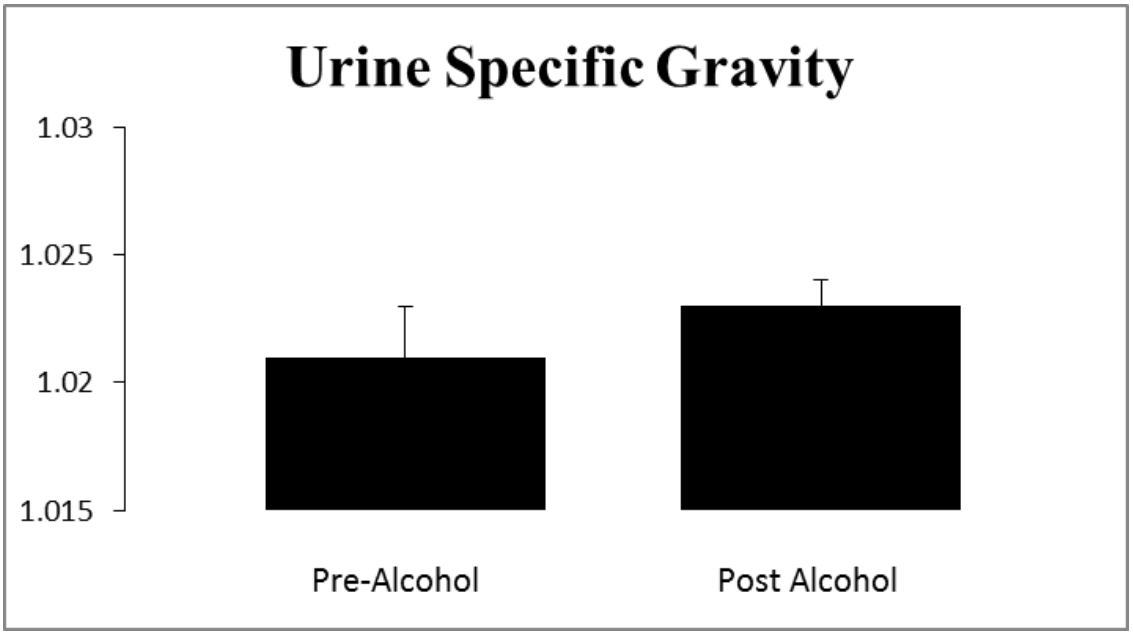

Figure 1: The data shown are urine specific gravities measure via refractometer before alcohol consumption as well as 12 hours post alcohol consumption. The data shown are 1.021 ± 0.002 and 1.023 ± 0.001. 12 hours post alcohol urine specific gravity and pre consumption urine specific gravity were analyzed and determined to be statistically not different ($p > 0.05$). Data are presented as mean ± SEM.

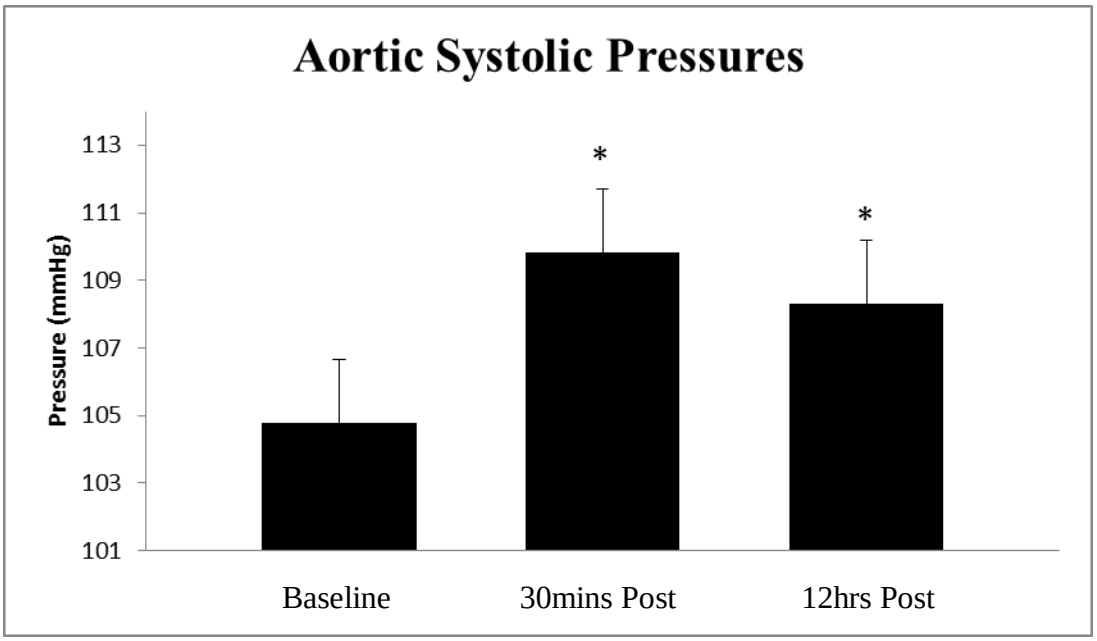

Figure 2: The data shown are aortic systolic pressures measure at baseline, 30 minutes following alcohol consumption, and 12 hours following alcohol consumption. The data shown are 104.765 mmHg ±1.905, 109.824 mmHg ± 1.898, and 108.294 mmHg ± 1.886. Data are presented as mean ± SEM. *Significance at $p < 0.05$ noted at baseline versus 30mins post as well as baseline versus 12hrs post.

