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Effects of Pre-Workout Caffeine Supplementation on Post-Exercise Hypotension

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ABSTRACT

Post-exercise hypotension (PEH) is believed to play a major role in the antihypertensive health benefits of exercise. While it has been shown that resistance exercise is effective at eliciting PEH, commonly consumed sports supplements may attenuate or completely eliminate that response. Caffeine, a popular stimulant, is often consumed prior to exercise. Therefore, the purpose of this study was to investigate the effects of pre-workout caffeine supplementation on the post-exercise hypotensive response in adults with above normal blood pressure. Participants (n = 5) were recreationally resistance trained men and women who consumed placebo or caffeine (3 mg/kg bodyweight) 45-minutes prior to exercise. The resistance exercise session consisted of four sets of 10 reps for bench press, cable row, leg press, and shoulder press at 70-75% one repetition maximum. Blood pressure and heart rate were measured pre-exercise, during exercise, and 90 minutes post-exercise. Caffeine supplementation resulted in significantly greater SBP at 30, 50, 60, 70, and 80 minutes post-exercise compared to placebo condition. These findings indicate that pre-workout caffeine supplementation eliminates the post-exercise SBP hypotensive response that was observed in the placebo condition and should be avoided if the antihypertensive effects of resistance training are to be fully achieved

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INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in the United States and accounts for more than 600,000 deaths each year (64). There are multiple risk factors, modifiable and non-modifiable alike, associated with the development of CVD. These risk factors include, but are not limited to, physical inactivity, diet, cigarette smoking, obesity, dyslipidemia, and hypertension (64). Hypertension (HTN) is considered the most important and strongest contributor to CVD and it currently affects nearly half of U.S adult population (65). As a modifiable risk factor, hypertension can be improved through the modification of long-term lifestyle habits. Diet and exercise are at the forefront of lifestyle modifications as they have proven effective in preventing and treating HTN alone or in combination (66).

The acute decrease in blood pressure (BP) following exercise is known as post-exercise hypotension (PEH) and is believed to play a major role in the antihypertensive health benefits of exercise (23). Traditionally, aerobic exercise has been favored over resistance exercise in prescriptions and recommendation guidelines for the prevention and management of HTN (46). However, more recently resistance exercise has been recognized to be just as effective as aerobic exercise at acutely lowering BP (12, 36, 46). Resistance exercise has been shown to acutely lower BP by 3 mmHg, however greater decreases are observed in those with hypertension (6 mmHg) and even larger in non-white hypertensives (10 - 14 mmHg) (36). As resistance training has only recently been

observed as an effective method in BP management, research is in its infancy. As such, the ideal characteristics of the resistance exercise intervention remain largely unknown.

While it has been shown that resistance exercise can elicit PEH, certain sports supplements may attenuate or eliminate the BP related health benefits when taken in conjunction with exercise. The use of sports supplements has become widely popular and the industry continues to grow with at least 55,000 different products available in the United States that account for nearly $30 billion in spending (14, 60). A place of significant growth in the industry has been multi-ingredient pre-workout supplements (MIPS) and energy drinks (29). The primary ingredient in such products is caffeine due to its effect on the central nervous system and its stimulant properties (29). Additionally, caffeine is the most widely consumed substance in the world and nearly 90% of Americans consume some form each day whether through coffee, energy drinks, MIPS or otherwise (53). In particular, caffeine and its associated supplements have gained in popularity for fitness enthusiasts and recreationally active individuals who do not necessarily require the ergogenic benefit of caffeine to perform (53). Furthermore, it has been postulated that caffeine may attenuate or eliminate the BP related benefits of exercise attributed to PEH. Despite the widespread consumption of caffeine and its recognition as a substance that affects blood pressure (18, 53), very few studies have investigated its effect on PEH. The inherent lack of research leaves a critical question unanswered: do these popular, unnecessary supplements do more harm than good?

Of the existing literature, most of the research focuses on the interaction of caffeine and aerobic exercise. To our knowledge, only two studies have investigated the effects of caffeine on the PEH response following resistance exercise, and the findings have been conflicting (3, 58). For example, Souza et al., (58) concluded that in normotensive adults, 4 mg/kg of caffeine 45 minutes prior to resistance exercise at 70% 1RM for 3 sets of 10 resulted in a greater 9-hour ambulatory BP measurement across all time points compared to placebo (58). However, PEH was still observed with caffeine consumption (58). In contrast, Astorino et al (3) concluded that caffeine intake (6 mg/kg) prior to intense resistance exercise (70-80% 1RM) for 4 sets of maximum reps completely eliminated the PEH response during 75 minutes of seated rest in normotensive and prehypertensive men. The opposing findings of the studies by Astorino et al (3) and Souza et al (58) may be attributed to the variation in methodology regarding dosage, exercise volume, and time course of PEH observation. Given the novelty of the research, variability in methods, and conflicted outcomes, more research is necessary to determine if caffeine consumption negates the blood pressure related health benefits of exercise. As the sports supplement industry continues to grow and prevalence of HTN steadily rises, understanding the effects of one on the other has become increasingly important. Therefore, the purpose of this study is to investigate the effect of pre-exercise caffeine consumption on the post-exercise hypotensive response following resistance training in recreationally trained men and women with above normal blood pressure.

REVIEW OF LITERATURE

Acute Blood Pressure Response to Exercise

During dynamic aerobic exercise, systolic blood pressure (SBP) increases linearly with exercise intensity, while a maintenance or slight decrease of diastolic blood pressure (DBP) is observed (23). A "normal" blood pressure (BP) response during exercise, as defined by the American College of Sports Medicine, is an increase in SBP by 10±2 mmHg per metabolic equivalent (MET), although this is still a matter of debate due to individual variances and minimal empirical evidence (16). The change in exercising BP is determined by cardiac output, total peripheral resistance, and sympathetic activity (19).

The rise in SBP is largely due to the increase of cardiac output (CO) in order to meet the metabolic needs of the active muscle (23). Increases in heart rate and contractility due to withdrawal of parasympathetic tone and the subsequent increase in sympathetic activity contributes to the observed increase in cardiac output. The metabolic needs of the muscle are further assisted by the redistribution of blood flow through vasoconstriction of the gastrointestinal and renal vessels and a concurrent blunting of skeletal muscle vasoconstriction due to release of vasodilators, such as adenosine and nitric oxide (NO) in the active muscle (23). The reduction in systemic vascular resistance due to the vasodilation of skeletal muscle arterioles and concurrent increases in heart rate

observed at increasing intensities of exercise, leave DBP mostly unchanged during acute exercise (23).

The blood pressure response during exercise differs by individual, as well as by exercise mode and intensity. The previously described response (SBP increasing linearly with workload and DBP decreasing or remaining the same through a large increase in CO and a decrease in vascular resistance) typically applies to acute aerobic exercise. However, both SBP and DBP typically react more significantly during resistance training due to a more modest increase of CO, an increase or no change in vascular resistance, and mechanical compression/constriction of vessels (23). The BP response during resistance training is cyclical and dependent on the specific phase of the lift: increases during concentric contraction, decreases at completion of the movement, increases again through eccentric contraction in the lowering phase. For both aerobic and resistance training, blood pressure rapidly returns to baseline at termination of exercise, often returning to levels below the pre-exercise baseline. This transient reduction in blood pressure is known as post-exercise hypotension (PEH) and is thought to be one of the acute benefits to exercise (23)**.**

Post-Exercise Hypotension

The phenomenon of a transient decrease in blood pressure following exercise was first observed in 1898 by L Hill after he monitored blood pressure for 90 minutes post 400-yard dash (27). This phenomenon is now termed post-exercise hypotension. Since the original observation, PEH has been demonstrated in both normotensive and

hypertensive men and women with a variety of exercise prescriptions (27). This review will cover the various exercise prescriptions that have been utilized to elicit PEH, as well as discuss the internal physiological mechanisms and other external factors that impact this response. Several factors have been identified to impact the magnitude and duration of the PEH response, including the exercise mode, intensity, and inherent BP of the subject.

Aerobic Exercise and PEH

The effects of aerobic/endurance training on PEH has been extensively researched (15, 19, 24, 28). It is generally accepted that PEH occurs in a dose-response fashion to the exercise intensity and duration, however some have observed no difference in the magnitude of PEH based on intensity or duration (Ham06).

