The Effects of Caffeine Supplementation and Withdrawal on Muscular Power, Strength and Endurance in Physically Active, Habitual Caffeine Consumers

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Thesis directed by

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Abstract of Thesis

The Effects Of Caffeine Supplement and Withdrawal on Muscle Power, Strength, and Endurance in Physically Active, Habitual Caffeine Consumers

Caffeine has strongly demonstrated to be an ergogenic aid in aerobic activity and equivocally found beneficial for anaerobic activity. This study compared independent effects of caffeine withdrawal, chronic and acute caffeine supplementation on muscle peak torque, average power, perceived exertion (RPE) and perceived pain index (PPI) during isokinetic exercises in habitual caffeine consumers. Physically active subjects (n=33) participated in a placebo-controlled study with four independent sessions. Repeated-measures ANOVA and paired t-tests were used for analyses with an alpha <0.05. Subjects withdrew from caffeine for 4 days, supplemented 5mg·kg of caffeine for 3 days and consumed 6mg·kg of caffeine or matched placebo 1 hour before final testing. Caffeine withdrawal showed significant decreases in knee extension peak torque 7.5 N-m (60°·s^{-1}), 3.9 N-m (30-repetitions at 180°·s^{-1}) 5.5 N-m (isometric @30°) and 8.2 N-m (isometric @90°). Knee flexion peak torque decreased 2.8 N-m (180°·s^{-1}) and 3.0 N-m (30-repetitions at 180°·s^{-1}). Average power for extension decreased 6.6 N-m (60°·s^{-1}) and flexion by 8.1 N-m (180°·s^{-1}). Average power decreased 5.9 N-m and 7.5 N-m during 30-repetitions at 180°·s^{-1}. Following chronic and acute caffeine supplementation there were no differences in RPE, PPI, peak torque or average power. The current study demonstrated that caffeine withdrawal significantly decreased performance in moderate-to-high caffeine consumers, while chronic and acute caffeine consumption did not significantly affect performance.
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Chapter 1- Introduction

Caffeine is the most popular, widely used drug in the world. In the United States approximately 90% of adults consume caffeine daily. Because of its ergogenic benefits the National Collegiate Athletic Association (NCAA) regulates caffeine consumption for collegiate athletes if concentrations of caffeine in urine exceed 15 ug/ml. The urinary caffeine level allowable by the International Olympic Committee (IOC) is below 12ug/ml. For a 70 kg person, this would equate to about 5-6 cups of coffee 1 hour before testing. There is evidence that caffeine increases oxygen uptake, catecholamine release, and metabolic rate. Studies have demonstrated that caffeine can be a positive ergogenic aid for aerobic exercise; however, the studies of the anaerobic effects of caffeine are equivocal. It is a possibility that differences in study design and training status could explain the disparate findings of the effect of caffeine on strength performance. The mechanism(s) that provide aerobic ergogenic benefits of caffeine (such as glycogen sparing) would not benefit many anaerobic athletes; however, it has been argued that caffeine supplementation can increase catecholamine response, thus decreasing pain perception to allow for more repetitions. In addition, caffeine has been studied to work as an antagonist to block adenosine from binding with adenosine receptors. Therefore, the ergogenic benefit of caffeine can be due to the central nervous system and the blunting of pain by the blocking of adenosine receptors. Otherwise, caffeine has been observed to increase maximal muscular voluntary activation and torque by advocating the central modulation and efficiency of motor unit activity.
Habitual caffeine consumption may alter the metabolic responses following caffeine ingestion and therefore, may dampen caffeine’s ergogenic benefits.\textsuperscript{4,18,20,29,33} Caffeine dependence can occur in individuals who consume as little as 100mg of caffeine or 170 mL·day\textsuperscript{-1} of coffee.\textsuperscript{31} Consequently, anyone who consumes a cup of coffee a day can be susceptible to caffeine withdrawal symptoms. Symptoms of caffeine withdrawal can begin as early at 12-24 hours, usually peaking at 24-48 hours and can last about 7 days. It can take as little as 3 days of caffeine exposure to experience withdrawal symptoms.\textsuperscript{14} The tolerance is associated with an up regulation of adenosine $A_1$ or $A_2$ receptors and post-receptor events.\textsuperscript{14} Caffeine withdrawal can be associated with headaches, mood shifts, irritability, anxiety, depression, drowsiness and fatigue.\textsuperscript{15}

The habitual use of caffeine in participants has been considered in many anaerobic caffeine studies; however the detrimental effects of withdrawal symptoms have not been tested. Furthermore, habitual caffeine consumption’s impact on strength performance and muscle activation has been rarely studied. The current study not only visited the anaerobic effects of chronic and acute caffeine supplementation, but it also considered any effects that withdrawal may have on performance in physically active, habitual caffeine consumers.

Several performance measures were compared (torque, power, endurance and pain perception) before and after caffeine withdrawal in physically active, habitual caffeine-consumers. It was hypothesized that the subjects would have an increase in pain perception and decrease in performance after withdrawing from caffeine. In addition, it is hypothesized that there would be no difference in pain perception or performance after
re-introducing caffeine. Lastly, it was hypothesized that the subjects would have an increase in performance and decrease in pain perception following acute caffeine supplementation. These findings could benefit athletes, the military and the physically active that regularly consume caffeine to understand any positive or negative effects caffeine may have on physical performance.

Chapter 2- Literature Review

Caffeine’s Mechanisms for Ergogenic Benefit

Catecholamines

The most abundant catecholamines in the human body are epinephrine (adrenaline) and norepinephrine (noradrenaline). Epinephrine and norepinephrine are released from the adrenal medulla as a response to the “fight or flight” mechanism when the Sympathetic Nervous System (SNS) is stimulated. Caffeine is identified to stimulate secretion of epinephrine that could produce a variety of secondary metabolic changes to promote an ergogenic action. \(^4,19,20\) Stuart et al., found that caffeine produced a 51% (±11%) increase in mean epinephrine concentrations. \(^17\) However, rarely have studies found an increase in levels of norepinephrine. \(^19,21\)

Consistent reports state that caffeine enhances endurance because caffeine stimulates epinephrine secretion, which results in the mobilization of free fatty acids (FFA). The increased amount of fuel of FFA to active muscles contributes to the Randle effect. The Randle Effect is the theory that increased fat oxidation helps to spare muscle
glycogen stores and increase sympathetic activity.\textsuperscript{21} The Randle Effect suggests that utilizing fat oxidation results in glycogen sparing and is considered to be an ergogenic benefit of caffeine on aerobic metabolism. However, since fat oxidation is not the primary fuel for anaerobic metabolism, the Randle Effect is not known to be a mechanism for ergogenic enhancement in anaerobic metabolism. Conversely, the increase in catecholamines enhances muscle glycogenolysis (in contrast to sparing of muscle glycogen in prolonged activities) can generate great anaerobic metabolism, lactate formation and muscle power output.\textsuperscript{19}

\textit{Adenosine Antagonist}

One explanation that caffeine can be an anaerobic ergogenic aid could be due to caffeine’s ability to inhibit the binding of adenosine to adenosine receptors in the CNS and therefore, reduces the perception of exertion.\textsuperscript{17} Caffeine is similar to adenosine’s structure and able to bind to the cell membrane receptors for adenosine, therefore blocking their action.\textsuperscript{21} When caffeine works as an antagonist, it can increase sympathetic nerve activity.\textsuperscript{18} A\textsubscript{1} Adenosine receptors are associated with G\textsubscript{i} protein input into adenylate cyclase and decreases intracellular cAMP (cyclic adenosine monophosphate). Adenosine A\textsubscript{1} receptor activation produces proprioceptive or pain enhancing properties by increasing, cyclic AMP levels in the sensory nerve terminal. Cyclic AMP helps as a secondary messenger and has a role in nociceptive processing.\textsuperscript{22} The role caffeine plays as an adenosine antagonist can block the perception of pain and serve as an analgesic.
Caffeine is understood to have analgesic properties. A number of studies showed caffeine effect on pain perception, as well as muscular effort. 9,11,12,14,16,23-25 The majority of these studies subjectively measured the subject’s pain using a pain scale. One objective study done by Plaskett and Cafarelli, used constant sensation contractions to objectively quantify the force of sensation. 26 Plaskett and Cafarelli, demonstrated a reduction in force sensation in the first 10-20 seconds of an isometric knee extension contraction after caffeine supplementation. 26 Several locations in the CNS and PNS have sensations of force and pains are modulated. 26

Muscle Activation

Caffeine may alter muscle activity at multiple points along the motor pathway. Caffeine has been observed to increase maximal voluntary activation and torque. 10 These observations advocate that the central modulation of motor unit activity is altered by caffeine. 10 Data from Kalmar and Cafarelli, 9 demonstrate that caffeine has an ergogenic effect on peak force generated and muscular endurance. Several studies support that caffeine increases muscle activation through a central mechanism, however, these studies do not suggest in depth mechanisms responsible for the effects. 9,26,27 It has been suggested that caffeine improves the efficiency of motor unit activation by decreasing the perception of pain and opposing the decline in motor unit activation and muscle firing rates. 9,10

Another explanation that caffeine may enhance muscle activation is due to the caffeine’s antagonist properties to adenosine receptors. Caffeine’s ability to block the
inhibitory effects of adenosine may increase drive from the motor cortex, therefore, potentially increasing a subject’s a capability to excite a motor unit pool.\textsuperscript{9,28} The theory behind this is that it could increase synaptic input to the cell body of the alpha-neuron, therefore increasing the excitability and threshold to facilitate maximal activation.\textsuperscript{9,28}

**Aerobic Benefits and Caffeine Consumption**

There are a number of studies supporting caffeine as an ergogenic aid for aerobic exercise.\textsuperscript{7-10,20,21,24} The proposed explanation for the ergogenic benefits on caffeine on aerobic performance is the Randle Effect. The Randle Effect considers sparing muscle glycogen by enhancing fat mobilization and metabolism.\textsuperscript{6,12} Since, fat oxidation does not provide fuel for short during, high intensity exercise, and muscle glycogen is not the limiting factor, caffeine may not be an ergogenic aid for anaerobic metabolism.