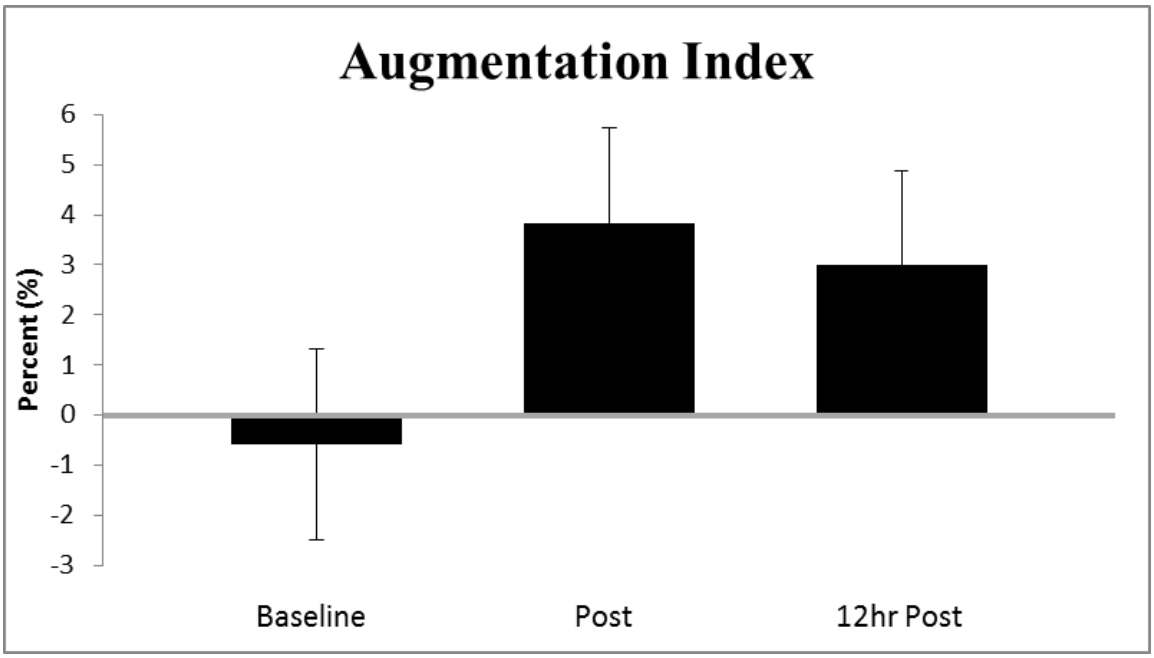

Figure 3: The data shown are augmentation indices measured at baseline, 30 minutes following alcohol consumption, and 12 hours following alcohol consumption. The data shown are -0.588 % ±2.067, 3.824 % ± 2.039, and 3.000 % ± 2.372. Data are presented as mean % ± SEM. No significant difference was determined.

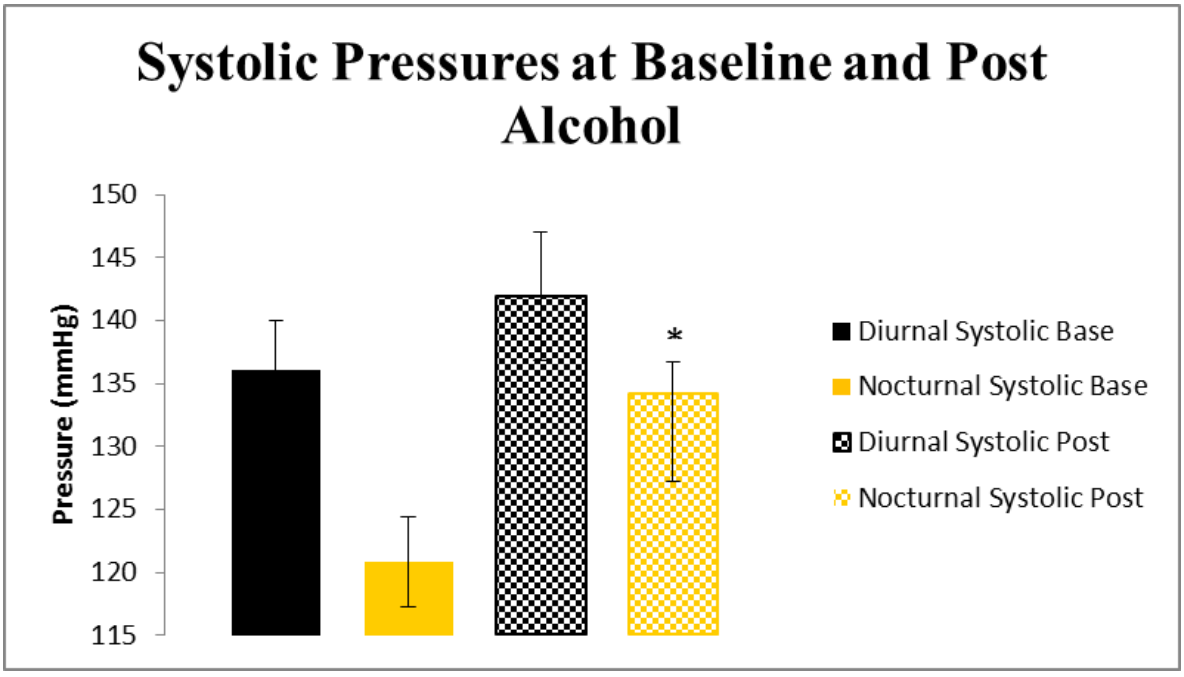

Figure 4: The data shown are systolic pressures measured at baseline and following alcohol consumption. The data shown are 136.118 mmHg ±3.912, 120.847 mmHg ± 3.579, 141.941 mmHg ± 5.105, and 134.194 mmHg ± 6.949. Data are presented as mean ± SEM. *Significance at $p < 0.05$ noted at baseline nocturnal systolic versus nocturnal systolic post alcohol.