Eicher and colleagues (19) determined that varying exercise intensities on a cycle ergometer elicited significantly different PEH responses. The subjects, 45 prehypertensive males aged 18-55, completed a control trial of 45-minute seated rest and three separate exercise trials at low (40% VO_{2peak}) and moderate (60% VO_{2peak}) intensity for 40 minutes and vigorous (100% VO_{2peak}) intensity until volitional fatigue. Each trial was followed by 45 minutes of seated recovery with BP automatically measured every 3 minutes. Participants were then fit with an ambulatory blood pressure cuff (ABPM) to assess the PEH response for 9 waking hours. As the intensity increased, the greater the PEH response (Vigorous: -11.7/-4.9 mmHg; Moderate: -5.4/-2.0 mmHg; Low: -2.8/-1.5 mmHg). As a result, PEH occurred in a dose-response fashion with each 10% increase in

intensity, SBP and DBP fell by 1.5 mmHg and 0.6 mmHg, respectively (19). Similarly, a study conducted on 23 normotensive males and females found a more significant PEH response with more intense exercise (24). Subjects completed three randomly assigned 45-minute sessions on a cycle ergometer at low, moderate, and vigorous intensity (30%, 50%, & 70% VO_{2peak}). As intensity increased, the greater and longer the PEH response (24). Conversely, Cornelissen et al (15) determined an equally significant PEH response following 50 minutes of aerobic exercise at low (33% HHR) and vigorous (66% HHR) intensities. The study population included trained and untrained normotensive individuals (15). A study conducted on hypertensive older males also demonstrated a non-significant difference in PEH at low (40% VO_{2MAX}) to moderate (60% VO_{2MAX}) intensity (47). Despite the earlier findings that suggest intensity has no impact on PEH, recent research continues to support the dose-response fashion of aerobic associated PEH.

Resistance Exercise and PEH

Resistance training is often supplemented to aerobic training in HTN prevention and treatment. However, the effect of resistance training on PEH is new and not widely studied. Similarly, to aerobic training, there is believed to be a dose-dependent response of PEH following resistance training, but again no consensus has been reached due to 1) general lack of studies and 2) conflicting evidence from existing studies. Rezk et al (54) sought to determine whether lower (40% 1RM) or higher intensities 80% 1RM) of resistance training would induce a greater PEH response. Participants were normotensive adults who completed 6 upper and lower body exercises for 3 sets of 20 reps. Both

intensities resulted in PEH of the same duration, but high intensity elicited a greater magnitude (54). Similarly, Duncan and colleagues (17) investigated the extent of PEH in 16 trained normotensive and prehypertensive men. Participants randomly completed both low (40% 1RM) and high (80% 1RM) intensity sessions with 3 sets of back squat, bench press, and deadlift. The study found that recovery blood pressure was significantly lower following the high intensity compared to low intensity (17). On the contrary, a study evaluated the effect of low intensity (40% 1RM) resistance training on PEH in medicated hypertensive women (41). The exercise sessions included 3 sets of 20 reps for bench press, leg curl, biceps curl, and back squat. The low intensity exercise significantly decreased blood pressure, which persisted for 10 hours post (41). Lastly, a recent 2016 meta-analysis evaluated 30 studies on the effect of resistance training on PEH and concluded that both low and high intensities elicit similar reductions in blood pressure following training (12).

External Factors in PEH

In addition to the exercise prescription parameters, there are a variety of external factors proposed to influence PEH; gender, diurnal variation, recovery posture, inherent blood pressure, and caffeine (37).

Inherent Blood Pressure

Inherent blood pressure is perhaps the most important and well-established of these external factors. Typically, prehypertensive and hypertensive individuals experience a more dramatic and prolonged PEH response compared to normotensives

(11, 50). This response follows the “baseline law” which states that individuals with a greater initial BP will experience the greatest drop in BP following exercise (46). Accordingly, unmedicated hypertensive subjects would be expected to experience a greater magnitude of PEH compared to medicated hypertensives whose baseline BP is closer to “normal” as well as prehypertensive and normotensive individuals.

Gender

It has been hypothesized that men and women may experience PEH differently based on the varying gender specific physiological responses and adaptations to exercise as well as the presence or absence of a menstrual cycle (40, 51). However, these hypotheses have not been supported as many studies show no significant difference in PEH between men and women of similar resting blood pressure (49, 55) and no significant difference in the pattern and overall occurrence of PEH during various phases of the menstrual cycle (20, 35). To put it simply, the menstrual cycle can be broken into two overarching phases: The follicular phase and the luteal phase, both of which are commonly divided into early, mid, and late phase categories (52). Estrogen levels are highest during late follicular (LF) and mid luteal (ML) phases, while levels are lowest during the early follicular (EF) phase (52). The cardioprotective effect of estrogen has recently led to question if and how fluctuating levels of estrogen during the menstrual cycle can affect the PEH response. Presumably, the first study to investigate the menstrual cycle phase on PEH, Esformes et al (20) concluded that the PEH response is similar in pattern, but different in magnitude. The subjects were eight eumenorrheic

young women who completed 3 separate exercise trials at 80% lactate threshold for 30 minutes on a cycle ergometer during the EF, LF, and ML phases. The post-exercise response was measured for 45-min in the supine position. In addition to the similar overall PEH response, it was also observed that the magnitude of DBP and MAP were significantly lower during recovery compared to rest in solely the EF phase, which led to the conclusion that the PEH response was buffered in the LF and ML phases when estrogen levels are naturally higher (20). The major limitation of the study was the absence of blood or urine tests to ensure participants were in varying phases of the menstrual cycle based on estrogen levels as up to 40% of women may have cycles that are considered short, anovulatory, and/or inadequate (52). This lack of determination may have resulted in some subjects not experiencing the normal and expected variations in estrogen in each phase, which could have led to skewed results. Arguably a more robust study, Lynn et al. (35), determined that PEH is largely unaffected by the menstrual cycle and estrogen. Subjects of this study were apparently healthy males and females (M = 14, F = 14). All females were eumenorrheic and not on any oral contraceptive for at least 6 months. The exercise trial(s) consisted of 60 minutes cycling at 60% VO_{2PEAK}. Males completed one trial while females completed three separate trials in the EF, LF, and ML phase determined through blood samples. Post-exercise blood pressure was measured for 90 minutes in the supine position. There was no statistically significant difference in pattern or magnitude of PEH between men and women, as well as no significant difference between phases (35). Contrary to Esformes et al (20), a lower baseline BP was

observed in the ML phase compared to the EF and LF phases, however the baseline differences did not directly affect the overall PEH response (20, 35). Lastly, a handful of studies have shown a difference in PEH mechanism of action based on gender; a decrease in CO is responsible for PEH in men, while a reduction in SVR is responsible in women (40, 51). Still, despite the mechanical differences, research has yet to document a significant difference in PEH between genders. From these studies, it can be concluded that gender does not affect PEH and the inclusion of women is not only plausible, but necessary. Due to the novelty of research on the direct effect of menstrual cycle on PEH, it would be advantageous to test all female participants in the same phase or have female subjects complete two separate trials: a phase when estrogen is low (EF) and a phase when estrogen is high (LF or ML).

Diurnal Variation

Diurnal variation, the physiological changes that occur specific to time of day, are an important external factor in regard to the magnitude of PEH (43). Some studies agree that PEH is more dramatic in the afternoon compared to the morning presumably due to the morning-associated decrease in vasodilatory substances and increase in sympathetic tone (4, 31). However, a recent study found that when circadian variation is controlled for, PEH is not significantly different in the morning vs. evening (9). This process of controlling for circadian variation is extensive and time-consuming, so it may not be plausible for many studies. Research on diurnal variation and PEH is limited and

conflicted, therefore it may be necessary to conduct trials at the same time of day and possibly limit trials to the afternoon to eliminate the effect of diurnal variation.

Recovery Posture

Recovery posture, seated vs supine, has been postulated to play a role in PEH. Seated recovery exacerbates venous pooling by positioning vasodilated vessels below the heart (6). As a result, venous return is diminished as well as preload, stroke volume, and cardiac output. Consequently, a fall in blood pressure occurs. The supine recovery position equalizes the effect of gravity on the body and venous blood and pressure is distributed more evenly, leading to the thought that supine recovery could potentially reduce the effect of PEH (44). In terms of practicality, both recovery positions can be correct based on the population in question and the time of day exercise would be performed. For example, an exercise trial conducted at night would necessitate the supine recovery position as the population who would exercise at night presumably lies down to sleep after exercise. On the other hand, for morning or afternoon exercise the seated or standing position may be more practical as the population would typically be in either one of these positions during waking hours. In conclusion, it is necessary to report which recovery position is utilized as well as to choose a recovery position based on the practical application of results. While the external factors that elicit physiological changes and the subsequent PEH responses are highly variable, the internal physiological factors have been elucidated.

Internal Physiological Mechanisms of PEH

Cardiac output and total peripheral resistance are major determinants of arterial BP; therefore, any change must be attributed to either an increase or decrease in one or both variables, which can occur due to central and/or vascular mechanisms (26). It has been proposed that the transition from exercise to rest causes an imbalance in these two determinants as cardiac output decreases rapidly, although not back to resting levels, while the reduction in SVR is more sustained resulting in lower arterial pressures.

Recent research has focused on the sustained vasodilation of active muscles as the primary internal mechanism of PEH due to changes in the baroreflex that manifests as a reduction in SVR. Essentially, at the onset of exercise, the baroreflex arc begins to operate at a higher level thereby increasing sympathetic tone. The termination of exercise "resets" the baroreflex, decreasing sympathetic tone further than baseline levels.