However, consideration of the participant’s regular caffeine consumption has been minimal in research studies. Bell et al,\textsuperscript{7} reported the difference in magnitude and duration of the ergogenic effects of caffeine of users verses nonusers. Bell found that endurance for caffeine users improved roughly 20%, while endurance increased by 30% for caffeine nonusers.\textsuperscript{7} A later study by Bell et al., studied the effect of repeated caffeine ingestion on repeated exhaustive exercise endurance with nine male caffeine users.\textsuperscript{8} Results showed that overall caffeine consumption in the morning increased time to exhaustion by $31.3 \pm 18\%$ compared to the placebo group. However, re-dosing with caffeine in the evening did not show any further ergogenic effect. Therefore, Bell’s findings showed that caffeine consumption at lower blood concentrations can show the
same ergogenic effects during subsequent bouts of exhaustive exercise; specifically, blood caffeine concentrations greater than 27 \( \mu \text{mol L}^{-1} \) for caffeine users to experience aerobic ergogenic effects.

In 1999, Kalmar et al., studied caffeine’s ergogenic effect on endurance of a person’s quadriceps muscle group by holding the 50% of maximal voluntary contractions (MVC) to fatigue. Kalmar et al. considered the participants caffeine consumption and limited the study to participants who consumed less than 2 cups of coffee (or equivalent) per week. This study only selected male participants because the luteal phase of the menstrual cycle can delay the elimination of caffeine. In addition, oral contraceptives can reduce the activity and breakdown of caffeine and can increase its half-life. Prior to this study, participants were asked to abstain from consuming caffeine one week before and throughout the study. The protocol of Kalmar et al, examined four parts; H reflexes, MVC, brief submaximal contractions, and sustained submaximal contractions. The only significant findings showed that caffeine subjects increased the ability to sustain 50% MVC (increased 25.8% posttests for caffeine group). Therefore, the conclusion of Kalmar et al., only demonstrated an ergogenic benefit of caffeine on muscular endurance.

**Anaerobic Effects**

The mechanisms of caffeine shown to benefit aerobic performance (Randle Effect) would not support caffeine as an ergogenic aid for anaerobic exercise. However, an abundance of studies have demonstrated caffeine’s ergogenic benefit during anaerobic
exercise. Upon closer examination, overall analysis of caffeine’s benefit for anaerobic exercise has been equivocal. A review study in 2010 analyzed 11 studies on the ergogenic effect of caffeine on resistance training and found that 6 of the studies (54%) demonstrated significant enhancements after caffeine-mediated supplementation. Since carbohydrates are not a limiting factor for high-intensity short-term exercise, there must be other explanations for the ergogenic effect of caffeine. Other potential mechanisms of caffeine that may benefit anaerobic performance are the decrease in pain perception, which could lower a psychological limiting factor and could increase output. Caffeine can decrease pain perception by the increase in catecholamines responses or acting as an antagonist to adenosine by binding to adenosine receptors.

In 2008, Hudson et al., showed that 6 mg·kg\(^{-1}\) caffeine significantly enhanced resistance-training performance during leg extension and arm curl exercises by increasing total repetitions. In leg extensions, 47% of caffeine participant’s performance exceeded the predetermined number of total repetitions (≥ 5 reps), while 53% exceeded repetitions in set 1 alone. In arm curls, caffeine participants increased 53% in total repetitions and 47% in set 1 (p<=0.05). Furthermore, Hudson et al., considered caffeine’s effect on pain perception, hypothesizing that caffeine inhibits pain perception allowing participants to perform more repetitions. There was not a significant difference in reported perceived exertion between the placebo and caffeine group, however since the caffeine group was able to perform more repetitions it was believed caffeine inhibited the perceived exertion to allow for more repetitions.
On the other hand, Beck et al., found no significant difference in performance of leg extensions when supplementing 201 mg of caffeine. This dosage was significantly less than the one used in the previous study, however. Beck et al., did find that 201 mg of caffeine enhanced bench press performance. Beck’s study suggested that the acute effects that caffeine has on anaerobic work could depend on the type of activity performed, the dosage of caffeine and the characteristics of the participants. Characteristics such as, caffeine sensitivity; individuals who do not regularly consume caffeine may show greater ergogenic effects compared to habitual caffeine users. In addition, the training status of the subject may affect caffeine’s ergogenic impact. Astorino’s et al. review also acknowledged that the difference of caffeine’s effect during high-intensity exercise might be due to the different training statuses of the subjects.

Green et al. found that caffeine helped increase performance on leg press only on the latter sets. Green’s study looked at both men (n=13) and women (n=4). The results of this study showed that leg press repetitions increased in set 2 and significantly increased in set 3. However, this study did not show any difference in the number of repetitions for bench press in any of the sets. All in all, Green’s study demonstrated that caffeine consumption provided ergogenic benefits during resistance training by increasing number of repetitions to failure during leg press. Green et al., discussed that the ergogenic benefit of caffeine might be due to the central nervous system and the blunting of pain by the blocking of adenosine receptors. This study also suggests that the effect of caffeine may be limited to larger-muscle groups. Green et al., findings were consistent with Stuart et
al., which showed a larger effect of caffeine during the second half of testing in simulated rugby.\textsuperscript{17}

**Dynamic Strength**

Limited research has been done on caffeine’s effect during isokinetic dynamometry. Increased motor unit activation during MVC of the knee extensors following caffeine ingestion has been shown.\textsuperscript{9} Duncan et al., demonstrated that caffeine ingestion increased dynamic muscle torque at 30° s\(^{-1}\), 150° s\(^{-1}\) and 300° s\(^{-1}\) contraction speeds and muscle activity of the quadriceps muscle in non-habitual caffeine users, trained men.\textsuperscript{16} Bazzucchi et al., found similar results that showed caffeine supplementation improves muscle performance during short-duration maximal dynamic exercise by demonstrating that elbow extensors increased maximal torque values throughout dynamic contractions at all angular velocities.\textsuperscript{15} Lastly, A study of isometric submaximal contractions at different knee angles found a significant increase with caffeine supplementation. Caffeine increased time to fatigue by 15\% at 30° and 13\% at 90° knee angles.\textsuperscript{30}

In contrast, Bond, et al. found caffeine to have no anaerobic ergogenic effect of muscle function during low, moderate and high contracting velocities on isokinetic force exerted at 30°, 150°, and 300° s\(^{-1}\).\textsuperscript{31} In addition, Jacobsen et al., found no significant change in isokinetic strength tests of the knee extensors and flexors at 30°, 150°, and 300° s\(^{-1}\) angular velocities in highly trained athletes with similar habitual caffeine intake.\textsuperscript{32} Madigan and Willems found no significant difference after caffeine
supplementation in the muscle activity of the vastus lateralis and biceps femoris on isokinetic strengths and muscle activity. This study examined the isometric strength at specific angles, whereas the majority of other studies assessed dynamic strength on the isokinetic machine. Therefore, further research may benefit by studying multiple sets of the resistance exercises on an isokinetic dynamometer can help explain these discrepancies.

**Caffeine Sensitivity**

The proposed metabolic response to caffeine is the increase in plasma catecholamines. Robertson et al., found that habitual caffeine consumers showed a decrease on the effect of caffeine on plasma and urinary catecholamines during rest. If that is the case, then how does habitual caffeine ingestion impact the ergogenic effects of caffeine on habitual caffeine users during exercise?

The habitual use of caffeine could further alter the effects that caffeine has on athletic performance. A standard oral dose of pure caffeine for most of these studies is 6 mg·kg⁻¹ of body weight, which is relatively equivalent to about the caffeine in four to five cups of coffee. About 1 hour after consumption of 6 mg·g⁻¹ caffeine, the plasma concentration would be approximately 40μmol·L⁻¹. The half-life of caffeine is known to be approximately 3-4 hours. It would be beneficial to understand when an ergogenic aid should be ingested in order to make the most of its ergogenic properties. To the best of our knowledge, caffeine sensitivity has not been accounted for in a number of these studies looking at the ergogenic benefit of caffeine.
Van Soeren et al., compared regular caffeine users (daily caffeine intake 761.3±11.8mg/day) vs. nonusers and discovered a difference in the degree of increase in plasma epinephrine following caffeine ingestion for users during exercise. Nonusers who supplemented caffeine increased 0.98±0.13 at 30 min and 0.27±0.13 nM at 60 min after exercise; comparatively to 0.54±0.08 and 0.66±0.08 nM of the placebo nonuser group. While in users, plasma epinephrine concentrations were 0.21±0.03 in the placebo trial, increased with caffeine to 0.35±0.07, and 0.25±0.02 nM in double caffeine trial. Caffeine users plasma epinephrine levels increased to 1.16±0.17, 1.29±0.13 and 1.77±0.39 nM 30 minutes after exercise. Additionally, Bangsobo et al., found that chronic caffeine consumers dampened the epinephrine response during strenuous exercise with daily supplementation for 6 weeks. After 6 weeks, caffeine continued to increase fat metabolism; although the epinephrine responses were less.