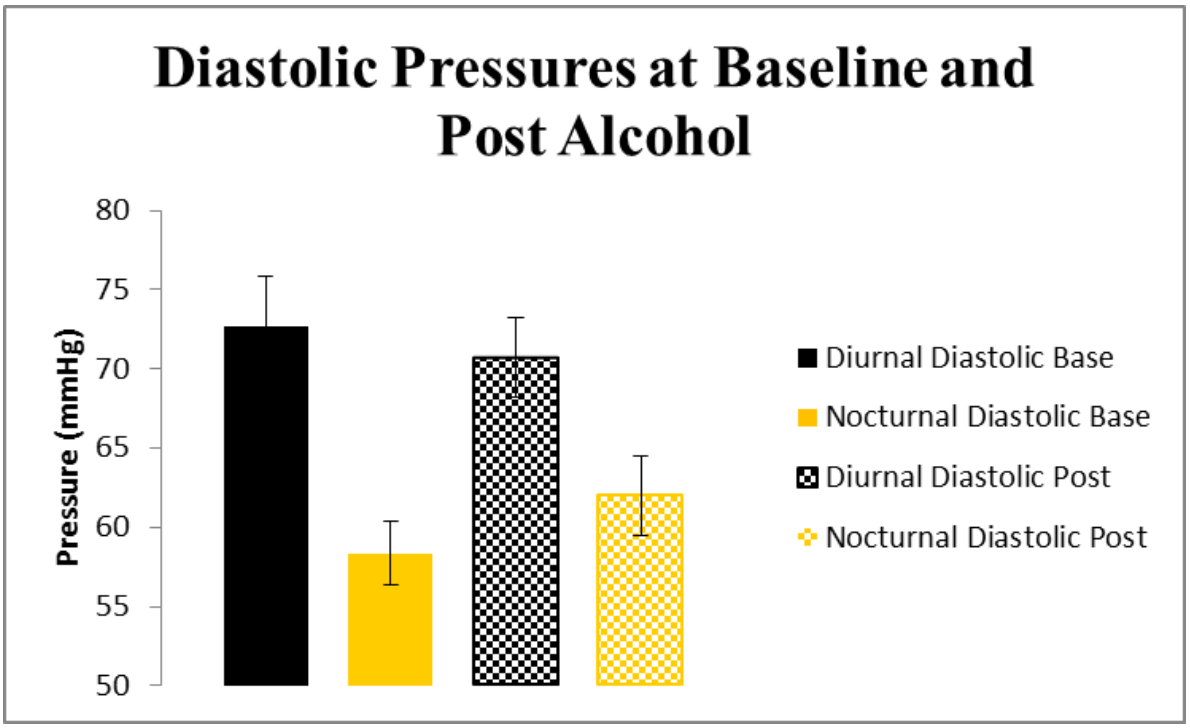

Figure 5: The data shown are diastolic pressures measured at baseline and following alcohol consumption. The data shown are 72.706 mmHg ±3.119, 58.354 mmHg ± 2.006, 70.706 mmHg ± 2.479, and 61.994 mmHg ± 2.551. Data are presented as mean ± SEM. No significant differences were determined.

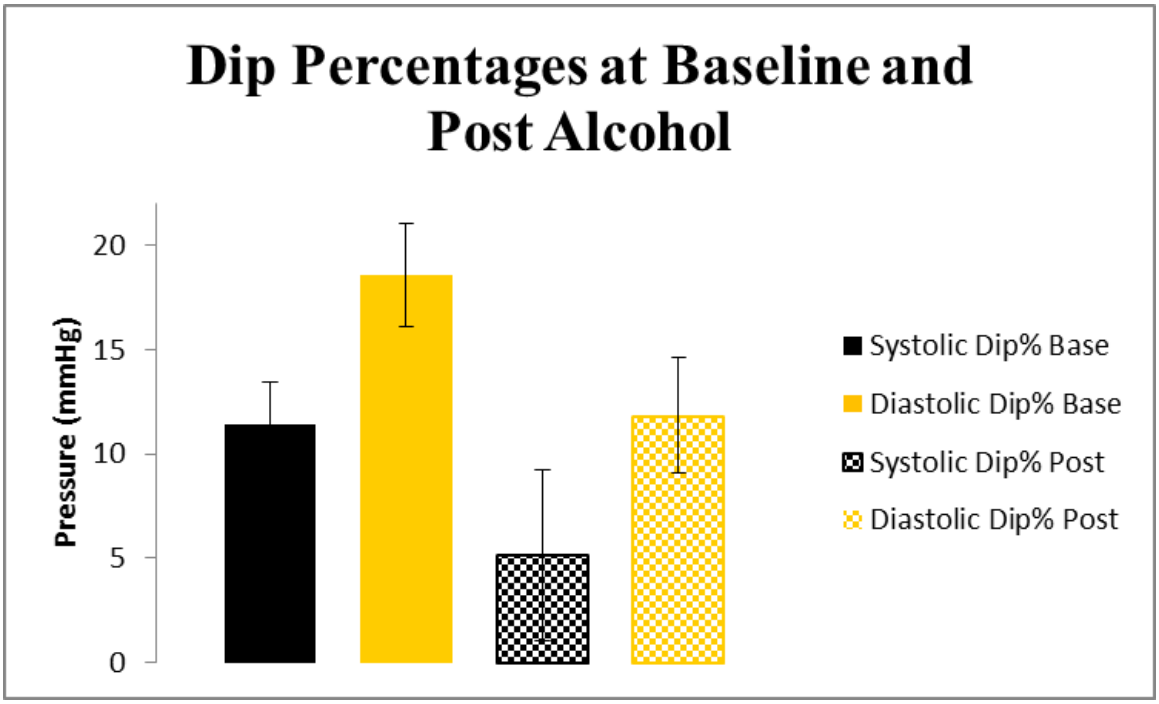

Figure 6: The data shown are percentages of blood pressure dip measured at baseline and following alcohol consumption. The data shown are 11.437 % ± 2.014, 18.522 % ± 2.473, 5.136 % ± 4.102, and 11.818 % ± 2.756. Data are presented as mean ± SEM. No significant differences were determined.