Alongside the decreased sympathetic nerve activity, an increase in vasodilatory substances occurs (26). Of particular importance, the increased release of nitric oxide and adenosine as a response to acute exercise is believed to play an important role in PEH. These factors work together to cause a reduction in SVR in the active muscles as well as non-exercising tissues, suggesting that PEH is part of a systemic response (26). While the internal physiological factors have been elucidated the external factors that elicit these changes and the subsequent PEH response are more variable.

Overview of Caffeine

Caffeine is the most widely consumed substance in the world with nearly 90% of the American population consuming some form of caffeine each day (53). It is naturally found in chocolate, coffee, and tea, and is an added ingredient in soda, energy drinks, and sports supplements (61). The greatest contribution of caffeine intake, 98%, is attributed to caffeinated beverages. Levels of ≤ 400 mg/day, equivalent to four cups of coffee, has been established as safe in the general population. Certain sub-groups, such as adolescents, pregnant or breastfeeding women, and hypertensive adults (≤ 200 mg/day) have more stringent recommendations for safe caffeine intake without adverse effects (59). The average adult, 18-55 years of age, consumes 200 mg/day (61). Because of its widespread consumption, the physiological effects and pharmacokinetics of caffeine has been extensively researched.

Intake and Metabolism

Alsabri et al (1) offer a thorough review on caffeine intake and metabolism. Caffeine can be consumed in a variety of forms, such as those previously mentioned, as well as in the form of chewing gums, tablets/capsules, and powder as caffeine anhydrous. Caffeine is rapidly and readily absorbed following oral consumption with 99% of the substance absorbed in 45 minutes. Overall absorption of caffeine does not differ by forms, however initial absorption rates do vary. Gum, compared to tablets/capsules, is absorbed more rapidly with absorption beginning in the mouth through buccal mucosa. Dependent on the form of administration, peak blood levels of caffeine are reached 30-60

minutes after ingestion. As an amphiphilic molecule, caffeine ($C_8H_{10}N_4O_2$) is soluble in both water and lipids. Because of this quality, caffeine can cross all biological membranes, including the blood-brain barrier and placenta. Only 10-30% of caffeine is found bound to plasma protein, which demonstrates caffeine's ability to efficiently and freely distribute across all tissues. The average half-life of caffeine is 3-5 hours. However, half-lives as little as 1.5 hours and as much as 9 hours have been recorded in research. Caffeine is metabolized in the liver by the CYP1A2 pathway where it is broken down into three major metabolites: Paraxanthine (84%), Theobromine (12%), and Theophylline (4%). Metabolism and elimination are affected by individual variations, such as age, obesity, pregnancy, and genetic variations in the enzyme responsible for caffeine metabolism. Physiological and environmental factors such as smoking, use of oral contraceptives, grapefruit consumption, and altitude also impact rate of metabolism and elimination, subsequently influencing half-life. Elimination of caffeine is by first order kinetics and only a small percentage is excreted in urine due to the reabsorption of caffeine by the renal tubules following glomerular filtration (1).

Caffeine as an Ergogenic Aid

Keisler and Armsey (33) provide an extensive review of caffeine as an ergogenic aid. The use of caffeine to enhance exercise performance is widespread and supported by evidence-based results. It has been shown to increase alertness, improve cognitive performance, increase time to fatigue, and decrease perception of work, all of which are beneficial for exercise performance. As a result of caffeine’s ability to cross all biological

membranes and affect all tissues, a specific mechanism of action regarding caffeine and exercise performance has yet to be established. Over the years there have been many proposed mechanisms to explain the ergogenic effect of caffeine. Perhaps the earliest proposed mechanism comes from Powers and colleagues who observed increased free fatty acid oxidation during aerobic exercise. It was thought that this led to a delay in depletion of muscle glycogen stores, a decrease in lactic acid production, and consequently the ability to exercise longer. However, current research does not support these findings, which suggest other potential mechanisms of action to explain the ergogenic effect of caffeine (33).

Similarly, it has been proposed that through the inhibition of the enzyme phosphodiesterase, muscle glycogen is spared by an increase in fat oxidation (33). More specifically, the enzyme phosphodiesterase is responsible for the breakdown of cyclic adenosine monophosphate (cAMP). The inhibition of phosphodiesterase leads to an accumulation of cAMP which will activate the hormone lipase. Lipase stimulates lipolysis and as a result, free-fatty acids are released and transported to active tissue for energy. The dosage required to elicit a physiological response in humans would be toxic and therefore this mechanism is also unlikely to describe the ergogenic effect of caffeine (33).

Research has indicated that caffeine consumption activates ryanodine receptors within skeletal muscle, which leads to increased calcium release from the sarcoplasmic reticulum (33). It is hypothesized that activation of ryanodine receptors also leads to

increased sensitivity of the muscle fiber to calcium and decreased activity of the sarcoplasmic reticulum calcium pump. The effect is mediated by stored levels of calcium and dosage of caffeine. Research has shown supraphysiological levels of caffeine would be required to generate an ergogenic effect (33).

Perhaps the most popular and plausible mechanism of action is the ability of caffeine to act as a non-specific antagonist on adenosine receptors in the brain and peripheral tissues (33). Although some research suggests a reduction in muscle pain and perceived force as a result of adenosine receptor blockage within skeletal muscle, much is still unclear regarding adenosine and skeletal muscle. Therefore, the key mechanism regarding caffeine and exercise performance is believed to occur within the central nervous system. Caffeine and its main metabolite, paraxanthine, cause a cascade of events opposite to the function of adenosine, which is responsible for the feeling of tiredness/sleepiness. As a result, caffeine has been shown to delay or even prevent feelings of fatigue. The release of the neurotransmitter's dopamine, serotonin, acetylcholine, and epinephrine are controlled and inhibited by adenosine. Caffeine consumption prevents the action of adenosine and encourages the release of neurotransmitters, which is associated with the ergogenic effects seen with caffeine (33).

Vascular Effects of Caffeine

Echeverri et al (18) provide an extensive review on the vascular effects of caffeine. Although caffeine is one of the most widely consumed substances around the world, its effect on the cardiovascular system is not completely understood. The main

cardiovascular component affected is believed to be blood pressure. Acutely, a 200-250 mg dose of caffeine raises SBP and DBP in normotensives by 3-14 mmHg and 4-13 mmHg respectively. The rise in blood pressure with caffeine occurs in line with plasma concentration; BP begins to increase within 30 minutes following consumption and reaches maximal levels at 60-120 minutes. The primary vasopressor mechanisms of caffeine include its ability to antagonize adenosine receptors, and to a lesser extent, its direct and indirect action on the endothelium and vascular smooth muscle cells (VSMC).

As previously discussed, caffeine acts as an adenosine A_1 and A_2 receptor blocker and thereby restricts the vasodilatory function of adenosine. As a result, plasma concentration of adenosine accumulates and an increase in sympathetic tone, circulating catecholamines (specifically norepinephrine), and peripheral vascular resistance is observed. The cumulative effect is indirect vasoconstriction that manifests as an increase in blood pressure (18).

As one of the most extensive tissues in the human body, the endothelium is responsible for many aspects of vascular biology. The most important function here is the maintenance of VSMC tone through an intricate balance in the release of vasoconstrictors and vasodilators, particularly nitric oxide. Caffeine activates endothelial ryanodine receptors which stimulates the release of calcium from the endoplasmic reticulum. Cytoplasmic calcium binds to the protein calmodulin which forms a complex that enhances the activation of nitric oxide synthase. Therefore, caffeine directly results in the release of nitric oxide from the endothelium that rapidly diffuses into VSMC. The end

result of this process is vasodilation and improved endothelial cell function at rest. However, caffeine and exercise results in decreased endothelial cell function, presumably due to the duality of caffeine's role in endogenous nitric oxide production based on rest or exercise. The vasodilation effect of caffeine may be antagonized by the simultaneous inhibition of adenosine receptors. The effect on adenosine is believed to be the predominating cardiovascular mechanism, due to lack of in vivo research and the large doses proposed to be necessary to elicit the calcium response of the endothelium and VSMC. Lastly, the effect of caffeine on post-exercise hypotension is largely unknown (18).

Influence of Habituation

In regard to chronic intake of caffeine, research has shown an inconclusive contribution to hypertension and other cardiovascular disease, which is believed to be as a result of long-term intake increasing tolerance to the pressor effect (42). The influence of habituation on the ergogenic and cardiovascular effect of caffeine is not completely understood. Previously, it was hypothesized that caffeine-naive individuals experience greater ergogenic effects than habitual caffeine users, however recent research has reported conflicting results. Some report no difference while others report a blunting of erogenicity (25, 48). The key mechanism believed to be responsible for the reduction in ergogenic effect experienced with habitual caffeine intake is the up-regulation of adenosine receptors and increased speed of the CYPA12 enzyme (34). The dosage and time required to elicit habituation is not definitive, but most research has established

>300 mg/day for at least three days (21, 48). The blunted ergogenic response could potentially be offset by consuming doses greater than usual prior to exercise or through short-term withdrawal leading up to an event (34). Due to conflicting results and an unclear understanding on the effect of caffeine habituation, it may be advantageous to avoid using caffeine-naive individuals in research that is aimed at determination of and/or effect on physiological responses.