Correspondingly, a later study by Van Soeren et al. tested caffeine users with no withdrawal, after 2-day withdrawal and after 4-day withdrawal. The latter study demonstrated an increase in plasma epinephrine in response to exercise and caffeine regardless of the state of habituation or withdrawal. Comparatively, in non-caffeine users, Graham et al. found that a moderate dose of caffeine increased epinephrine levels; while, Tarnopolsky et al. demonstrated that 6 mg·kg⁻¹ caffeine supplementation in caffeine users showed no changes in epinephrine during moderate exercise (70% VO₂max). However, Bangsbo et al. found a dampened epinephrine response during exercise with caffeine supplementation in chronic caffeine users.
Although, these studies contradict each other, they both confirm that the chronic consumption of caffeine can alter metabolism. Individuals can develop a tolerance and/or dependency for caffeine. The tolerance is associated with an up regulating of adenosine A₁ or A₂ receptors and post-receptor events. Caffeine withdrawal can be associated with headaches, mood shifts, irritability, anxiety, depression, drowsiness and fatigue. It can begin as early at 12-24 hours, usually peaking at 24-48 hours and can last about 7 days. It can occur after as little as 3 days of caffeine exposure to experience withdrawal symptoms. Robertson et al. showed that after several days of caffeine ingestion (750mg/day) blunted the catecholamine response of caffeine. Additionally, Bangsbo et al. demonstrated that after 6 weeks of caffeine supplementation, plasma levels of epinephrine reduced with exercise alone and when caffeine was consumed prior to exercise.

One aspect that has not been clearly studied is the effect of caffeine tolerance and the effect that caffeine withdrawal could negatively have on athletic performance. Habitual caffeine consumption may impact strength performance and muscle activation but has minimally been taken into consideration with many of the caffeine studies. This study intends to demonstrate the inter-individual variation; the response of caffeine sensitivity, and caffeine tolerance has on athletic performance. We would like to account for the variable daily caffeine consumption, caffeine dependencies to examine how caffeine sensitivity alters its ergogenic properties and to study if withdrawal symptoms of habitual user negatively affect performance.
Caffeine Withdrawal

Habitual caffeine consumption may alter the metabolic responses following acute caffeine consumption and therefore, may dampen the caffeine’s ergogenic benefits. Caffeine dependence can occur in individuals who consume as little as 100mg of caffeine or 170mL · day\(^{-1}\) of coffee. Therefore, anyone who consumes a cup of coffee a day can be susceptible to caffeine withdrawal. Symptoms of caffeine withdrawal are reported to begin 12-24 hours after the last dose and can last up to 9 day.

It has been hypothesized that short-term withdrawal from dietary caffeine may result in an enhancement of caffeine-induced responses, including increase in plasma epinephrine during exercise. An acute 3 mg · kg dose of caffeine after a 4 day withdrawal in habitual caffeine users showed significant improvements on endurance cycling performance. Although, these habitual caffeine consumers reported withdrawal symptoms including headaches, fatigue, feeling less focused and unmotivated. In accordance, Van Soeren et al. found no effect on caffeine-induced increases in endurance during high-intensity exercise compared with acute withdrawal; even though all of these subjects reported headaches, fatigue, lethargy, and flulike symptoms following acute withdrawal between 2 and 4 days. Furthermore, Hetzler et al. did not find any alterations in substrate utilization during submaximal exercise after acute withdrawal. Collectively, these studies support a common suggestion that caffeine withdrawal periods do not influence the ergogenic potential in endurance exercises following administration of an acute caffeine dose. Therefore, we can recommend that at least 4 days of
caffeine withdrawal can re-sensitize individuals to the metabolic effects of acute caffeine consumption.

Similarly, caffeine withdrawal can affect mental alertness and performance, which in turn can affect physical output. A double blind study by Rogers et al., studied the effects of overnight caffeine abstinence and caffeine administration in habitual users.\textsuperscript{41} Caffeine withdrawal resulted in detrimental effects during a computerized test at 10:30AM following withdrawal and more severe effects later in the afternoon.\textsuperscript{41} The subjects complained of symptoms that were greater sleepiness, lower mental alertness and poorer performance on reaction time, choice reaction time and recognition memory tasks. On the other hand, caffeine supplementation had no effect on medium-high caffeine consumers and non-low caffeine consumers.\textsuperscript{41} Rogers et al. suggested that the caffeine-increased anxiety/jitters on motor control could offset the benefit of caffeine in non-low users. Beneficially, caffeine enhanced physical performance in both medium-high and non-low caffeine consumers.\textsuperscript{41} All in all, this study showed that medium-high caffeine consumers gain no acute benefit for mental alertness and performance due to their habit.\textsuperscript{41}

**Physiological Interaction with Trained Individuals**

Caffeine appears to have a more predictable impact on highly trained individuals.\textsuperscript{21} It could be that highly trained individual’s muscles are more responsive to stimuli as an adaptation of training, or it could be that highly trained individuals have greater mental discipline.\textsuperscript{21} It has been found that exercise training altered the effects of adenosine on
adipose tissue. Likewise, Mauriege et al. found differences between obese and lean women in adenosine sensitivity between adipocytes. LeBlanc et al. found that, at rest, trained athletes had an increased response to caffeine compared to untrained individuals, including a larger increase in epinephrine, FFAs and resting metabolism.

The research comparing the effects on caffeine on trained and untrained individuals is limited. The review study of caffeine’s ergogenic effect on anaerobic metabolism, by Astorino et al. contemplated that the difference of caffeine’s effect during high-intensity exercise might be due to the different training statuses of the subjects. The current study would like to consider the varying effects caffeine could have on the physically active.

**Chapter 3- Methods**

**Study Design**

The study uses a double-blind, cross-over, parallel design, consisting of two intervention sessions and at least two familiarization sessions. The subjects reported to the lab for several familiarization sessions in attempt to minimize a learning effect with the isokinetic exercise testing. Following the baseline measure, the subjects withdrew from caffeine for 4 days and were tested after the withdrawal phase. Lastly, caffeine was added back and the subjects supplemented 5 mg·kg of caffeine for three days to mimic and control their caffeine consumption. On the last testing day, the subjects were randomized into groups and either consumed a 6 mg·kg caffeine supplement or placebo, waited an hour for the effect and concluded their testing (Table 2).
Subjects

Thirty-three physically active subjects (N=33; 30 females, 3 males) participated in this study. Two subjects dropped out of the study for reasons unrelated to the intervention. Potential subjects were required to be physically active for at least 6 months prior to testing which included strength training at least 3 times per week, and the subjects were moderate to high caffeine consumers. Physical active and caffeine consumption was defined by their self-report on questionnaires. Hormonal phases were considered in female participants and limited their data collection to the luteal phase of their menstrual cycles. Change in hormone levels in women could potentially alter the dependent variables (i.e. RPE, PPI). Current study controlled the intervention sessions during the same phase of menstruation to limit extraneous variables estrogen may have with caffeine.

Subjects were recruited by emails to George Washington University varsity athletes and emails through the Milken School of Public Health List Server email group to undergraduate and graduate students. For participation in the study, the subject received a Starbucks gift card and the result of their composition testing was shared with them.

Details of the study were provided to all eligible subjects prior to their giving informed consent. The George Washington University Institutional Review Board approved all the study procedures.
Table 1. Participant demographic information - physically active, moderate to high caffeine consumers (n=33)

<table>
<thead>
<tr>
<th></th>
<th>Value ± SD</th>
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<tbody>
<tr>
<td>Gender</td>
<td>30 women, 3 men</td>
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<tr>
<td>Age (years)</td>
<td>21±1</td>
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<tr>
<td>Weight (kg)</td>
<td>60.25±6.79</td>
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<tr>
<td>Height (m)</td>
<td>1.67±0.06</td>
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<tr>
<td>Body Mass Index (kg·m⁻²)</td>
<td>21.67±1.94</td>
</tr>
<tr>
<td>Body fat %</td>
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**Testing Protocol**

Subjects performed at least two familiarization sessions that mimicked the testing sessions in order to minimize the variance attributable to learning effects. Familiarization sessions repeated until primary dependent variables (e.g. peak torque extension at 60°·s⁻¹) did not vary by more than ten percent. The highest measures found within 10% were used as the baseline measures.

Following baseline testing, the subjects refrained from caffeine for four days and were tested again following the withdrawal period (T1). Following the withdrawal testing, the subjects supplemented with 5 mg·kg⁻¹ of caffeine (provided in two 2.5 mg·kg⁻¹ capsules taken separately) for three days before the final testing to control their caffeine consumption and mimic their moderate habitual use of caffeine.

During the final session (T2), subjects were randomly stratified and assigned to the placebo or caffeine group for T2 and matched based on isometric peak torque relative to their body mass. The subjects ingested either caffeine (6 mg·kg⁻¹ of body weight) or volume matched placebo (Metamucil®). A coin flip was used to determine which of the
matched pair received the caffeine or the placebo. The subjects waited an hour before performing the exercise tests. Caffeine is rapidly absorbed and plasma concentrations typically reach peak levels in about one hour. At various points in testing, they completed side effects questionnaires to ensure they were not experiencing any health problems that might result from the supplementation (Figure 1).

**Testing Session Protocol**

[Diagram showing testing schedule]

Figure 1. Outlines the daily testing schedule when the subjects reported to the lab.