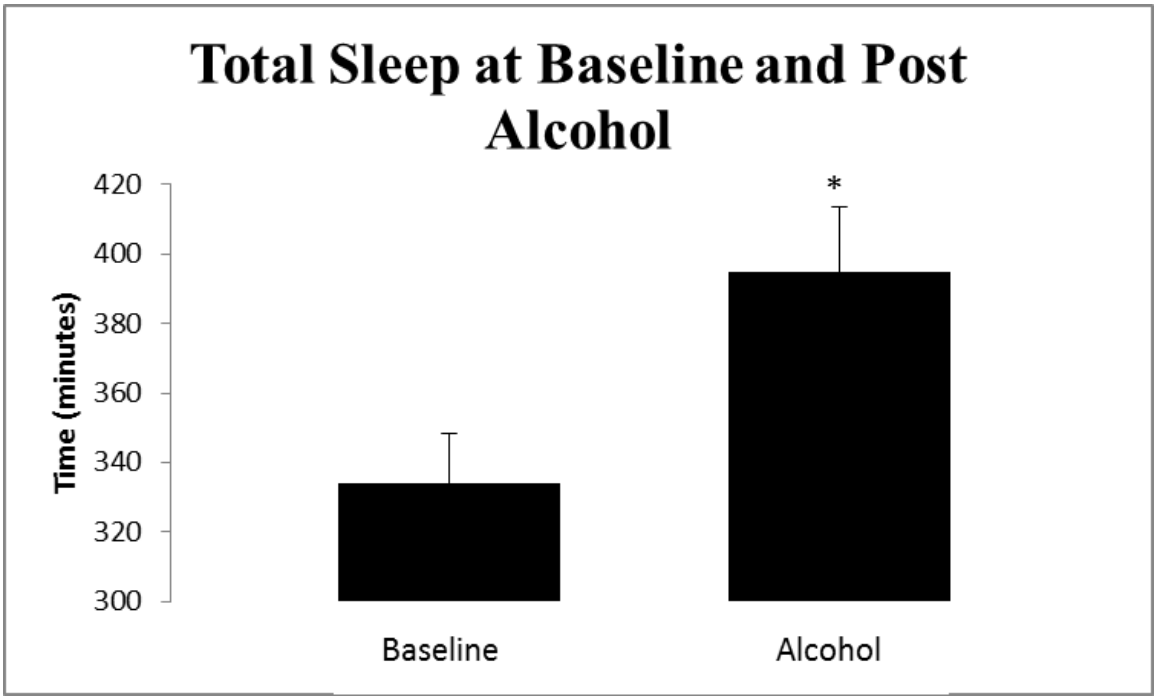

Figure 7: The data shown are time (minutes) of total sleep measured at baseline and following alcohol consumption. The data shown are 333.882 minutes ± 14.681 and 394.882 minutes ± 18.626. Data are presented as mean ± SEM. *Significance at $p < 0.05$ noted at baseline total sleep versus post alcohol total sleep.

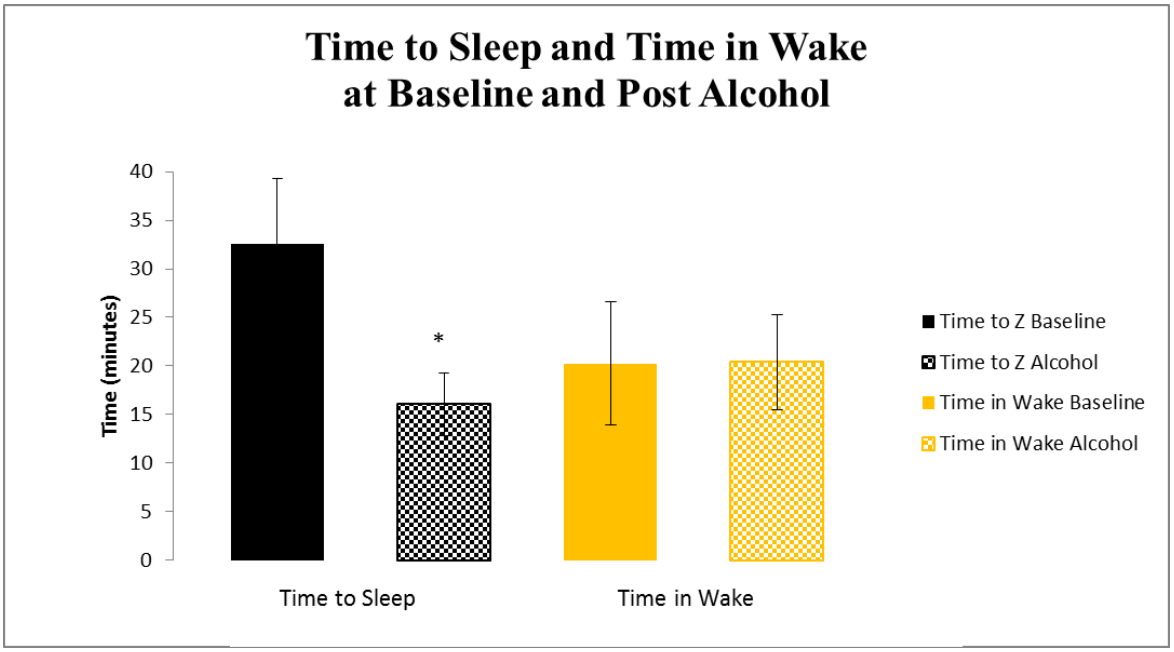

Figure 8: The data shown are times (minutes) measured at baseline and following alcohol consumption. The data shown are 32.529 minutes ± 6.805, 16.059 minutes ± 3.185, 20.235 minutes ± 6.337, and 20.412 minutes ± 4.882. Data are presented as mean ± SEM. *Significance at $p < 0.05$ noted at baseline time to sleep versus post alcohol time to sleep.

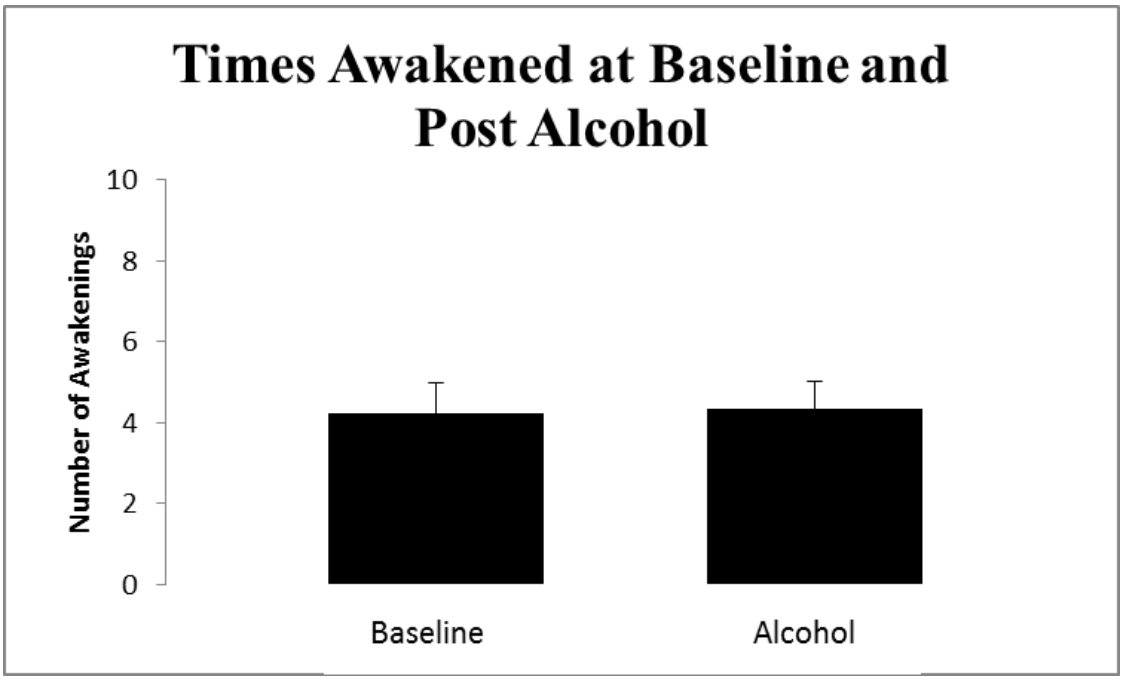

Figure 9: The data shown are number of times awakened measured at baseline and following alcohol consumption. The data shown are 4.235 ± 0.076 and 4.353 ± 0.653. Data are presented as mean ± SEM. No significant differences were determined.