Caffeine and Post-Exercise Hypotension

Despite the widespread consumption of caffeine and recognition as a stimulant that acutely affects blood pressure, very few studies have investigated the effect of caffeine consumption on post-exercise hypotension. Of the existing literature, outcomes are conflicting.

To determine the effect of caffeine on recovery hemodynamics, Souza et al (58) recruited 15 healthy adults (12 Males, 3 Females) with recreational resistance training experience to participate in the double-blind, placebo controlled, crossover study. All participants were considered light caffeine habituated, which was defined as an average daily intake of less than 250 mg. Prior to the study, participants were instructed to abstain from caffeinated beverages, vigorous exercise, and alcohol for at least 72 hours prior to testing. All participants had 1RM tests administered for the following lifts: Lat pulldown, knee flexion, chest press, knee extension, bicep curls, leg press at 45 degrees, and triceps curls. At least 72 hours later, participants completed either the caffeine or placebo trial between the morning hours of 8:00 and 9:00 am. Resting BP values were taken after 10

minutes of seated rest using an automated blood pressure device. Once baseline values were recorded, participants randomly received an identical capsule of either placebo or caffeine. All participants received both capsules and completed the trial on non-consecutive days. The caffeine capsules contained 4 mg/kg of caffeine. Participants would then wait 45 minutes before completing the exercise session. At the end of the 45 minutes, blood pressure and other hemodynamic values (cardiac output, stroke volume, and peripheral vascular resistance) were measured. The exercise session consisted of a 5-minute warm-up and then 3 sets of 10 reps at 70% 1RM with 90 seconds of rest between each set. The exercises were the same as listed above for 1RM assessment. Blood pressure and hemodynamic variables were assessed again 15 minutes post-exercise as well as blood pressure measured every 30 minutes for 9-hours post with an ambulatory blood pressure monitoring device. Most significantly, caffeine ingestion resulted in greater blood pressure across all time points when compared to placebo, however PEH was still present (58).

Two years later, the same research team sought to determine the influence of varying doses of coffee on PEH in hypertensive adults (57). Subjects were both genders (9 females, 3 males) between the ages of 40-55 who participated in regular jogging for at least three months, but were overweight with controlled hypertension. All subjects were instructed to abstain from caffeinated beverages for at least 48 hours prior to the study. Baseline values were measured after 10 minutes of seated rest with a standard mercury sphygmomanometer. The intervention included four separate exercise sessions on a cycle

ergometer for 40 minutes at 60-80% max heart rate. For 120 minutes post-exercise, blood pressure was assessed in 10-minute intervals in the seated position. Particularly unique to this study, participants ingested caffeine up to 30 minutes post-exercise depending on the dosage. Each participant randomly received all four caffeine interventions: CAF1: 150 ml of coffee once at 10 minutes post for a total of 144 mg caffeine; CAF2: 150 ml of coffee twice at 10 and 20 minutes post for a total of 288 mg caffeine; CAF3: 150 ml of coffee thrice at 10, 20, and 30 minutes post for a total of 432 mg caffeine; DESC: 150 ml decaffeinated coffee thrice at 10, 20, and 30 minutes post for a total of 108 mg caffeine. Both forms of coffee were sourced from the same manufacturer and were prepared with 500 ml of boiling water and sweetened with sugar. Blood pressure was measured every 10 minutes for a total of 120 minutes using a standard mercury sphygmomanometer. Post-exercise hypotension was observed at all time points in DESC as well as at 10, 20, and 90 minutes in CAF1. Systolic BP was increased in CAF2 and CAF3 at all time points and DBP was increased at each time point for all three caffeinated interventions. However, statistical significance was only found at 10 minutes post-exercise in CAF2 and CAF3 when compared to CAF1. These results suggest that one dose of caffeine is enough to blunt the systolic PEH response, while two and three doses completely eliminate PEH and instead result in a post-exercise hypertensive response (57).

A 2006 study by Notarios and colleagues (45) investigated the effect of intravenous caffeine on the post-exercise blood pressure response based on the hypothesis that caffeine blocks the vasodilator action of adenosine. The subject

population included 14 healthy, middle aged adults. In this double-blind, placebo controlled, crossover study participants completed two separate testing days at least one week apart. Participants were instructed to abstain from caffeinated food and beverages for at least 72 hours and to consume their last meal at least 2 hours before the trial. Prior to the exercise session, blood pressure was measured with a sphygmomanometer and then an antecubital catheter was inserted into the right arm forearm. Over the time course of 20 minutes, 4 mg/kg of caffeine or placebo were intravenously infused. After infusion, participants sat in the upright position for 10 minutes before exercise. The exercise session was a graded cycle ergometer test that increased intensity by 17 Watts per minute until volitional failure, which was determined by a respiratory exchange ratio greater than 1.1 or the inability to maintain pedaling speed. At termination, participants completed an active recovery on the bike for two minutes. Post-exercise blood pressure was assessed for 10 minutes post. The key result was that caffeine completely eliminated the PEH response over the 10-minute recovery period (45)

Astorino et al (3) concluded that regardless of caffeine ingestion, intense resistance training completely eliminated the PEH response. The present study was conducted on 14 resistance trained normotensive and prehypertensive men. Prior to the study, participants were educated on caffeinated foods and beverages and were instructed to avoid consumption for at least 48 hours prior to the two testing days. Upon arrival at the testing facility, baseline blood pressure was measured after 5 minutes of rest with an automated blood pressure device. Shortly after, participants 1RM was measured for

bench press, leg press at 45 degrees, bilateral row, and barbell shoulder press. One week after baseline measurements, participants returned for testing at the same time of day. Participants were randomly assigned to receive caffeine (6 mg/kg) or placebo, both of which were provided in identical capsules. One hour after ingestion of caffeine or placebo, participants began the resistance training protocol. In the one-hour time frame, resting BP measurement was taken for 30 minutes every 10 minutes. As a warm-up, participants walked to the fitness center and completed 8-10 reps of bench press. For the actual exercise intervention, participants completed 4 sets of maximum repetitions at 70% 1RM on bench press and shoulder press and 80% of 1RM on leg press and bilateral row. Following the exercise session, participants returned to the lab for 75 minutes of seated recovery with BP measured every 25 minutes. Participants returned one week later for the opposite treatment. The study found no change in DBP between placebo or caffeine, but SBP was higher post-exercise with caffeine consumption. The PEH response was not observed with either placebo or caffeine (3).

In contrast to the above studies, Anunciaco and colleagues (2) reported caffeine intake does not interfere with recovery blood pressure. Participants in the study were 10 healthy, physically active, normotensive men. Prior to the exercise sessions, participants were instructed to avoid alcohol and caffeine consumption as well as any vigorous activity for at least 72 hours. Each participant was evaluated for both treatments at least 72 hours apart. Resting blood pressure was measured after 10 minutes of seated rest and followed by ingestion of either caffeine (4 mg/kg) or placebo in identical capsules. Blood

pressure was measured again for one-hour post-ingestion in 10-minute intervals before the exercise session. Participants completed 50 minutes of aerobic exercise on a cycle ergometer at 60% VO_{2PEAK}. The test was followed by 60 minutes of seated rest with BP assessed every 10 minutes with an automated device. Results from the study found no significant difference in BP before, during, or after exercise following caffeine consumption when compared to placebo. Therefore, this study suggests caffeine has no impact on aerobic PEH (2).

Finally, a few studies have determined the effect of caffeine on PEH as a secondary outcome measure (10, 63). The first study investigated the acute effect of caffeine as an ergogenic aid in anaerobic exercise (63). Participants were 19 highly trained male athletes aged 18-40 years. Prior to the study participants were asked to abstain from any caffeine for 48 hours and fast for 8-12 hours. Upon arrival, resting measurements were obtained and participants were given a commercially made shake with caffeine (5 mg/kg) or without caffeine. Fifteen minutes after participants consumed the shake, a standardized breakfast was served. An hour after consumption of the shake, participants began the exercise intervention. The anaerobic exercise session included a 10-minute warm-up, 3 exercise tests with 60 second rest between each, of leg press, chest press, and the Wingate. Blood pressure was measured post-exercise for an unspecified amount of time and the result was a significant increase in systolic PEH with caffeine compared to placebo (63). Conversely, Bunsawat et al (10) evaluated the effect of caffeine on autonomic recovery following aerobic exercise in 18 young and apparently

healthy adults. Participants were instructed to refrain from caffeine, alcohol, food, and strenuous physical activity for at least 12 hours before testing. As a crossover study, participants were evaluated in both conditions and all tests were completed at the same time of day (7:00 am - 10:00 am). After 15 minutes of supine rest, baseline measurements were obtained and then participants ingested either a 400 mg caffeine or placebo capsule. A VO_{2MAX} treadmill test was administered 45 minutes after. Once the test was finished, participants rested in the supine position while measurements were performed at 5, 15, and 30 minutes. The significant finding of this study regarding blood pressure was that compared to baseline, caffeine significantly increased DBP at all time points while no difference in SBP was observed (10).