In an effort to control for extraneous variables, subjects were instructed to refrain from caffeine, alcohol and moderate-intensity exercise for 24hr prior to T1 or T2 testing. They also recorded their diet 24hr prior to T1 and were instructed to replicate this diet record prior to T2. Subjects were also instructed to fast for 4-6 hours prior to testing. Text message and email reminders were sent daily to the participants during the intervention periods to support compliance.
**Study Protocol**

<table>
<thead>
<tr>
<th>Screening</th>
<th>Familiarization</th>
<th>Baseline</th>
<th>T1 Withdrawal</th>
<th>T2 Chronic Supp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Training status</td>
<td>Weight Blood Pressure Heart Rate</td>
<td># Vertical Jump Handgrip Isokinetic Isometric Eccentric Fatigue</td>
<td>DXA, BIA, RMR, Urine</td>
<td>Day 0 Weight Blood Pressure Heart Rate</td>
</tr>
<tr>
<td>Caffeine consumption</td>
<td>Repeat EAM again if not within 5-10% of Familiarization</td>
<td><em>Vertical Jump Handgrip</em> Isokinetic* Isometric Eccentric* Fatigue* #</td>
<td># Supplement or Placebo</td>
<td>Day 3 Weight Blood Pressure Heart Rate</td>
</tr>
<tr>
<td>Medical Hx</td>
<td></td>
<td></td>
<td>Meal</td>
<td></td>
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<tr>
<td>Health Status</td>
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<td></td>
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</tr>
<tr>
<td>Informed Consent</td>
<td></td>
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<td></td>
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</tbody>
</table>

**Variables and Equipment**

Heart Rate (HR) and Blood Pressure (BP) were measured at the beginning of each testing session to help determine if it was safe for them to participate in the exercises (systolic BP <140mmHg). A Dual-energy X-ray Absorptiometry (DXA) was conducted to determine the subjects’ percent body fat (%BF) and fat-free mass (FFM). The independent variables were caffeine withdrawal and caffeine supplementation.
The dependent variables studied were measures of peak torque and peak power on an isokinetic dynamometer for extension and flexion at various speeds. Isokinetic peak torque and power were tested in the subjects dominant leg at 60°•s\(^{-1}\), 180°•s\(^{-1}\), and 300°•s\(^{-1}\). The goal of these 3 sets was to target high, moderate and low intensities of concentric muscle contraction. The various isokinetic sets were chosen to examine muscle activation effect of caffeine. Short duration endurance was assessed in 30 repetitions at the moderate intensity of 180°•s\(^{-1}\) to study caffeine’s effect on pain perception. Isometric peak torque was measured and 120% of isometric peak torque was used for resistance in eccentric sets on their non-dominant leg. The goal of the eccentric exercises was to elicit pain and impose muscle damage to consider if there were any differences in pain perception between the intervention sessions and groups.

In addition, subjective variables of Rating of Perceived Exertion (RPE) and Perceived Pain Index (PPI) were recorded after each exercise test. An RPE scale is a psychophysiological scale, meaning that it calls on the mind and body to rate one’s perception of effort by measuring feelings of effort, strain, discomfort, and/or fatigue experienced.\(^{32}\) We used a 15-category scale developed by a Swedish psychologist Gunnar Borg.\(^{32}\) The Borg RPE scale ranges from 6-20. We used a Visual Analog Scale (VAS) to record perceived pain index.

**Statistical Analysis**

Data were analyzed using SAS 9.3 Statistical software. Dependent t-tests were used to test the study hypotheses between baseline and withdrawal phases with an alpha probability level of less than 0.05. Dependent t-tests were used for the comparison of
baseline to T1 or T2, while independent t-tests were used for T2 comparisons between groups. Repeated measures Analysis Of Variance (ANOVA) was used to determine the differences in RPE, PPI and eccentric exercises between the three time points ($B_0$, $T_1$, and $T_2$). Statistics were generated for all absolute and relative body weight values for peak torque and peak power.

Chapter 4- Results

Withdrawal (T1)

Significant differences in peak torque for knee extensors were observed following 4 days of caffeine withdrawal in four out of the six exercises (Figure 2). Knee extension peak torque at $60^\circ \cdot \text{s}^{-1}$ decreased by 7.5 N-m ($92\pm21 \text{ vs. } 84\pm25$ N-m; $p=0.006$); performance during 30 repetitions at $180^\circ \cdot \text{s}^{-1}$ decreased from $69\pm16$ to $65\pm14$ N-m ($p=0.016$); isometric peak torque at $30^\circ$ of knee flexion decreased by 6 N-m for knee extensors ($54\pm16 \text{ vs. } 48\pm10$ N-m; $p=0.05$); and isometric peak torque performed at $90^\circ$ of knee flexion declined by 8.2 N-m ($102\pm39 \text{ vs. } 94\pm38$ N-m; $p<0.001$). No statistically significant differences were observed in peak torque for knee extensors performed at $180^\circ \cdot \text{s}^{-1}$ or at $300^\circ \cdot \text{s}^{-1}$ following caffeine withdrawal.
Figure 2. Comparison of baseline peak torque to peak torque following 4 days of caffeine withdrawal for knee extensors. Data presented are mean values ± standard error. * Indicates a p<0.05.

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Peak Torque (N-m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>Withdrawal</td>
</tr>
<tr>
<td>60°·s⁻¹</td>
<td>100±10</td>
</tr>
<tr>
<td>180°·s⁻¹</td>
<td>80±10</td>
</tr>
<tr>
<td>300°·s⁻¹</td>
<td>60±10</td>
</tr>
<tr>
<td>Fatigue @ 180°·s⁻¹</td>
<td>40±10</td>
</tr>
<tr>
<td>Isometric @ 30°</td>
<td>20±10</td>
</tr>
<tr>
<td>Isometric @ 90°</td>
<td>10±10</td>
</tr>
</tbody>
</table>

Significant differences in peak torque for knee flexors following caffeine withdrawal were observed in two out of the six exercises (Figure 3). Knee flexion peak torque at 180°·s⁻¹ decreased by 2.8 N·m (40±12 vs. 37±10 N·m; p=0.049), while performance during 30 repetitions at 180°·s⁻¹ decreased 3 N·m from 40±9 to 37±10 N·m (p=0.04). There were no statistically significant differences in peak torque for knee flexors performed dynamically at 60°·s⁻¹ and 300°·s⁻¹ or isometrically at 30° and 90° of knee flexion following caffeine withdrawal.
Figure 3. Comparison of baseline peak torque to peak torque following 4 days of caffeine withdrawal for knee flexors. Data presented are mean values ± standard error. * Indicates a p<0.05.

Average power for extension (Figure 4) at 60°·s⁻¹ decreased 6.6 N-m (78±23 N-m vs. 72±19 N-m; p=0.015) and flexion average power (Figure 5) at 180°·s⁻¹ decreased 8 N-m (86±37 vs. 78±29 N-m; p=0.05) following caffeine withdrawal. There were no statistically significant differences observed in average power for knee extensors at 180°·s⁻¹ or knee flexors at 60°·s⁻¹. At 300°·s⁻¹ there no significant differences for extension or flexion average power.

Fatigue performance during 30 repetitions at 180°·s⁻¹ showed significant differences for both extension and flexion average power following caffeine withdrawal. Extension average power decreased 6 N-m (135±35 vs. 129±31 N-m; p=0.039); while flexion average power decreased 7.5 N-m (68±24 vs. 61±22 N-m; p=0.02).
Figure 4. Comparison of baseline average power to average power following 4 days of caffeine withdrawal for knee extensors. Data presented are mean values ± standard error. * Indicates a p<0.05.

Figure 5. Comparison of baseline average power to average power following 4 days of caffeine withdrawal for knee flexors. Data presented are mean values ± standard error. * Indicates a p<0.05.
Eccentric exercises for knee extensors were performed for 3 sets. Resistance for knee flexion was $60^\circ \cdot \text{s}^{-1}$ and $300^\circ \cdot \text{s}^{-1}$ for knee extension. Relative resistance was used from 120% maximal voluntary contraction (MVC) of the subject’s extension peak torque measured isometrically at $90^\circ$ of knee flexion. Knee extension peak torque performed eccentrically (direction of knee flexion) decreased by 6.65 N-m in set 1, 6.92 N-m in set 2 and 4.54 N-m in set 3 (109±46, 106±41 and 103±37 N-m vs. 102±28, 99±31 and 99±30; p=0.14) following caffeine withdrawal (Figure 6). Average eccentric knee flexion power was lower for the first set for both baseline and following caffeine withdrawal (38±19 vs. 40±16 watts). Average power increased for set 2 and was very close between baseline and withdrawal measures (44±24 and 44±16). In set 3 average flexion power decreased for baseline (41±22) and withdrawal (43±16 watts; p=0.01) (Figure 7).
Figure 6. Comparison of baseline eccentric peak torque and eccentric peak torque following 4 days of caffeine withdrawal for knee extensors over 3 sets. Data presented are mean values ± standard error. * Indicates a p<0.05.

Figure 7. Comparison of baseline average power and average power following 4 days of caffeine withdrawal for knee extensors over 3 sets. Data presented are mean values ± standard error. No significant differences were observed.

Chronic Caffeine Consumption
Caffeine was reintroduced by supplementing 5mg·kg\(^{-1}\) (two 2.5mg·kg\(^{-1}\) capsules) for three days. Following chronic caffeine supplementation compared to baseline there were no differences in peak torque or average power observed for any of the exercises at various speeds. As hypothesized there would be no difference between chronic caffeine supplementation and baseline, as the goal was to control and mimic the habitual caffeine consumption of the subjects.

**Acute Caffeine Supplementation vs. Placebo (T2)**

Following 3 days of chronic caffeine supplementations the subjects were separated into two different groups (caffeine vs. placebo) and dependent exercise variables that were relative to each participant’s body mass were analyzed. Knee flexion peak torque at 60\(^{\circ}\)·s\(^{-1}\) (0.85±0.23 vs. 0.66±0.18 N·m/kg; p=0.03) and 300\(^{\circ}\)·s\(^{-1}\) (0.61±0.11 vs. 0.58±0.22 N·m/kg; p=0.02) were statistically significantly higher in acute caffeine supplement group compared with placebo. As seen in figures 8-11, subjects who consumed acute caffeine performed higher on the various exercises compared with the placebo group; however, most of the results were not statistically significant. This could be due to splitting the sample size into two unequally sized groups and therefore only having half of the statistical power.
Figure 8. Comparison of peak torque of knee extensors between a group that ingested 6mg·kg of caffeine and a placebo group. Data presented are mean values ± standard error. There are no statistically significant differences in peak torque for knee extensors between the groups.