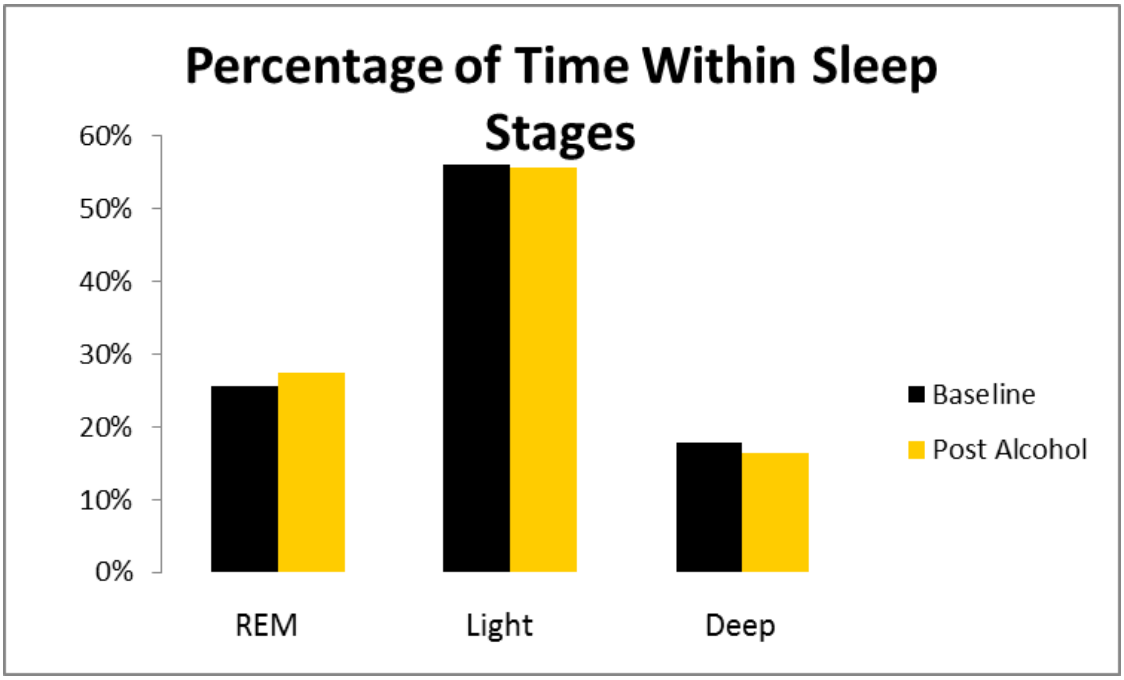

Figure 10: The data shown are percentages measured at baseline and following alcohol consumption. The data shown are 85.118 minutes ± 0.10024, 108.353 minutes ± 0.12038, 186.941 minutes ± 0.09899, 219.529 minutes ± 0.11382, 59.647 minutes ± 0.0143, and 64.941 minutes ± 0.028. Percentages shown are 25.493%, 27.439%, 55.990%, 55.594%, 17.865%, and 16.446%. Data are presented as mean ± SEM. No significant differences were determined between baseline sleep stage percentages and post alcohol sleep stage percentages.

Conclusion

The results from the present study show that heavy consumption of alcohol in a sample of college age males can have marked effects on both hemodynamics and sleep architecture. It is well known that chronic alcohol consumption contributes to increased cardiovascular risk (Lang et al., 1987, Marmot et al. 1994, Puddey et al., 1988); however, no studies have been conducted pertaining to acute bouts of binge drinking in a college-aged male sample in relation to hemodynamic and sleep architecture variables. Although at baseline, subjects were mildly dehydrated, evidenced by the lack of significant difference in urine specific gravities, dehydration may be ruled out as a possible cause for the significant differences. Dehydration has been shown to result in similar findings and has a large impact on vascular health and function (Gonzalez-Alonso et al., 1995). The present results indicate that dehydration did not account for the noted differences in hemodynamics.

As previous research has shown (Foerster et al., 2009, Keil et al., 1989, Wakabayashi et al., 2010), alcohol consumption yielded significant results particularly in aortic systolic blood pressure. This study gives a novel view of the effects in that at both time intervals of 30 minutes post consumption and 12 hours post consumption when compared to baseline measures, significant increases in aortic systolic blood pressures were determined. As evidenced, acute alcohol consumption resulted in an increase in systolic pressure that was seen throughout the sleeping period and into the following morning. The full duration of the effects from acute alcohol ingestion is still unknown, and future research is needed to

expound further on the findings of the present research. This extended period of increased cardiac workload likely has direct effects on the entire cardiovascular system and serves as a catalyst for the formation/progression of other risk factors. Increased aortic systolic pressure can increase the likelihood of further arterial stiffening and arterial wall insult (Safarova et al., 2012). Higher aortic systolic pressures can also reduce the sensitivity of pressoreceptors, thus further impairing autonomic regulation (Mandyam et al. 2012, Michas et al., 2012, Moller et al., 2007, Parati and Esler, 2012).

Because of increased cardiac workload, risk factors associated with cardiovascular disease, specifically hypertension, can be potentiated (Urbina et al., 2011). Following alcohol consumption, nocturnal systolic blood pressure was significantly increased when compared to baseline measures. These data indicate that acute alcohol ingestion results in transient hypertension in the aorta. Because elevated aortic systolic pressures have such a strong impact on peripheral circulation, this puts individuals at risk for many hypertension related cardiovascular diseases. Significantly elevated nocturnal blood pressure is highly correlated to increased risk of cardiovascular disease (Hansen et al., 2011, Yano and Kario, 2012a, Yano and Kario, 2012b). Non-statistically significant increases in diurnal systolic pressures as well as diurnal and nocturnal diastolic pressures were observed. Though findings were not significantly different, changes due to alcohol ingestion can have strong clinical significance. Because our findings observed short-term hypertension lasting up to 12 hours after acute alcohol ingestion, a number of effects can follow ranging from arterial insult, directly due to increases in pressure, to impairments in baroreflex sensitivity (Davis et al., 2012). This extended time period of elevated systolic blood pressure can have a marked

effect on many aspects of cardiovascular health, particularly arterial compliance and autonomic auto-regulation (Michas et al., 2012).