METHODS

Participants

Men and women between the ages of 18-65 years, with elevated BP (SBP 120-129 mmHg and/or DBP: >80 mmHg) or stage 1 hypertension (SBP: 130-139 mmHg and/or DBP: 80-89 mmHg) were recruited for this study. Interested participants were initially asked questions regarding caffeine consumption, physical activity habits, resting blood pressure, and medical history. Participants were considered recreationally resistance trained (2-3 days/week for ≥ 2 months with prior technique experience with the assigned lifts) and caffeine-habituated (≥ 200 mg/day). Participants were excluded if they were pregnant or currently breastfeeding and/or used any medication or supplement with cardiovascular effects. Additionally, participants were excluded if they were current smokers or had smoked in the last 6 months. Participants were apparently healthy with no reported signs or symptoms of cardiovascular disease as indicated by a pre-participation screening questionnaire. All participants signed an informed consent. This study was approved by the Stephen F. Austin State University Institutional Review Board.

Protocol

General Design: For this study, a randomized, double-blind, placebo-controlled, crossover design was implemented in which the post-exercise blood pressure response was observed following resistance exercise with and without caffeine supplementation. Participants were asked to report to the lab on 4 separate occasions over the course of approximately 8 days. A sample study timeline is provided in Figure 1. Participants were asked to fast for at least 2 hours prior to any visit as well as refrain from caffeine, alcohol, and exercise for at least 24-hours. Participants were instructed to maintain a similar diet in the 24-hours prior to any visit.

Blood Pressure Screening & Anthropometric Measures: Potential participants who met the inclusion criteria came to the Fitness and Human Performance Lab for official blood pressure (BP) screening to determine whether or not they satisfied the elevated or stage 1 hypertensive criteria. After 10 minutes of seated rest in a quiet, temperature-controlled room, BP was measured with a properly fit automatic oscillometric cuff (Omron Intellisense, Japan) on the participants left arm. The test-retest reliability of the cuff was previously determined with a Pearson R of .972 for SBP and .948 for DBP. Participants were instructed to sit with back supported and feet flat on the ground with arm rested at heart level. Additionally, participants were asked to remain quiet and still throughout measurements. Blood pressure was measured every 2 minutes for a total of 3 measurements. The average of the 3 measurements was used to determine blood pressure status. These procedures were repeated a second time, at least 24 hours

later, in order to confirm BP status. Following BP screening, anthropometric values of eligible participants were recorded: height, weight, and body fat percentage (DEXA).

Maximum Strength Assessment: One-repetition maximum (1-RM) tests were performed at least 72 hours prior to intervention. A specified 5-10 repetition warm-up was completed once participants were given instructions on proper form and safety. Following the warm-up, participants performed a 1RM assessment according to Baechle and Earle (5) guidelines for barbell bench press, seated 45º leg press, barbell shoulder press, and cable row. A conservative, near maximal load was estimated in which the participant was able to complete 2-3 reps. If successful, the participant rested for 2-4 minutes and then attempted a 1RM by increasing the weight by 5-10% for the upper body lifts and 10-20% for lower body. If unsuccessful, the load was decreased by 2.5-5% for upper body lifts and 5-10% for lower body. This process was repeated 3-5 times until the participant was able to properly execute only one complete repetition (5).

Post-Exercise Hypotension Intervention: The two exercise trials in which post-exercise blood pressure was measured occurred at least 72-hours apart. In order to eliminate the morning-associated diurnal variations in BP, all trials were conducted between the hours of 3:00 and 7:00 pm (31). Upon arrival at the lab, participants were asked to verbally confirm whether or not they refrained from caffeine, alcohol, and exercise for at least 24-hours. Then, participants sat in a quiet, temperature-controlled room for 10 minutes. After seated rest, baseline BP was measured as previously described and the average of 3 measures was recorded.

Once baseline BP measurement was complete, participants consumed 12 ounces of sports drink with either caffeine (3 mg/kg of body weight) dissolved in the beverage or the same sports drink without caffeine (placebo) in a randomized, double-blinded fashion. The look and flavor of the beverage was identical for the caffeine and placebo trials.

Forty five-minutes following beverage consumption, participants completed a brief warm-up (10 minutes) and then a resistance exercise session that consisted of 4 sets of 10 repetitions with 90 seconds rest between sets for the following exercises: bench press and shoulder press at 70% 1RM and 45º leg press and cable row at 75% (3). Heart rate, rating of perceived exertion, and the number of reps achieved was recorded following each set during the exercise bouts. Additionally blood pressure was measured by the same automatic device following the 4^{th} set of each exercise.

Once the resistance exercise session was complete, participants returned to the seated position and post-exercise blood pressure was measured every 10 minutes for 90 minutes.

Statistical Analysis

A 2-way (condition x time) repeated measures ANOVA was used for statistical analysis. Using the mean values for each dependent variable, main effects for condition (caffeine and placebo) and time (pre-beverage, pre-exercise, immediately post-exercise, and 10, 20, 30, 40, 50, 60, 70, 80 and 90 min post-exercise) were determined, as well as any condition x time interaction. Significant main effects were followed up with pairwise

comparisons (least significant differences). Interactions were followed up with dependent t-tests between conditions at a given time point. All statistical analyses were performed in SPSS.

RESULTS

Subject demographic and BP screening data are displayed in Table 1. Maximal strength (1RM) testing data are displayed in Table 2. Workout data for the two conditions are presented in Table 3. There we no differences between conditions for workout volume (reps completed), perceived intensity (RPE), or any of the physiological measures recorded between sets (HR and BP).

The mean values for SBP from 45-minutes pre-exercise prior to beverage consumption to 90 minutes post-exercise for each condition are displayed in Figure 2. There was a main effect for condition ($p = 0.017$), time ($p = 0.017$), and a trend towards a significant condition x time interaction ($p = 0.088$). The interaction was followed up by dependent t-tests that revealed significantly greater SBP at 30, 50, 70, and 80 minutes post-exercise for the caffeine compared to placebo condition. There was also a strong trend toward significant ($p < 0.06$) between condition differences at the PRE-EX and 70 minute post-exercise time points. Pairwise comparisons for time revealed significantly greater SBP pre-exercise, 45 minutes after beverage consumption (PRE-EX) compared to pre-beverage consumption (PRE-BEV). The average change in SBP from pre-exercise prior to beverage consumption to 20-90 minutes post-exercise for each condition is displayed in Figure 3. A dependent t-test revealed a statistically significant difference between conditions ($p < 0.005$).

The mean values for DBP from 45-minutes pre-exercise

prior to beverage consumption to 90-minutes post-exercise for each condition are displayed in Figure 4. There was a main effect for time ($p = 0.034$), but no main effect for condition or condition x time interaction

The mean values for MAP from 45-minutes pre-exercise prior to beverage consumption to 90-minutes post-exercise for each condition are displayed in Figure 5. There was no main effect for time ($p = 0.106$), but a trend towards significance for condition ($p = 0.07$), as well as towards a significant condition x time interaction ($p = 0.075$). The interaction was followed up by dependent t-tests that revealed significantly greater MAP only at the pre-exercise (PRE-EX) time point, 45 minutes after beverage consumption for the caffeine compared to placebo condition. There was also a trend toward significant ($p < 0.10$) between condition differences at the 20 and 70 minutes post-exercise time points. The average change in MAP from pre-exercise prior to beverage consumption to 20-90 minutes post-exercise for each condition is displayed in Figure 6, although the differences were not significant ($p = .237$).

The mean values for HR from 45-minutes pre-exercise prior to beverage consumption to 90-minutes post-exercise for each condition are displayed in Figure 7. There was a main effect for time ($p < 0.001$), no main effect for condition ($p = 0.202$), and a significant condition x time interaction ($p = 0.034$). The interaction was followed up by dependent t-tests, but no significant between conditions differences were found at any particular time point. However, the immediately post-exercise time point ($p = 0.051$) appears to be driving the condition x time interaction observed. Pairwise comparisons for

time revealed significantly greater HR immediately post-exercise (IPE), and at 10, 20, and 30 minutes post-exercise compared to before exercise prior to beverage consumption (PRE-BEV), regardless of condition.

DISCUSSION

The aim of the present study was to investigate the effects of pre-exercise caffeine supplementation on the post-exercise hypotensive response to a bout of resistance training in recreationally trained adults with above normal blood pressure. Key findings of the study include: (a) caffeine (3 mg/kg) significantly increased pre-exercise SBP; (b) caffeine resulted in significantly greater post-exercise SBP at 30, 50, 60, 70, 80 minutes compared to placebo; and (c) while resistance exercise at 70-75% 1RM did result in systolic-PEH (-4 mmHg), the hypotensive response was reversed by caffeine supplementation (+4 mmHg).