Figure 9. Comparison of peak torque of knee flexors between a group that ingested 6mg·kg of caffeine and a placebo group. Data presented are mean values ± standard error. Statistically significant differences in peak torque for knee flexors were found at 60°·s⁻¹ and 300°·s⁻¹.
Figure 10. Comparison of average power of knee extensors between a group that ingested 6mg·kg of caffeine and a placebo group. Data presented are mean values ± standard error. There are no statistically significant differences in average power for knee extensors between the groups.

Figure 11. Comparison of average power of knee flexors between a group that ingested 6mg·kg of caffeine and a placebo group. Data presented are mean values ± standard error. There are no statistically significant differences in average power for knee flexors between the groups.
Rating of Perceived Exertion

The only statistically significant (p<0.05) difference in RPE between baseline and following caffeine withdrawal was following the eccentric sets. The RPE decreased by 0.6 following caffeine withdrawal period compared to baseline (13.90±1.54 vs. 13.27±1.86; p=0.02); which was contrary to our hypothesis. There were no significant differences for resting RPE, and RPE following handgrip, isokinetic and fatigue exercises.

Perceived Pain Index

There were no significant differences in PPI following any of the exercises between baseline and caffeine withdrawal period. However, the subjects’ reported statistically significant differences in PPI at rest. The subjects PPI decreased by 3.8 at rest following a caffeine withdrawal period (8.40±10.12) compared to baseline (12.17±14.17;p=0.05).

Chapter 5- Discussion

Caffeine has been shown to be an ergogenic aid for aerobic activity. The theory behind caffeine’s performance enhancement with aerobic exercise is due to the enhanced utilization of fat oxidation and sparing of muscle glycogen (Randle Effect). The Randle effect would not support caffeine as an ergogenic aid for anaerobic activity. Nevertheless, caffeine has also shown to increase catecholamine response, decrease pain
perception and increase muscle activation, which could benefit both aerobic and anaerobic activities.\textsuperscript{11,13,16}

The increase in catecholamines can facilitate anaerobic metabolism, lactate formation and muscle power output by enhancing muscle glycogenolysis (in contrast to sparing of muscle glycogen in prolonged activities).\textsuperscript{20} Due to caffeine’s effect to increase secretion of epinephrine, a variety of secondary metabolic changes can promote an ergogenic action and corresponding muscle activation.\textsuperscript{4,20,38} By this means, caffeine can alter muscle activity at multiple points along the motor pathway to increase maximal voluntary activation.\textsuperscript{10} Another mechanism is caffeine’s ability to work as an antagonist to block adenosine from binding with adenosine receptors. As a result, the ergogenic benefit of caffeine can be due to the central nervous system and the blunting of pain by the blocking of adenosine receptors.\textsuperscript{13-14,21,39} Caffeine’s ability to block the inhibitory effects of adenosine may increase drive from the motor cortex, in turn, potentially increasing a subject’s a capability to excite a motor unit pool.\textsuperscript{9,28} Accordingly, the theory suggests an increase in synaptic input to the cell body of the alpha-neuron, therefore increasing the excitability and threshold to facilitate maximal activation.\textsuperscript{9,28}

Habitual caffeine consumption may alter the metabolic responses following caffeine ingestion and therefore, may dampen caffeine’s ergogenic benefits.\textsuperscript{4,35-36,39} The current study examined the anaerobic effects of chronic and acute caffeine supplementation also considered any effects that withdrawal may have on performance in physically active, habitual caffeine consumers. Robertson et al., found that habitual caffeine consumers showed lower plasma and urinary catecholamines concentration.
compared to nonusers during rest.\textsuperscript{34} That showed that caffeine users had a decreased catecholamine response following caffeine consumption at rest. If that is the case, then how does habitual caffeine ingestion impact the ergogenic effects of caffeine on habitual caffeine users during exercise? Bangsobo et al., found that chronic caffeine consumption dampened the epinephrine response during strenuous exercise with daily supplementation for 6 weeks.\textsuperscript{35} The results of the current study support these previous findings, as there was a statistically significant decrease in exercise performance following caffeine withdrawal in habitual caffeine consumers. Knee extensor peak torque (Figure 2) and average power (Figure 5) decreased at the higher intensity ($60^\circ \cdot s^{-1}$) following withdrawal; whereas, knee flexors’ peak torque (Figure 3) and average power (Figure 5) decreased at the moderate intensity ($180^\circ \cdot s^{-1}$). It was hypothesized that physical performance would decrease following caffeine withdrawal, but not that there would be a discrepancy among knee extensors and flexors. The differences found could correlate with the force-velocity curve. The amount of force production muscles are capable of producing can vary with the type and velocity of contraction due to the differences in cross-bridge mechanics and the rate at which cross-bridges can be formed. One is shown to be stronger and produce more force at slower speeds, compared to faster speeds where less force is needed and produced.\textsuperscript{46} Knee extensors are predominantly stronger than knee flexors. The normal hamstring: quadriceps ratio is considered to be 2:3 (hamstrings between 50-80\% as strong as quadriceps) through the full range of knee motions. However, the ratio often is higher at higher speeds.\textsuperscript{47} The difference in muscle strength and ratio between the hamstring (flexors) and quadriceps (extensors) can explain why
there may only be a difference for knee extensors at the stronger, higher intensity and knee flexors at the moderate intensity.

**Short Endurance**

Short endurance exercises of 30 repetitions showed significant decreases for all dependent variables measured: flexion peak torque, extension peak torque, flexion average power and extension average power. It is not surprising that endurance performance significantly decreased following caffeine withdrawal in habitual consumers considering the scientific literature strongly supports caffeine supplementation as an ergogenic aid for endurance performance. However, due to the short duration of the 30 repetitions, ergogenic benefits from this study would not arise from the sparing of muscle glycogen. The mechanism in this study responsible for the decrease in performance in short duration endurance exercise following caffeine withdrawal is possibly due to increased pain perception or rating or perceived exertion. Caffeine affects the central nervous system and the blunting of pain by the blocking of adenosine receptors. During withdrawal, the subject could feel an increase in rating of perceived exertion or pain perception thus decreasing their performance and increasing fatigue. Although, the subjects did not report differences in rating of perceived exertion or perceived pain index, it could be correlated with their significant decrease in performance and thus there was no reported difference in their perception.

Results reported by Madigan and Willems found no significant difference in isometric contractions of quadriceps following caffeine supplementation. The current study found that extension peak torque significantly decreased at 30° (5.5 N-m) and 90°
(8.2 N-m) of knee flexion following withdrawal, however there were no significant differences for knee flexors at either angle following caffeine withdrawal.

**Pain Perception**

One of the main mechanisms believed to be responsible for caffeine’s ergogenic benefit during anaerobic activity is due to the decrease in pain perception. It was hypothesized that caffeine would decrease perceived pain and thus increase performance because of the strong scientific research on caffeine’s ability to blunt pain and increase performance.\(^{19}\) Conversely, the subjects did not report any differences in perceived pain index. Contrary to the hypothesis, the subjects only reported a difference of a lower rating of perceived exertion for the last 3 eccentric sets following withdrawal. RPE decreased 0.6 in the eccentric sets following withdrawal compared to baseline (p=0.05). Though, as predicted the subjects generated less force production in all eccentric sets following withdrawal (6 N-m less) which could explain their lower rating of exertion due to lower muscular output may explain why the subjects reported a lower RPE.

**Caffeine Supplementation**

Notably, a previous study showed a significant increase in muscle torque for all isokinetic speeds (30°·s\(^{-1}\), 150°·s\(^{-1}\) and 300°·s\(^{-1}\)) following caffeine ingestion (6mg·kg) compared to placebo.\(^7\) The study demonstrated acute caffeine consumption improves muscle performance during short duration muscle contractions for dynamic torque in knee extensors and flexors.\(^{16}\) Duncan, et al. study believed it was due to the adenosine antagonism and increased motor unit activation.\(^{16}\) However, Bond et al. found that 5
mg·kg of caffeine had no ergogenic benefit on muscle function in low, moderate and high contracting velocities (30°, 150° and 300°s⁻¹) for knee extension and flexion peak torque and power on an isokinetic machine. These results found that following chronic caffeine supplementation for three days had no significant effects on performance compared to baseline. It was hypothesized that there would be no difference following chronic caffeine consumption in habitual caffeine consumers as the goal was to mimic their normal habitual caffeine consumption. In addition, there were no statistically significant differences between acute caffeine supplementation and placebo. Visibly the data appear to demonstrate a difference between the caffeine and placebo group, however the statistical power was too low to support the differences between the groups. With an addition of more subjects to the data a statistical significance may be found.

**Limitations**

Under the circumstances, the largest limitation of this study was relying on subject compliance. The specific assumptions were that the subjects in fact withdrew from caffeine, supplemented according the plan, and controlled their exercise and pre-testing diet. Caffeine markers were not measured in this study to ensure their compliance. Several side effects questionnaires were recorded throughout the study to consider any differences between baseline, withdrawal, chronic, and acute supplementation to monitor their symptoms. Another limitation of the study could be that the subjects knew they were refraining from caffeine and the first part of the study was not blinded, which consequently could have led to bias.
The parallel, double blind component of the study separated the subjects into two groups thereby reducing the statistical analysis to half the power compared to baseline and withdrawal phase where statistically significance was found. Further data collection with new subjects will continue to compare the acute effects of caffeine supplementation following controlled caffeine consumption in moderate to high caffeine consumers. Further investigations on caffeine’s effects on participants should use caffeine markers to guarantee desired caffeine levels.