No significant differences were noted in arterial compliance measures. When comparing pulse wave velocities, a slight change was observed. Contrary to available research, statistical significance was not witnessed. Because of this, further research is needed. Augmentation index measures revealed a similar situation to pulse wave velocity in that changes were observed without obtaining statistical difference. Because aortic systolic pressure and nocturnal blood pressures were significantly elevated when compared to baseline, compliance measures such as pulse wave velocity and augmentation index were expected to have statistical significance attributed to the difference between baseline and post alcohol measures (Lewandowski et al. 2012).

The present research showed decreases in both nocturnal systolic dip and nocturnal diastolic dip (Pall et al., 2012, Sasaki et al., 2012). No significant differences were determined between post-alcohol measures and baseline measures, which can be attributed to an outlier in our sample. This outlier showed effects that were not congruent with the mean of the rest of the group, which affected the group mean. This is likely attributed to aerobic training status of the individual, as this variable was not controlled. Observable differences in nocturnal dip were measured, but these differences did not reach statistical significance. Again, though statistical significance was not achieved, clinical importance was obtained in that blood pressure dip was greatly reduced, which is highly correlated to cardiovascular disease progression (Tsioufis et al., 2011).

There were no significant findings in this study relating acute alcohol consumption to

number of awakenings and time in deep sleep in comparisons of baseline and post alcohol consumption, contrary to previous research (Van Reen et al., 2011, Vinson et al., 2010). One significant finding was the difference in time taken to fall asleep. Alcohol showed a significant decrease from baseline data. This illustrates one common problem associating acute alcohol ingestion and sleep. Alcohol is commonly used as a sleep aid, possibly due to the results from this study, which showed reduction in time to sleep, but as evidenced earlier, even acute ingestion can result in transient hypertension which progresses risk factors associated with CVDs. This further reiterates the point that alcohol should not be used as a sleep aid because acute consumption may have deleterious effects. Time spent in deep sleep and number of awakenings showed no significant difference as previously hypothesized (Van Reen et al., 2011, Vinson et al., 2010). The percentage of time spent in each stage of the sleep cycle was not found to be significantly different. Therefore, the interrelationship of how alcohol affects sleep architecture should be studied further.

The current investigation suggests that an acute bout of heavy alcohol consumption among young males may influence the nocturnal BP system and may impact the progression of hypertension related cardiovascular disease due to the increase in aortic systolic blood pressure. Progressions of these diseases are being seen at earlier ages and can be exacerbated by factors such as alcohol consumption. The present findings, which showed a significant increase in aortic systolic blood pressure and nocturnal systolic blood pressure, can be an important mechanism as to how alcohol intensifies the progression of hypertension related cardiovascular disease. These pressure increases can have profound effects on many facets of the cardiovascular system. These effects can range from

impairment of autonomic auto-regulatory mechanisms (Davis et al., 2012) to aspects of hemodynamics (Lewandowski et al. 2012).

Limitations

The most glaring limitation of this study is that the results only apply to males. Further research is needed in order to expound upon how females are affected by acute alcohol ingestion. Another limitation faced during the research process was that subject aerobic training status was not controlled. We did, however, control for exercise throughout the duration of the study to exclude any affects brought on by acute exercise. Another limitation can be attributed to a lack of power to detect differences based on the sample size (N=17). A larger sample could result in an observed significance value.

Future Implications

The connection between alcohol use and hypertension is well documented yet the mechanism remains elusive. Many areas of the cardiovascular system are affected and these effects have consequences which further impact the system. This study showed that acute ingestion of alcohol can result in increases in aortic pressure, which can have a profound impact on the health and functionality of the entire cardiovascular system from a clinical perspective (Friedman and Logan, 2009). An increase in aortic pressure of 4-5mmHg was observed 30 minutes post consumption as well as 12 hours post consumption. Because of the extended period in which the aorta was experiencing an increased workload, nocturnal brachial blood pressure was also found to be significantly increased. These changes can drastically affect hemodynamics as well as baroreflex sensitivity (Michas et al., 2012, Moller et al., 2007) and can occur very early in the cascade of events which progress to

cardiovascular disease. The findings of this study illustrate how a singular acute bout of alcohol ingestion can impact risk factors for the development of cardiovascular disease.

A single bout of alcohol ingestion resulted in up to 12 hours of elevated aortic pressures, which is supported by previous research (Wakabayashi, 2005); however, the duration for which these pressures remain elevated is still unknown. Future research is needed to determine the duration of aortic systolic pressure as well as any other risk factors for the progression of cardiovascular disease. More research observing nocturnal blood pressure dipping following an acute bout of alcohol ingestion is also needed. It may be that this period of increased aortic pressure is the direct mechanism behind baroreceptor blunting which diminishes the presence of a nocturnal blood pressure dip following acute ingestion of alcohol in a young healthy cohort of men.

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Appendix A

From: Dr. Stan Aeschleman, Institutional Review Board Chairperson
RE: Notice of IRB Approval by Full Board Review
Study #: 13-0116

Study Title: Sleep, Individual Differences, Blood Flow, and Alcohol Use in College Males
Submission Type: Initial
Approval Date: 2/18/2013
Expiration Date of Approval: 11/19/2013

This submission has been approved by the above IRB for the period indicated above.

Investigator's Responsibilities:

Federal regulations require that all research be reviewed at least annually. It is the Principal Investigator's responsibility to submit for renewal and obtain approval before the expiration date. You may not continue any research activity beyond the expiration date without IRB approval. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.

You are required to obtain IRB approval for any changes to any aspect of this study before they can be implemented except to eliminate apparent immediate hazards. Should any adverse event or unanticipated problem involving risks to subjects occur it must be reported immediately to the IRB. Best wishes with your research!