The observed systolic PEH following resistance exercise, as well as the absence of diastolic PEH, is supported by previous data (13, 17, 22, 30, 32, 56). It is postulated that diastolic PEH does not occur when there is a decrease in venous return and baroreflex with a subsequent decrease in CO accompanied by an increase in PVR (54). Contradictory to the present findings, there are studies that have observed both systolic and diastolic PEH (8, 38, 54). These differences may be due to differences in methodology and participant characteristics between studies. For example, it appears that those with higher baseline BP (8), less training experience (38), and lower intensity/volume is more effective at eliciting diastolic PEH (54). Nonetheless, the current exercise prescription was effective at eliciting systolic PEH and the purpose of

the present study was to investigate whether or not caffeine supplementation would eliminate this response.

Because of its' stimulatory effects, caffeine has been postulated to mitigate the hypotensive response following exercise. While the current resistance exercise prescription did result in PEH, caffeine supplementation not only eliminated PEH, but instead caused a hypertensive response. As a more novel area of research, the corresponding data is limited. To our knowledge, only three studies have investigated the effect of caffeine on post-resistance exercise BP and the current body of literature has similar, yet divergent conclusions (3, 58, 63). The caffeine-associated increase in post-exercise systolic BP, and change in duration of PEH, was observed in all three studies. As for DBP, the overarching consensus was that caffeine had no significant effect. On the contrary, a study did report that regardless of caffeine supplementation, intense resistance exercise eliminated the PEH response (3), while another reported that, although caffeine significantly increased SBP, PEH was still present at early time points (58). Both studies, and the present, prescribed resistance exercise of 70-80% 1RM, yet the caffeine dosage and other methodology varied.

To start, Souza et al., (58) used a 4 mg/kg caffeine dose and implemented 9-hour ABPM. The use of ABPM, as opposed to BP measurement within a controlled setting, adds some external validity, while sacrificing internal validity. The lack of, or unreported, control for activity during the 9-hour BP measurement window may have influenced the overall appearance of PEH in the caffeine and placebo condition (58). As such, the

present study assessed BP in a controlled setting, in the seated position, to expand upon the baseline understanding of how caffeine may influence the PEH response. The current methodology did account for external validity through the use of seated recovery vs supine, as well as allowing subjects to partake in activities such as scrolling their phone, doing homework, listening to music/podcasts, etc., while remaining seated, between the BP measures. Souza et al. (58) also used a higher dose than the current study, albeit just a 1 mg/kg difference, the dose still equaled more than the amount of caffeine found in an average cup of coffee and pre-workout supplement.

Conversely, Astorino et al., (3) suggested PEH was eliminated due to intense resistance exercise. However, it is difficult, and possibly erroneous, to completely attribute the lack of PEH to 1RM intensity as subjects performed maximal reps to failure for 4 sets (3). It is plausible that the increased volume masked the hypotensive response as other resistance exercise PEH studies have observed PEH at a similar intensity (8, 17, 22, 30, 54). The present study prescribed a more commonly implemented exercise prescription within the general population (4 sets of 10 reps at 70-75% 1RM) and still observed PEH in the placebo condition. Besides the increase volume in the Astorino study, the prescribed caffeine dose was double that of the present study (6 mg/kg) and is significantly greater than that of a cup of coffee or pre-workout supplement (3). Again, we observed similar deleterious effects of caffeine on PEH with not only half the dose, but a more realistic dose of pre-workout caffeine. As such, the results of the present study support the use of intense resistance exercise as an alternative anti-hypertensive

therapeutic approach as well as highlights the unintended consequences of pre-workout caffeine consumption.

A possible explanation behind the caffeine-induced pressor effect shown with SBP is likely the antagonization of adenosine receptors (18, 33). As a result, plasma levels of adenosine accumulate and an increase in sympathetic tone, circulating catecholamines, and peripheral vascular resistance (PVR) occurs. Thus, the vasodilatory effect normally observed post-exercise is reduced or eliminated (33). The decrease in sympathetic tone and PVR following exercise are strongly believed to be defining characteristics of PEH (23, 27). Based on results of the present study, we speculated that caffeine may offset the decrease in both factors, and in turn, cause vasoconstriction that manifests as the elimination of PEH.

Given the current findings, the present study is not without limitation. One limitation was the small sample size (n =5). Despite the limited sample size, the large effect size in the systolic PEH response still allowed for the study to be adequately powered (> .80) for this particular dependent variable. A larger sample may help clarify the effect of caffeine on DBP and MAP post-exercise. Participants were largely college-aged, Caucasians with slightly above normal BP. As such, caution should be used when extrapolating the results of this study to other populations, as subject characteristics (race, age, BP status) can greatly influence PEH. Another limitation was the absence of hemodynamic variable measurement (CO, SV, PVR, HRV) that could have given more insight into the observed PEH response and specific mechanisms responsible. Lastly,

despite best efforts in matching the taste of both beverages, all participants complained of a bitter taste in the caffeine condition. This introduces a potential bias and influence of PEH results, but highly unlikely that participants were able to significantly manipulate the physiological BP response.

Future research should include more subject populations, including medicated and nonmedicated hypertensives, as they are likely to benefit the most from resistance exercise and the benefits of the PEH response. Even a small 2 mmHg decrease in SBP is associated with a 14% and 9% reduced risk of stroke and coronary artery disease, respectively (62). More attention should also be placed on the manipulation of various factors of the exercise prescription (intensity, total volume, rest, etc). In regard to the specific caffeine-PEH relationship, future research should include supplementation with popular pre-workout blends that include caffeine, as other supplements in these blends may also impact blood pressure. Lastly, future research should investigate the effect of caffeine on hemodynamic variables of PEH to gain a deeper, more robust understanding of their relationship.

Once more, the present study supports the use of resistance exercise in the early management of high blood pressure development and it underscores the potential cardiovascular health risks of caffeine prior to resistance exercise. This is particularly true if blood pressure is a concern, which is the case for a large majority of the population (64). Almost 50% of U.S. adults have HTN and another 30% are considered to have elevated BP (64). Therefore, nearly 80% of Americans should be mindful of blood

pressure and perform exercise for the health-related benefits. The sports supplement industry, particularly energy drinks and MIPS, has grown exponentially, and continues to market these products to the general population as a necessity (29, 53). However, these individuals do not require the ergogenic benefit of caffeine and this study suggests they should avoid pre-workout caffeine supplementation as it negates the critical anti-hypertensive benefit of PEH.

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Table 1. Demographic, body composition, and resting blood pressure values obtained from initial fitness screening of individuals with above normal blood pressure.

Variables	Men (n = 3)	Women (n = 2)	Total (n = 5)
Age (years)	23 ± 2	25 ± 5	23 ± 3
Weight (kg)	88 ± 6	70 ± 25	80 ± 16
Height (in)	69 ± 1	64 ± 3	67 ± 3
Body Fat (%)	31 ± 14	34 ± 12	32 ± 12
Systolic Blood Pressure (mmHg)	127 ± 6	125 ± 8	126 ± 6
Diastolic Blood Pressure (mmHg)	71 ± 10	82 ± 2	76 ± 9
Mean Arterial Pressure (mmHg)	90 ± 6	97 ± 3	92 ± 6
Heart Rate (bpm)	74 ± 9	74 ± 9	74 ± 8

All values represent mean ± SD. Blood pressure and heart rate values averaged across two screening visits.

Table 2. Maximal strength (1-repetition maximum) values from initial fitness assessment of individuals with above normal blood pessure.

Variables	Men (n = 3)	Women (n = 2)	Total (n = 5)
45º Leg Press	333 ± 115	185 ± 59	274 ± 119
Barbell Shoulder Press	53 ± 22	29 ± 5	43 ± 21
Cable Row	77 ± 24	45 ± 13	64 ± 25
Bench Press	87 ± 43	36 ± 10	67 ± 41

All values represent mean ± SD. All units in kg.

Table 3. Comparison of resistance exercise session data (4 exercises x 4 sets x 10 reps) for placebo and caffeine conditions in individuals with above normal blood pressure (n = 5).

Variables	Placebo	Caffeine	p - value
Total Reps	158 ± 5	159 ± 3	0.374
Rating of Perceived Exertion	13 ± 1	13 ± 2	0.737
Heart Rate (bpm)	143 ± 19	149 ± 25	0.150
Systolic Blood Pressure (mmHg)	123 ± 3	125 ± 9	0.567
Diastolic Blood Pressure (mmHg)	65 ± 9	67 ± 8	0.589

All values represent mean ± SD. p-values from dependent t-test comparing conditions. RPE and HR data averaged from the end of each set. BP data averaged from end of each exercise. Exercises included leg press, bench press, cable row, shoulder press.