**Practical Applications**

The significance of this study is to examine not only the positive ergogenic effects of caffeine but also any detrimental withdrawal effects on performance in physically active, moderate to high caffeine consumers. This information could benefit athletes, the military and the physically active whom regularly consume caffeine to understand any positive and/or negative effects caffeine may have on physical performance.
References


Appendices

1. Recruitment Flyer

Caffeine Consumers Wanted

We are looking for physically active individuals, who consume caffeine on a regular basis for a research study. If you fit the requirements below, there are over $300 in incentives for participating in the study.

Requirements:
- Must be physically active
- Must consume caffeine on a regular basis (coffee, energy drinks, caffeine supplements, etc.)

Incentives:
- Free DEXA scan (precise test to determine your body composition)
- Free resting metabolic rate test tailored to you (tells you exactly how your metabolism works, and how many calories your body needs)
- The results of the study will show you how caffeine affects your performance.
- Possible gift cards and/or coupons

Contact: Tara Hannings, Thannings@gwu.edu
2. Pre-Participation Health Screening

GWSPH – Laboratory of Exercise Physiology & Metabolism
Pre-Participation Health Screening

<table>
<thead>
<tr>
<th>Subject ID Number</th>
<th>Date</th>
<th>Age</th>
<th>Gender</th>
<th>Height</th>
<th>Weight</th>
<th>Race</th>
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<td></td>
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</tr>
</tbody>
</table>

The intent of this form is to evaluate your risk for an adverse exercise-related event. Please direct any questions pertaining to this form to laboratory personnel. Information you provide will be treated as personal and confidential. Do not put your name on this form.

Age | Gender | Height | Weight | Race |
--- | ------ | ------ | ------ | -----

Are you allergic or sensitive to caffeine containing products?  Yes  No

---

Section I. Known Cardiovascular, Pulmonary, and Metabolic Disease

Have you ever had (or currently have) any of the following? Circle “yes” or “no” for each disease:

a. Cardiovascular Disorders
- Cardiovascular disease (CVD)  Yes  No
- Angina (chest pain)  Yes  No
- Peripheral artery disease (PAD)  Yes  No
- Hypertension (high blood pressure)  Yes  No
- Cerebrovascular disease  Yes  No
- Heart clicks (abnormal heart sounds)  Yes  No
- Stroke  Yes  No
- Heart murmur  Yes  No
- Coronary artery disease (CAD)  Yes  No
- Emboli (abnormal blood particles)  Yes  No
- Heart attack  Yes  No
- Heart surgery  Yes  No
- Angioplasty (surgical opening of a heart artery)  Yes  No
- Phlebitis (inflammation of a vein)  Yes  No
- Anemia  Yes  No

b. Pulmonary Disorders
- Chronic obstructive pulmonary disease (COPD)  Yes  No
- Asthma  Yes  No
- Interstitial lung disease (tissues surrounding lung)  Yes  No
- Cystic fibrosis  Yes  No
- Emphysema (lung disease)  Yes  No
- Bronchitis (lung inflammation)  Yes  No

c. Metabolic Disorders
- Diabetes (type 1 or type 2)  Yes  No
- Thyroid disorders  Yes  No
- Renal (kidney) or hepatic (liver) disease  Yes  No

d. Other Disorders
- Cancer  Yes  No
Emotional disorders  Yes  No
Eating disorders  Yes  No
Osteoporosis (decreased bone mass/density)  Yes  No
Epilepsy  Yes  No

a. Have you been pregnant within the past year?  Yes  No

b. Do you have ANY disorders or problems not listed above?  Yes  No
If you answered “yes” please provide details:


c. Do you know or suspect of ANY reason (medical, health, or otherwise) why you should not participate in this study?  Yes  No
If you answered “yes” please provide details:


Section II. Major Signs and Symptoms Suggestive of Cardiovascular, Pulmonary, and Metabolic Disease

Have you ever experienced any of the following? Circle “yes” or “no” for each sign or symptom:

Pain, discomfort, tightness, or numbness in the chest, neck, jaw, or arms  Yes  No  
Shortness of breath at rest or with mild exertion  Yes  No  
Dizziness or fainting  Yes  No  
Difficult, labored, or painful breathing during the day or at night  Yes  No  
Ankle swelling  Yes  No  
Rapid pulse or heart rate (palpitations)  Yes  No  
Intermittent muscle cramping  Yes  No  
Known heart murmur  Yes  No  
Unusual fatigue or shortness of breath with usual activities  Yes  No  

If you answered “YES” to any of the above please explain the sign or symptom in more detail:


Section III. Atherosclerotic Cardiovascular Disease Risk Factors

Has your father or brother experienced a heart attack (or cardiovascular surgery) before the age of 55, or has your mother or sister experienced a heart attack (or cardiovascular surgery) before the age of 65?  Yes  No

Do you currently smoke, have quit smoking within the past 6 months, or are regularly exposed to large amounts of environmental tobacco smoke (e.g. second-hand smoke more than 4hr a day)?  Yes  No
Has your medical doctor ever told you that you have high blood pressure (hypertension) or are you on medication to control your blood pressure? Yes No

Has your medical doctor ever told you that you have high blood cholesterol (hypercholesterolemia) or are you on medication to control your cholesterol? Yes No

Total cholesterol: _____ LDL: _____ HDL: _____ Date Tested: ________

Has your medical doctor ever told you that you have an “impaired” or high fasting blood glucose level (measurement of blood glucose taken after you have not eaten for 12-14 hours) or impaired glucose tolerance following an oral glucose tolerance test (OGTT) (measurement of blood glucose taken after consuming a sugary drink or slice of bread)? Yes No

Fasting Glucose: ________ Date Tested: ________

Section IV. Medications

Please list any medications (prescription or over the counter) and any nutritional supplements that you have taken with the past 2 months.

Do you use recreational drugs of any kind? Yes No
Do you currently use tobacco of any kind? Yes No
Has your weight been unstable for the past month? Yes No

Do you know of any reasons why you should not participate in this research study?

☐ Yes ☐ No

If yes please state the reason: ________________________________

_____________________________________________________

_____________________________________________________

_____________________________________________________

By checking the box below I certify that all of the above is true, to the best of my knowledge.

☐ Check here Date: _________________

END OF FORM

Internal use only

This document has been reviewed by the researcher ☐ _______ (initial)
3. Caffeine Questionnaire

**Please record how many ounces you consume on an average day**

<table>
<thead>
<tr>
<th>Beverages</th>
<th>Ounces</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coffee</td>
<td></td>
</tr>
<tr>
<td>Decaf Coffee</td>
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<tr>
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<td>Green Tea</td>
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<tr>
<td>Espresso</td>
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<td>Energy Drinks</td>
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<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>12oz</td>
<td>16oz</td>
<td>20oz</td>
</tr>
</tbody>
</table>

**Please record any supplements you consume, quantity and form (scoop, bottle, tablet)**

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<thead>
<tr>
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<th>GNC Raw Ravage</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABK Speed Stacked Pumped</td>
<td>Gold Maximize Intense</td>
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<tr>
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<td>Image Sports ALARM</td>
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<tr>
<td>BPI L.M.E</td>
<td>Jack3D</td>
</tr>
<tr>
<td>BPI B4</td>
<td>Juggeruaut RP</td>
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<tr>
<td>BSN Endorush</td>
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<td>Muscle Pharm Assault</td>
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<tr>
<td>BSN N.O. Xplode TRP</td>
<td>MuscleTech Neurocore</td>
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<tr>
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<tr>
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<td>Octane Energy/sports drink</td>
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<td>Craze</td>
<td>ON AMIN.O.Energy</td>
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<td>Cytosport Monster Pap</td>
<td>Oxysite Pro</td>
</tr>
<tr>
<td>Force Factor HRX</td>
<td>Pre JYM</td>
</tr>
<tr>
<td>Force Factor HRX</td>
<td>Recline RTD</td>
</tr>
<tr>
<td>GAT Nitralax</td>
<td>Ripped Freak</td>
</tr>
<tr>
<td>GNC AMP (Pre-Post)</td>
<td>SportMax Preworkout Shot</td>
</tr>
<tr>
<td></td>
<td>Panic</td>
</tr>
</tbody>
</table>

**Please record how many tablets you consume on an average day**

<table>
<thead>
<tr>
<th>OTC Medicines</th>
<th>Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anacin</td>
<td></td>
</tr>
<tr>
<td>Appetite control</td>
<td></td>
</tr>
<tr>
<td>Dristan</td>
<td></td>
</tr>
<tr>
<td>Excedrin</td>
<td></td>
</tr>
<tr>
<td>Extra Strength Excedrin</td>
<td>Prescription</td>
</tr>
<tr>
<td>Midol</td>
<td></td>
</tr>
<tr>
<td>NoDoz</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prescription</th>
<th>Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefhot</td>
<td></td>
</tr>
<tr>
<td>Floctin</td>
<td></td>
</tr>
<tr>
<td>Darvon Compound</td>
<td></td>
</tr>
</tbody>
</table>

Please list any other sources of caffeine and quantity consumed ________________________________

---

Internal use only

Total average caffeine consumption _________ mg  Low □  Moderate □  High □
4. Physical Activity Questionnaire

Are you physically active?    Yes    No

How long have you consistently been participating in physical activity?

☐ 0-6 months    ☐ 6-12 months    ☐ > 12 months

How many times per week do you participate in exercise?

☐ 1-2 days    ☐ 3-4 days    ☐ 5-7 days

How long do you exercise per session?