Appendix B

Consent to Participate in Research

Information to Consider About this Research

Alcohol Use, Individual Differences, and Sleep in College Males

Principal Investigators: Jacqueline Belhumeur; Daniel Payseur
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Faculty Advisers: Lisa Curtin (curtinla@appstate.edu) and Scott Collier (colliersr@appstat.edu)

What is the purpose of this research?

The specific purpose of this study is to explore the relationships between blood pressure, individual differences (i.e., social, emotional, and behavioral differences), sleep, and alcohol use in college males. It is the intent of the primary investigators to write two Master's theses based upon the results of this study and to publish and present the results of this study in academic journals and at professional conferences.

Why am I being invited to take part in this research?

You are invited to participate because you are a healthy male between the ages of 21 and 25 years with no history of cardiovascular or other medical conditions or regular nicotine use. Additionally, you are not currently on any prescription medications that would be complicated by alcohol use and have previously consumed four alcoholic beverages in one sitting. You also have not been diagnosed with an alcohol use disorder and are not currently receiving any form of psychological service. A screening for alcohol abuse and dependence will be conducted before admitting you into the study. If you volunteer to take part in this study, you will be one of 25 males to do so.

What will I be asked to do?

The research procedures will be conducted at the Vascular Biology and Autonomic Studies Laboratory at the Blue Cross Blue Shields of North Carolina Institute for Health and Human Services on University Hall Drive in room 186C.

You already participated in the brief telephone interview and were informed that we would ask you to:

- Stop taking all over-the-counter medications and supplements for 72 hours prior to today and for the duration of the study
- Not consume alcohol 24 hours prior to today and to not drink alcohol during your time in the study (except for when we ask you to drink alcohol during the next lab visit)
- Bring a government-issues photo identification listing your birth date

In addition to the above:

- You will need to come here 3 times (today and two other days) over the course of 3-5 days (depending on your schedule) for a total of approximately 350 minutes or 5 hours and 50 minutes .

- You will need to continue abstaining from over-the-counter medications and supplements for the duration of the study

- You will need to abstain from exercise on days you visit the lab.

- You will not consume alcohol throughout the duration of the study (3-5 days) with the exception of the next visit to the laboratory when we will ask you to consume alcohol.

Here is a summary of what to expect during each lab visit:

First Session

The first visit will take approximately 80 minutes or 1 hour and 20 minutes. During this visit, we will conduct a series of noninvasive blood pressure tests, including pulse wave velocity, pulse wave analysis, and reactive hyperemia. This is so we can get an idea of how efficiently your blood moves throughout your body. At this time, you will also be given instructions on an ambulatory blood pressure cuff and a ZEO sleep band. This is so we can monitor the flow of your blood and the quality of your sleep over the course of a night before the alcohol consumption session at your second visit. You will be asked to provide a urine sample for assessment of hydration. You will be asked to wear both of these noninvasive devices while sleeping *the night before your second lab visit* (even if this is not the day immediately after your first lab visit). You will need to agree to have a friend drive you to the next session, or agree to take the AppalCart/taxi to and from the lab for the next session. You will receive $10 for your time.

Second Session

After 1-3 nights, you will return to the Vascular Biology and Autonomic Studies Laboratory for a second time at 5:30pm. You will also be asked to eat something two hours before arriving. Food bars and juice will be available in the event that you do not eat. This visit will take approximately 180 minutes or 3 hours and will involve the same blood pressure tests as before (i.e. pulse wave velocity, pulse wave analysis, and reactive hyperemia), additional biological measurements (i.e. height, weight, blood pressure, and body composition), and a series of individual differences measurements (i.e. personality, stress, socialization, sleep, and alcohol-related questions). At this time, you will also be asked to fill out a demographic questionnaire. Finally, you will be asked to consume enough alcohol so that your blood alcohol content reaches approximately .08. This is the equivalent of three to five drinks for most males. These drinks will consist of one part vodka and four parts tonic water and lime. Again, we ask that you not volunteer for this study if you have never consumed four alcoholic beverages in one sitting. Following the alcohol administration, you will be required to stay at the lab until your blood alcohol content returns to .02-.04, at which time we will

release you to a sober driver or escort you to the AppalCart which runs from the lab to the ASU campus until 9:09 PM. We will ascertain your blood alcohol concentration by having you blow into a handheld breathalyzer. We will also measure your blood pressure, pulse wave velocity, and reactive hyperemia after alcohol administration, in addition to assessing your hydration level via urinanalysis. You will be asked to wear the ambulatory blood pressure cuff and ZEO sleep band for a final night and return to the lab in the morning. This is so we can see how the alcohol affected your blood pressure and sleep following alcohol consumption. You will receive $20 for your time.

Third Session

Your third and final visit will take approximate 60 minutes or 1 hour. At this time you will be asked to return your ambulatory blood pressure cuff and ZEO sleep monitor. You will be asked to provide a urine sample for assessment of hydration.We will also conduct pulse wave velocity, pulse wave analysis, and reactive hyperemia tests for a final time. You will receive $10 for your time.

What are possible harms or discomforts that I might experience during the research?

To the best of our knowledge, the risk of harm and discomfort from participating in this research study is slightly more than you would experience in everyday life. Alcohol consumption will take place in a supervised laboratory setting and you will not be released until your blood alcohol content has returned to a safe level, as defined by the National Institute on Alcohol Abuse and Alcoholism. Additionally, you will not be allowed to operate a motor vehicle following the administration to prevent the risk of harming yourself or others; you will not be on any concurrent medications to prevent possible detrimental drug interactions; and you will be required to eat beforehand so that you are not drinking on an empty stomach. All measurements used in the lab are noninvasive and will cause no physiological harm. You may also experience some personal discomfort as you reflect upon your blood pressure feedback or responses to questionnaires. You have the right not to answer any individual questions. Finally, there is some risk that confidentiality could be breached but many safeguards are in place to prevent such harm (see below for list of precautions).

Measures

Body Composition Testing:

There are no known risks associated with this measure. It is essentially the same as stepping on a bathroom scale at home.

Reactive Hyperemia:

No substantial risks are associated with reactive hyperemia. Subjects may feel some discomfort in their arm during the portion of the test when blood is occluded to the arm. The sensation is similar to the "pins and needles" individuals feel if their arm "falls asleep." This feeling will immediately disappear once the occluding pressure cuff is released and blood flow returns to normal. This is a common technique employed to determine vascular function, and 5 minutes of occlusion is the minimum amount of time needed to yield accurate measures. No tissue damage is associated with this method.