Figure 1.

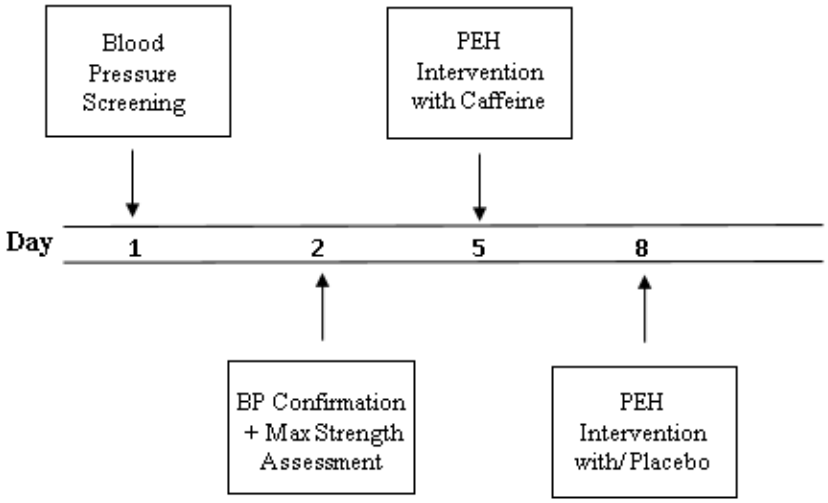
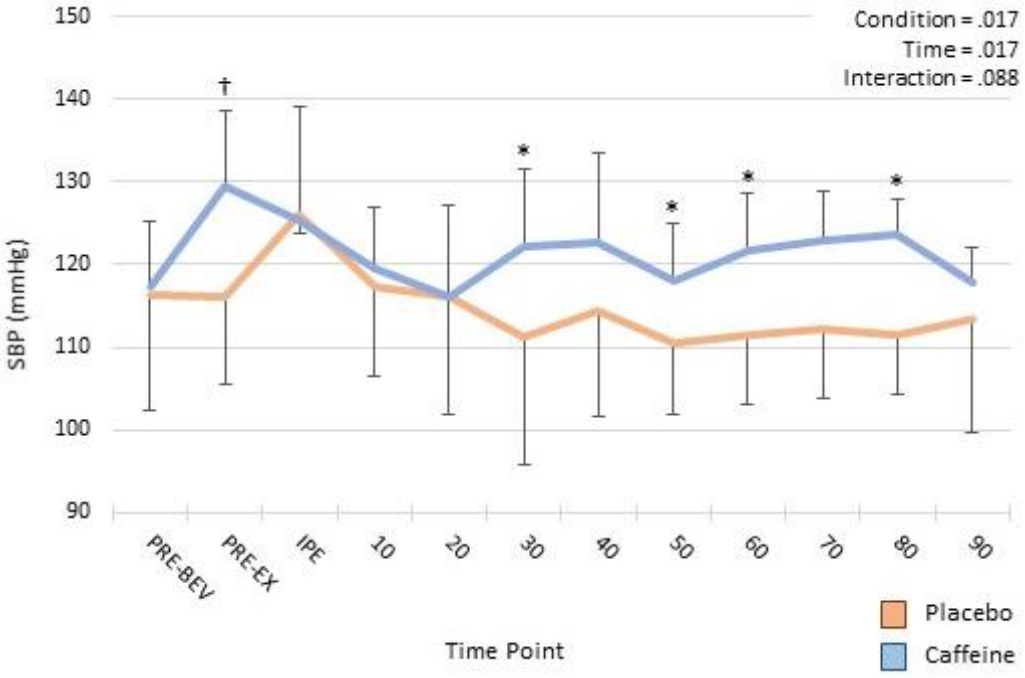


Figure 2



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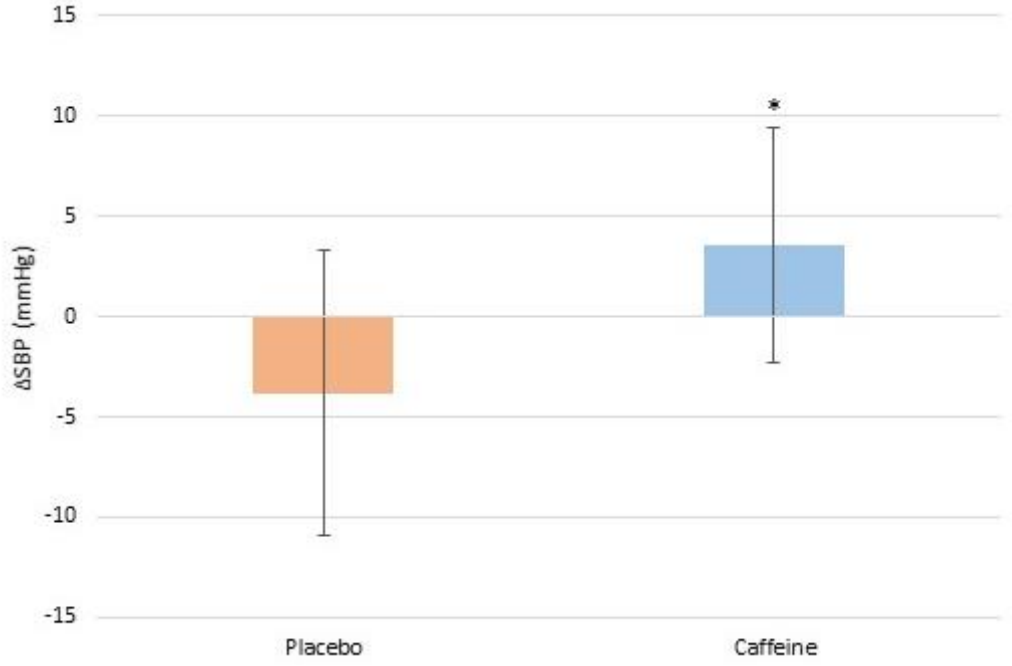

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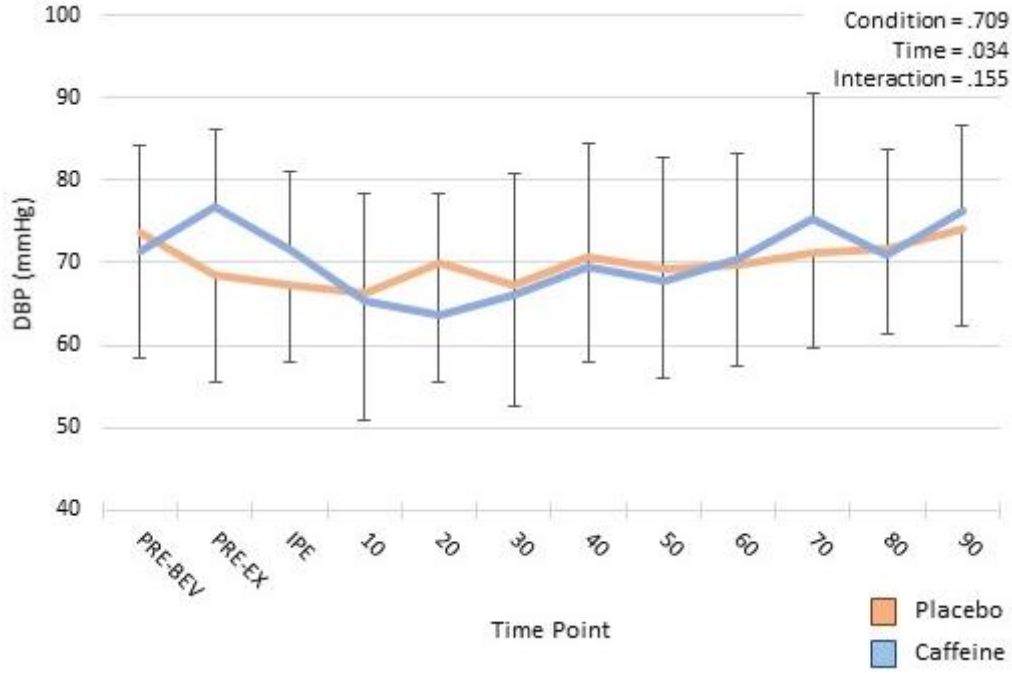