☐ < 30 mins    ☐ 30-60 mins    ☐ 60-90 mins    ☐ > 90 mins

What type of exercise(s) do you perform? (Check all that apply)

☐ Only Cardio    ☐ Both Cardio & Resistance Training
☐ Only Resistance Training    ☐ Organized sports
☐ Other ____________________

If you resistance train, on average

How many different exercises do you perform? ______

How many sets per exercise? ______

About how many repetitions in each set? ______

If you engage in cardiovascular activity, on average what is your effort?

☐ Maximal effort    ☐ Moderate effort (breathing deeply)
☐ Difficult effort    ☐ Difficult effort slight effort (lightly warm and perspiring)

If you participate in an organized sport, what sport ____________________
5. Side Effects Questionnaire

Participant #: _________  Testing Session: _______

Please rank the intensity of your symptoms (if any).

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No Symptoms</th>
<th>Some</th>
<th>Moderate</th>
<th>Significant</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in appetite</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Racing heart rate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shortness of breath</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxious</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irritable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drowsiness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blurred vision</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acid reflux</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

List any other unusual side effects and record the intensity

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Not at all</th>
<th>Somewhat</th>
<th>Moderate</th>
<th>Very</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
6. Borg's Rating of Perceived Exertion

<table>
<thead>
<tr>
<th>Rating</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>No exertion</td>
</tr>
<tr>
<td>7</td>
<td>Light</td>
</tr>
<tr>
<td>8</td>
<td>Somewhat hard</td>
</tr>
<tr>
<td>9</td>
<td>Hard (heavy)</td>
</tr>
<tr>
<td>10</td>
<td>Very hard</td>
</tr>
<tr>
<td>11</td>
<td>Maximal exertion</td>
</tr>
</tbody>
</table>
7. IRB Approved Informed Consent Form

GWU – Exercise Physiology & Metabolism Laboratory
Caffeine Withdrawal, Supplementation & Dynamic Strength Study
Informed Consent Form

Participant’s Name: ______________________________ Date: __________________________

The Effect of Caffeine Supplementation and Withdrawal on
Power, Strength and Endurance in Physically Active Habitual Caffeine Consumers

Description and explanation of study:

You are invited to participate in a research study investigating caffeine withdrawal and supplementation and its
effects on dynamic strength. If you agree to participate in the study, then you will be asked to some additional
private questions in a private setting to ensure that qualify for the study. If you qualify, then during the study
you will be asked to perform a number physical strength tests and some tests of hand-eye coordination. You
will also be asked to have your resting metabolism tested, your body fat percentage scanned, and to complete
five different questionnaires. After you become familiar with the testing procedures, the study intervention
will begin and require you to refrain from caffeine four days. We will then perform the same battery of tests to see
how you respond to caffeine withdrawal. Next you will supplement with caffeine capsules that we provide you
for three days. During this last testing session, you will perform the same battery of tests except you will do so
after taking a caffeine or placebo (inactive) supplement. This test will help to determine if taking extra caffeine
before exercise provides a benefit even when you have been normally ingesting caffeine. All testing sessions
will be conducted in the Exercise Physiology and Metabolism Laboratory in the Milken Institute School of
Public Health at The George Washington University. The testing sessions will be approximately two hours a
piece on two separate days during the one week intervention. This intervention period will be when you are
taking the provided caffeine capsules or refraining from caffeine ingestion. Prior to the intervention, you will
need to attend two to four familiarization (FAM) sessions so that you can become familiar with the testing
procedures. Overall, participation in this study will require about seven hours of your time over a 2-3 week
period.

The requirements for participation as a participant are as follows:
1) Between 18 and 25 years of age
2) Physically active at least 150 minute per week
3) Resistance training at least 3 times per week
4) Habitual caffeine consumer (at least 100mg per day or approximately 1 cup of coffee)
5) Willingness to participate in all 3 testing visits and at least 2 familiarization sessions
6) Willing to refrain from any sources of caffeine outside of the study criteria during the 7 day intervention
   period
7) Must be able to consume Metamucil and vegetarian softgel capsules
8) Must not use smoking tobacco (or in the past 6 months)
9) Must not have any chronic diseases (diabetes, cardiovascular, cancer, autoimmune) that require the use of
   medications and/or limit physical activity
10) Must not have any metabolic disorders including known electrolyte abnormalities, heart disease, arrhythmias,
    diabetes, thyroid disease or hypogonadism
11) Females must not have had a recent history of pregnancy or lactation (within the past 12 months) or intentions
to become pregnant within the next 6 months (as this status will alter your metabolism and low doses of
    radiation experienced during the DXA scans could be harmful to the fetus)

Approximately 50 participants (males and females) are being recruited for participation in this study and representation
from all racial and/or ethnic groups is encouraged.

Page 1 of 5
The study purpose and protocol has been explained to you including any risks and benefits associated with your participation. Please now thoroughly read this Informed Consent document. If you have any questions or concerns about the study, please direct those to the research team. Once you have completed reading this document, please provide your written informed consent by signing the last page. The Institutional Review Board has approved this study protocol. Following the Informed Consent procedure, you will need to complete medical, physical activity and caffeine consumption questionnaires. The medical history forms will include questions regarding history of illness and current medication usage. You will then be scheduled to return for your first familiarization session.

**Familiarization Sessions**

These familiarization sessions (FAM) are designed to help you get familiarized with the testing procedures and equipment. A number of the tests involved in this study have a "learning effect" with them meaning that your results may improve the more you do the test because you know more of what to expect from the test. Ultimately, you need to be able to demonstrate consistent results between the different FAM sessions in order to progress to the intervention based portions of the study.

For each session, we will begin by measuring your body mass, blood pressure (BP), and heart rate (HR). You will then be asked to complete a test to determine your reaction time (RT). An iPad application will be used that will measure the time it takes you to identify sequential numbers that are randomly arranged in a grid. The fastest time of three attempts will be recorded as your reaction time. Next you will perform the Purdue Pegboard Test that will assess your motor control. The Purdue Pegboard Test (PB) consists of taking a peg from a cup and inserting it into a hole as quickly as possible, firstly with the dominant hand, secondly with the non-dominant hand and thirdly, with both hands. During each test, you will have 30 sec to insert as many pegs as you possibly can. Lastly, there is a task of assembling pegs, collars and washers, alternating the dominant hand with the non-dominant where you will have 1 min to complete as many assemblies as possible. You will then perform exercise tests, including a vertical jump test, handgrip test, and four various tests on the Biodex System 3 Isokinetic Dynamometer.

For the physical exertion tests, the vertical jump test will consist of three attempts for maximal vertical jump height. You will be asked to jump as high as you can on a jump mat that will be recording your jump height. The handgrip test will require you to maximally squeeze a handgrip dynamometer (device that measures tension) with your dominant hand for three seconds for 3 trials to determine your maximal handgrip strength. You will then be asked to maintain 40% of your maximal strength for as long as you can without looking at the dial on the handgrip dynamometer. For the Biodex testing, two tests will be performed on your dominant leg and two tests will be performed on your non-dominant leg. Biodex testing requires you to be seated into a stable chair with the exercising leg secured to the dynamometer. Being secured to the chair might feel uncomfortable at first, but it is helpful to ensure that your knee joint is moving in the appropriate plane and that you are isolating the muscles in your thigh. On your dominant leg, we will test dynamic strength and power of your thigh muscles as you extend and flex your knee. This test will include 3 sets of various resistances and speeds. You will perform 5 repetitions (reps) at a high resistance and slow speed, 10 reps at moderate resistance and speed, and 15 reps at a low resistance and fast speed. No matter the speed or resistance, you will be asked to extend and flex you knee and strong and as powerfully as possible. The harder that you push, the more resistance the machine will provide. This is a type of resistance training and it is essential for measuring the maximal amount of torque and power that your thigh muscles can generate. On the same leg, you will then be asked to perform 30 repetitions at a moderate resistance. This exercise will make your leg very tired, but we ask that you give a maximal effort from beginning to end. On your other leg, we will test your isometric strength which requires you to hold a maximal contraction for 5 seconds at 2 different knee angles. Lastly, we will ask you to do eccentric work of your knee extensors for 3 sets of 5 repetitions. This test will require you to extend your knee and continue to contract your quadriceps muscles (front of the thigh) while the machine tries to pull your leg down. The arm will pull your leg down each time, but the goal is for you to resist it as much as possible. This will also be an exhaustive exercise that may cause muscle soreness.

Periodically throughout the testing sessions, we will also ask you to provide a subjective assessment of how you are feeling. We will ask you to provide us with a rating of perceived exertion (RPE) which is your perception of how hard you
were working during the exercise. This RPE scales ranges from a 6 meaning “not hard at all” to a 20 meaning “I could not do any more.” We will also ask you to rate your perceived pain intensity (PPI) in the specific muscles that you were working during an exercise. You will need to draw a vertical line along our PPI scale that will indicate the amount of pain that you felt that can range from “no pain at all” to “worst pain I have ever felt.” We will also want to monitor any potential side effects that you might feel from the caffeine withdrawal and supplementation, so we will periodically ask you to tell us about any potential changes in things like headaches, appetite, fatigue, nausea, stomach distress, etc.

You will then be asked to schedule a return to the lab within two to seven days of the initial FAM session for a subsequent FAM session. During this session and every one that follows, you will report to the lab in the afternoon after being fasted (no food) for 4-6 hours, and refraining from caffeine, alcohol and exercise for 24 hours. You are encouraged to take necessary medications and to consume water as you wish. For this 2nd FAM session you will go through the same battery of tests as the initial FAM session. The goal of FAM sessions is that you will be able to provide consistent results once you are familiarized with the testing protocols. Consistency in results will be defined if the results from FAM 1 and FAM 2 are within 5% of each other. If they are beyond 5% or if you are still unclear about some of the testing procedures, then you will need to return for additional FAM sessions until you can provide consistent results and no longer demonstrate a learning effect.