Pulse wave velocity:
There are no known risks associated with the Doppler ultrasounds used in this technique. A small Doppler sensor will be placed on the surface of the skin against the arteries in your neck, wrist, upper thigh, and ankle. The sensor uses ultrasound to measure the direction and speed of blood flow through an artery. No physical discomfort should be experienced during this assessment. Patient privacy will be upheld through the use of a curtain during the assessment of the femoral artery, as this is located near the pubic area.

Electrocardiography (ECG):
There are no known risks associated with standard ECG. A series of sensors will be placed on your chest. Trained technicians will perform all ECG preparation and measurements. Again, care will be taken to uphold patient privacy during preparation and assessments, as the chest area will need to be somewhat exposed for electrode placement.

Urine Specific Gravity (hydration assessment):
There are no known risks associated with Urine Specific Gravity. The specific gravity of these samples will be analyzed utilizing a refractometer to assess urine specific gravity. Once the urine sample has been analyzed for hydration it will then be immediately destroyed.
Ambulatory Sleep Monitoring:
Minor risk of discomfort is possible wearing the soft-fabric ZeoTM headband while sleeping. Because metallic fibers are used in the ZeoTM headband to transmit brainwave data, there is risk of skin rash or reaction in individuals who may be allergic to metals. Subjects will be informed to remove the device in such a case and contact one of the investigators.

Ambulatory Blood Pressure Assessment:
There are no known risks associated with ambulatory blood pressure assessment. A small cuff is placed around the upper arm and it is inflated similar to an arm blood pressure cuff. Subjects will be asked to wear this as they sleep. Subjects may feel slight discomfort in their arm with this cuff but this will disappear almost immediately when the cuff is released. A trained technician will demonstrate and fit the cuff for each subject.

AlkoSensor:
The AlkoSensor is a handheld breathalyzer. You will be asked to breathe into a disposable plastic tube for a few seconds and your breath alcohol content will be displayed on a display screen.

Are there any reasons you might take me out of the research?
If you do not use the ambulatory blood pressure cuff or ZEO sleep band as directed, we will have to remove you from the study. Additionally, if you cannot abstain from alcohol for 24 hours prior to initial testing as well as the duration of this study (3-5 days) we will have to remove you from the study. Also, abstaining from all prescription medications for 72 hours prior to the study and abstaining from exercise on lab days is required. Inability to do so will prompt your removal from the study. Finally, if you become uncomfortable at any point throughout the study, you may leave the study without penalty. You cannot, however, leave the lab after consuming alcohol until your BAC returns to a safe level and we know you have safe transportation.

What are possible benefits of this research?
By participating in this research, you may benefit by learning about the health of your cardiovascular system and how you react to alcohol. Additionally, the information gained from this research will enhance our understanding of the interrelation of blood pressure, alcohol, sleep, and individual differences.

Will I be paid for taking part in the research?
We will pay you for you for the time you volunteer while being in this study. You will receive $10 for your first and third visits and $20 for your second visit, for a total of $40 for your participation. You will receive payment each time you arrive at the lab.

What will it cost me to take part in this research?
It will not cost you any money to be a part of this research. Parking at the lab is free, as is the AppalCart. Recall that you may not drive to the second session, but must take the bus, a taxi, or have a friend drive you.

What if I get sick or hurt while participating in this research study?
If you need emergency care while you are at the research site, it will be provided to you. If you get hurt or sick when you are not at the research site, you should call your doctor or call 911 in an emergency. If your illness or injury could be related to the research, tell the doctors, or emergency room staff about the research study, the name of the Principal Investigators, and provide a copy of this consent form if possible. Call Jacqueline Belhumeur, at (804) 475-5503 or Daniel Payseur at (704) 530-8679 as soon as you can to let them know that you are hurt or ill. Please exercise caution regarding all activities regarding the alcohol administration session.

How will you keep my private information confidential?
Your information will be combined with information from other people taking part in the study. When we write up the study to share it with other researchers, we will write about the combined information. You will not be identified in any published or presented materials. All data entry and analysis will be conducted with statistical programs without using identifying information. Additionally, your identifiable information will be stored in a separate building from the rest of your information and will be deleted after three years. Your files, without identifying information, will be stored in the Vascular, Biological, and Autonomic Studies Laboratory office under lock and key.

Whom can I contact if I have a question?
The people conducting this study will be available to answer any questions concerning this research, now or in the future. You may contact the Principal Investigators at (704) 530-8679 (Daniel Payseur) or at (804) 475-5503 (Jackie Belhumeur). If you have questions about your rights as someone taking part in research, contact the Appalachian Institutional Review Board Administrator at 828-262-2130 (days), through email at irb@appstate.edu or at Appalachian State University, Office of Research and Sponsored Programs, IRB Administrator, Boone, NC 28608.

Do I have to participate?

Your participation in this research is completely voluntary. If you choose not to volunteer, there is no penalty or consequence. If you decide to take part in the study you can still decide at any time that you no longer want to participate. You will not lose any benefits or rights you would normally have if you do not participate in the study.

This research project has been approved on 2/18/2013 by the Institutional Review Board (IRB) at Appalachian State University. This approval will expire on 11/19/2013 unless the IRB renews the approval of this research.

I have decided I want to take part in this research. What should I do now?

Please indicate how you plan to get home at the end of the alcohol administration (second) session by checking one of the choices below:

____ Friend

____ AppalCart

____ Taxi

If you have read this form, had the opportunity to ask questions about the research and received satisfactory answers, and want to participate, then sign the consent form and keep a copy for your records.

_____

Participant's Name (PRINT) Signature Date

Vita

Daniel Keith Payseur was born in Lincolnton, North Carolina, to Keith and Delores Payseur. He graduated from West Lincoln High School in Lincolnton, North Carolina, in June 2006. The following autumn, he entered Appalachian State University to study Exercise Science; and in May 2010, he was awarded the Bachelor of Science degree. In the spring of 2012, he returned to Appalachian State University and began study toward a Master of Science degree in the field of Exercise Physiology. During his time there, he worked as a GA in the Vascular Biology and Autonomic Studies laboratory where he researched and presented multiple studies. He was awarded first place in the Inaugural Three Minute Research Competition as well as the Graduate Student Poster Competition in 2013. He also received a grant funded research assistantship through the National Institute of Health. The Master of Science in Exercise Physiology was awarded in May 2013.