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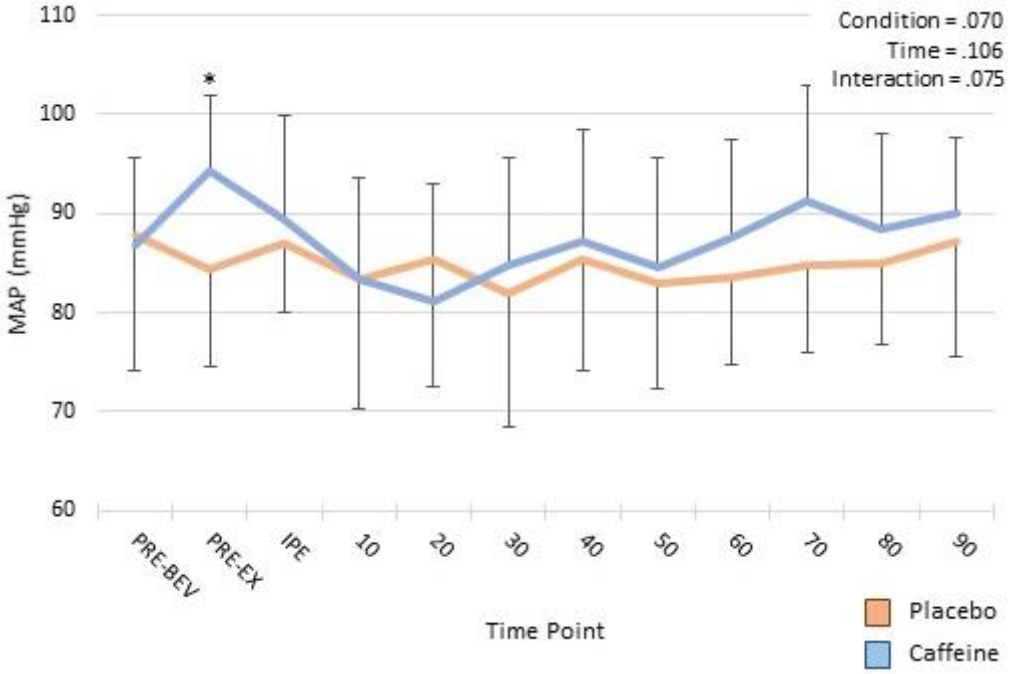

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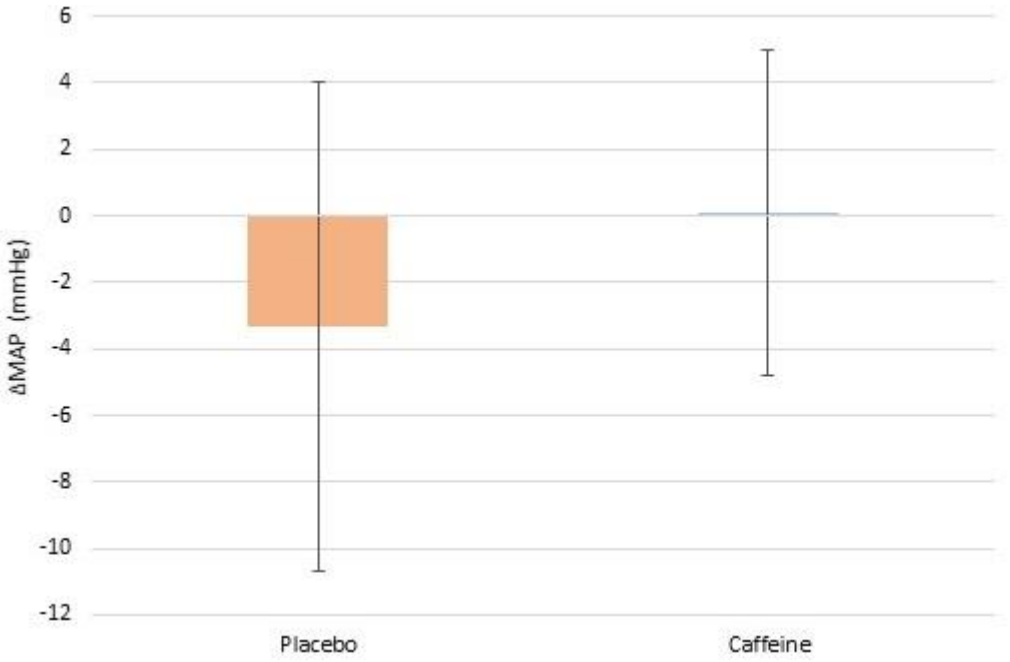

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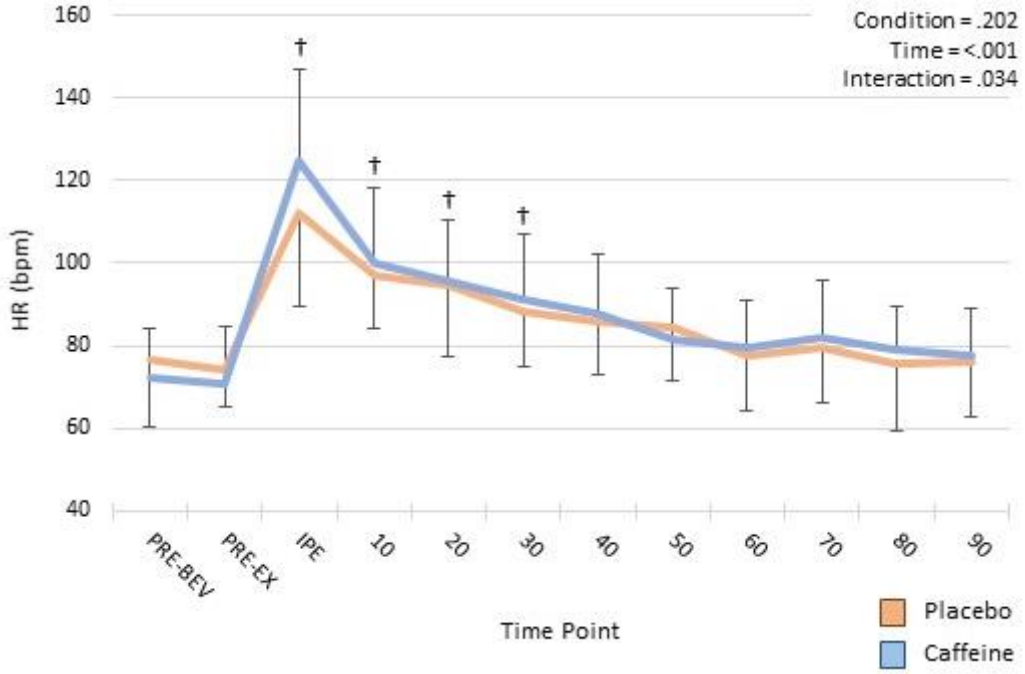
Condition = .202
Time = <.001
Interaction = .034
HR (bpm)
160
140
120
100
80
60
40
†
†
†
†
PRE-BEV
PRE-EX
IPE
10
20
30
40
50
60
70
80
90
Time Point
Placebo
Caffeine

Figure 1. Sample timeline for blood pressure screening, fitness assessment, and resistance exercise post-exercise hypotension (PEH) trials for randomized, double-blind caffeine and placebo conditions.

Figure 2. Systolic blood pressure (mmHg) pre-exercise before beverage consumption (PRE-BEV), 45 minutes post-beverage consumption prior to exercise (PRE-EX), immediately post-exercise (IPE), and at 10, 20, 30, 40, 50, 60, 70, 80, 90 minutes post-exercise for caffeine and placebo conditions. *****Significant difference ($p < 0.05$) between conditions at same time point. †Time point significantly different ($p < 0.05$) than PRE-BEV time point, regardless of condition.

Figure 3. Change in systolic blood pressure (mmHg) from pre-exercise before beverage consumption to post-exercise (20-90 minutes post) for caffeine and placebo conditions. *Significant difference ($p < 0.05$) between conditions.

Figure 4. Diastolic blood pressure (mmHg) pre-exercise before beverage consumption (PRE-BEV), 45 minutes post-beverage consumption prior to exercise (PRE-EX), immediately post-exercise (IPE), and at 10, 20, 30, 40, 50, 60, 70, 80, 90 minutes post-exercise for caffeine and placebo conditions.

Figure 5. Mean arterial pressure (mmHg) pre-exercise before beverage consumption (PRE-BEV), 45 minutes post-beverage consumption prior to exercise (PRE-EX), immediately post-exercise (IPE), and at 10, 20, 30, 40, 50, 60, 70, 80, 90 minutes post-exercise for caffeine and placebo conditions. *****Significant difference ($p < 0.05$) between conditions at same time point.

Figure 6. Change in mean arterial pressure (mmHg) from pre-exercise before beverage consumption to post-exercise (20-90 minutes post) for caffeine and placebo conditions.

Figure 7. Heart rate (bpm) pre-exercise before beverage consumption (PRE-BEV), 45 minutes post-beverage consumption prior to exercise (PRE-EX), immediately post-exercise (IPE), and at 10, 20, 30, 40, 50, 60, 70, 80, 90 minutes post-exercise for caffeine and placebo conditions. †Time point significantly different ($p < 0.05$) than PRE-BEV time point, regardless of condition.

VITA

Shelby Gibbs, a graduate of West Rusk High School, enrolled at Stephen F. Austin State University in Nacogdoches, Texas in the fall of 2014. She received a Bachelor of Science in Kinesiology with an emphasis in Fitness and Human Performance in May 2018. The following semester she enrolled in the Graduate School of Stephen F. Austin State University where she was employed as a graduate teaching and research assistant for the Kinesiology and Health Science Department.

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