Testing Session 1 (T1)

After your successful FAM session, you will be asked to withdraw from caffeine for four days. At this point you will return to the lab for your T1 session. You will need to write down all food and drink that you consumed on the day prior to this testing session as you will be asked to repeat this diet prior to your last testing session (T2). Initial measurements of body mass, HR, BP, BIA, RMR and urine sample will be taken, followed by the same exercise and motor control tests from your FAM trials that were described above (vertical jump, handgrip, Biodex).

Bioelectrical impedance analysis (BIA) will be used to measure total body water, intracellular fluid and extracellular fluid levels. This test requires you to lie still on a table for one minute while connected to the Quadscan BIA where a low energy, high frequency electrical current is passed through your body and the resistance of your body’s tissues is measured. This current is very small and most often too small to feel. The resting metabolic rate (RMR) test will require you to lie down and relax for 10 minutes while you breathe in and out of a tube. This directly measures the concentration of oxygen breathed out to measure your metabolism and also allows us to estimate how many calories that you burn each day at rest. You will also be asked to provide a urine sample for us in a collection cup. The specific gravity of the sample will be tested and it will then be stored in the freezer for future analysis of urinary caffeine levels.

At the end of T1, you will be given caffeine supplements for 3 days. You are to swallow one capsule twice a day for 3 days (2.5mg/kg each). You will be asked NOT to consume any other source of caffeine during these 3 days.

Testing Session 2 (T2)

T2 will begin after 3 days of caffeine supplementation following the same restrictions as the first testing session (no alcohol and exercise for 24 hours). You will follow the same 24 hour diet you recorded prior to T1. Body mass, BIA, HR, BP, RMR and urine sample will be taken again. In addition, on this last day of testing a DEXA scan will be measured before supplementation and the exercise tests.

Your percent body fat will be determined by an x-ray absorptiometry (DEXA) and will require you to lie on a table in a pair of shorts or a gown for about 6-11 minutes. The machine will emit a small dose of radiation. The dosage is 100x less than that encountered during a standard chest or dental x-ray or similar to what you would be exposed to on a cross country flight. The DXA is considered to be the most accurate test for assessing your percent body fat, muscle mass, and bone density.

Following these measurements, an acute caffeine supplement administration will be performed in a randomized, double-blind manner. This means that you will be randomly assigned to take either caffeine or a placebo. Neither you nor the
researchers will know to which group you were assigned. The supplements that you will be asked to swallow will be either caffeine-filled capsules (6 mg/kg) or Metamucil filled capsules and given with a snack.

The time commitment from you will be approximately 1 hour for each FAM. 1 hour for T1 and 2 hours for T2. FAM can be conducted whenever is convenient for you. The total time required is approximately 6-7 hours.

Table 1. Overview of Research Design

<table>
<thead>
<tr>
<th>Screening</th>
<th>Baseline (B0)</th>
<th>T1: Withdrawal</th>
<th>T2: Acute Supplement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Training status</td>
<td>Weight</td>
<td>Day 4</td>
<td>Day 9</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>HR &amp; BP</td>
<td>HR &amp; BP</td>
<td>HR &amp; BP</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>Reaction time</td>
<td>Reaction time</td>
<td>Reaction time</td>
</tr>
<tr>
<td>Reaction time</td>
<td>Pegboard test</td>
<td>Pegboard test</td>
<td>Pegboard test</td>
</tr>
<tr>
<td>Coffee consumption</td>
<td>Vertical Jump Handgrip*</td>
<td>Vertical Jump Handgrip*</td>
<td>Vertical Jump Handgrip*</td>
</tr>
<tr>
<td>Medical History</td>
<td>Isometric (Bd)*</td>
<td>Isometric (Bd)*</td>
<td>Isometric (Bd)*</td>
</tr>
<tr>
<td>ICD</td>
<td>Fatigue (Bd)*</td>
<td>Fatigue (Bd)*</td>
<td>Fatigue (Bd)*</td>
</tr>
<tr>
<td>Health Status</td>
<td>Reaction time</td>
<td>Reaction time</td>
<td>Reaction time</td>
</tr>
<tr>
<td>Reaction time</td>
<td>Pegboard test</td>
<td>Pegboard test</td>
<td>Pegboard test</td>
</tr>
<tr>
<td>Informed Consent</td>
<td>Repeat Baseline variables not within 5% of FAM</td>
<td>Repeat Baseline variables not within 5% of FAM</td>
<td>Repeat Baseline variables not within 5% of FAM</td>
</tr>
</tbody>
</table>

HR: Heart rate  BT: Reaction time  (Bd): Performed on the Blades  BP: Blood pressure  Pl: Pegboard test  BIA: Bioelectrical Impedance Analysis  RMR: Resting Metabolic Rate  DEXA: Body Fat Absorbometry

Possible risks and discomforts:
1) Caffeine ingestion may lead to an increased heart rate, anxiety, difficulty sleeping, nausea, restlessness, tremors, and/or increased urination.
2) Caffeine toxicity which could include symptoms such as severe nausea, vomiting, diarrhea, dehydration, severe tremors, confusion, headache, and/or fever.
3) Withdrawing from caffeine may lead to drowsiness, headaches, irritability, nausea, and vomiting.
4) Discomfort with collecting a urine specimen
5) Small doses of radiation exposure with the DEXA scan
6) Muscle soreness from the exercise tests

Steps to minimize risk to the participant:
1) You are of an age that has a relatively low incidence of health abnormalities.
2) You are less likely to show side effects of caffeine since you are a habitual caffeine user.
3) You will be instructed to ONLY ingest caffeine as instructed during the intervention period. This is not only important for the integrity of the study, but to also minimize any risk of caffeine toxicity. Common food items that you should avoid during this time include caffeinated soda, coffee, tea, chocolate or cocoa. Numerous dietary supplements and medications (e.g. Excedrin, Midol, ‘pre-workout drinks’) also contain large amounts of caffeine. You will be reminded to check food labels for caffeine and a complete list of caffeine containing products will be provided to you during the intervention.
4) You are required to be experienced at resistance training, so that you are less likely to be sore from the exercise tests.

5) Should an emergency arise, trained personnel will be available to intervene appropriately with CPR skills and in contacting emergency medical services. Tara Hannings is a certified athletic trainer (CPR and first aid certified) and is experienced in handling injuries, illnesses, and provided emergency care. This certification requires successful demonstration of skill in handling emergency situations that may arise in cardiovascular and pulmonary rehabilitation settings.

6) You will be informed to report any unexpected problems or adverse events that you may encounter during the course of the study.

7) You can withdraw from this study at any time.

The George Washington University has no mechanism to provide you compensation if you incur injuries as a result of participation in this research project. However, efforts will be made to make available the facilities and professional skills of the research staff. Tara Hannings, the research assistant, who is an employee with GW Athletics Sports Medicine as an athletic trainer will be on site at all times should a research-related injury or illness occur. In the event that it is determined that you need the attention of a physician, you will be referred to either your personal physician, the physicians at Medical Faculty Associates (MFA) or The George Washington Hospital.

Since this is a double-blind study, which means that neither the researcher nor you will know to which group you have been assigned. Upon completion of the study you will be informed as to which group you were assigned. In the event of a medical emergency, or you request that this information be divulged, the code will be broken prior to completion of the study. However, this will necessitate that you discontinue participation in the study.

You will be asked to leave the study if you begin to show any serious signs or symptoms that could be related to the testing or supplementation. You also may be asked to leave the study if you fail to comply with the testing requirements that are outlined above.

Potential benefits:
You will receive knowledge about your body composition and rest metabolic rate. The results of your body fat scan and resting metabolism test will be provided to you. A Starbucks or Dunkin Donuts gift card will be given following the completion of testing. The results of this study will provide you with insight on how caffeine affects your performance.
Consent:

Information about the procedures described above and the possible risks and benefits of the project have been explained. Whereas no assurance can be made concerning results that may be obtained, the researcher will take every precaution consistent with the best scientific practice. Questions concerning the research should be directed to Tara Hanings at (315) 264-3837 or Thahning@gwu.edu or Geoffrey Hudson, PhD at GJHudson27@gwu.edu. This project and this consent form have been reviewed by the Human Subjects Protection Review Committee, which ensures that research projects involving human subjects follow federal regulations. If you would like to discuss your rights as a research participant, or wish to speak with someone not directly involved in the study, please contact the George Washington University Office of Human Research at 202-994-2715, this is your representative.

I am aware that: Participation in this project is completely voluntary and I am free to withdraw at any time without penalty or prejudice, or loss of received benefits. In addition, all personal information is strictly confidential and no names will be disclosed. During the course of the study, my information will be identified by a letter-number combination. Any new information obtained during the course of this research that may affect my willingness to continue participation in this study will be provided to me. In addition, I will be informed of any unusual/abnormal clinical findings in which medical referral to my personal physician may be warranted. If I desire, I may request that this information be provided to my physician.

Consent to participate in this project is hereby given by the undersigned. A copy of this form has been given to me.

______________________________________________
Signature of the Research Participant

_______________________________
Date

Internal Use Only

I certify that I have explained to the above individual the nature and purpose of the potential benefits and possible risks associated with participation in this study. I have answered any questions that have been raised and have witnessed the above signature. I have explained the above to the volunteer on the date stated on this consent form.

______________________________________________
Signature of the Researcher Explaining the Study

_______________________________
Date

DO NOT SIGN ON OR AFTER EXPIRATION DATE OF: 01/15/2016

APPROVED
The George Washington University
Institutional Review Board

-FWA0005945-