

EFFECTS OF CAFFEINE SUPPLEMENTATION ON RESPIRATORY MUSCLE
STRENGTH AND ENDURANCE EXERCISE CAPACITY

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Chapter I

The Effects of Caffeine on Respiratory Muscle Strength and Endurance Exercise Capacity

Introduction

The respiratory muscles (i.e. the diaphragm, internal/external intercostals) are similar to other skeletal muscle in that they can become fatigued. The respiratory system is responsible for many actions; its primary role is to regulate the flow of oxygen and CO₂, a process known as gas exchange. The respiratory system works even harder when we exercise since there is an increased demand for oxygen for the working muscles. Prolonged endurance exercise at an intensity of >80% for 8-10 minutes has been shown to elicit respiratory muscle fatigue (RMF) in most subjects, trained and untrained (5,32). The National Heart, Lung and Blood Institute (NHLBI) defined muscle fatigue as “ a condition in which there is a loss in the capacity for developing force and or velocity of a muscle in response to a load and which is reversible by rest” (27). Possible causes of RMF have been proposed and include an accumulation of exercise-induced metabolites in the diaphragm

(4,51), reductions in available energy substrate (29), and competition for blood flow between respiratory and locomotor muscles (4,28,33).

A common non-invasive method to determine if RMF is present is to measure maximal inspiratory pressure (MIP) (taken at residual volume (RV)) and maximal expiratory pressure (MEP) (taken at total lung capacity (TLC)) (9). This method is a measure of global respiratory muscle strength to generate maximal force through inspiratory and expiratory efforts. The respiratory muscles are capable of being trained just like any other muscle in the human body. A study performed by Inbar et al. had subjects perform inspiratory muscle training 6 days a week for 10 weeks. After the training, subjects showed increased inspiratory strength (142.2 +/- 24.8 to 177.2 +/- 32.9 cm H₂O) as well as increases in respiratory muscle endurance (121.6 +/- 13.7 to 154.4 +/- 22.1 cm H₂O) (30).

Caffeine is a well-established ergogenic aid, which has been shown to prolong time to exhaustion during exercise. Caffeine helps to stimulate the CNS and energy metabolism in peripheral tissues, improved neuromuscular transmission and increased muscle contractility (7). It appears to be an ideal supplement for preventing RMF but the amount of literature on the association between caffeine and its effects on respiratory muscle function following intense exercise has not been investigated. The results of this study will not only benefit the athletic population for use of caffeine as an ergogenic aid but will also benefit those suffering from conditions like chronic obstructive pulmonary disease (COPD), neuromuscular weakness and prematurely born infants that need mechanical ventilation to aid in breathing (27).

Purpose

To determine the effects of caffeine supplementation on respiratory muscle strength/fatigue before and after endurance exercise. Additionally, the association between RMF and endurance performance will be determined.

Research Hypothesis

- 1) Caffeine supplementation will attenuate the magnitude of RMF following endurance exercise, as compared to placebo.
- 2) RMF will be lessened following the endurance exercise bout with caffeine supplementation and will be associated with an increased time to exhaustion.

Assumptions

The basic assumptions for the study include the following:

1. This study assumes that all participants were honest in all self reports of pain, previous injury and medical history.
2. This study assumes that participants will avoid intense aerobic exercise prior to the testing sessions.
3. This study assumes that participants will put forth maximal effort during all testing sessions.

Limitations

1. Participants may not be accustomed to performing maximal cycle performance tests.
2. Participants may be able to feel the effects of the anhydrous caffeine, which may bias their performance.

3. Participants may not be in adequate physical shape to perform the maximal cycle performance tests.

Significance of the Study

The body of evidence regarding RMF and caffeine supplementation is not substantial. The ergogenic effects of caffeine i.e. improving endurance performance, mobilizing free fatty acids and improving muscle contraction (7) can be beneficial to the respiratory muscles, especially the diaphragm. Since this study will be implementing exercise into the experimental design, the results will contribute to the limited body of evidence regarding caffeine supplementation and its effects on RMF during exercise.

Chapter II

Review of Related Literature

Respiratory Muscle Anatomy

The human respiratory system is responsible for many actions; its primary role is to regulate the flow of oxygen (O_2) and carbon dioxide (CO_2), a process known as gas exchange. The respiratory system works even harder when we exercise since there is an increased demand for oxygen for the working muscles. It not only works to bring oxygen rich air into our bodies, it also works just as hard to expel the CO_2 rich air and each action has its own set of muscles working to complete the task.

Inspiratory and Expiratory Anatomy and Physiology

Inspiration occurs when there is an active contraction of the respiratory muscles. The main muscle of inspiration is the diaphragm, which is a large dome shaped muscle that separates the abdominal and thoracic cavities. When the diaphragm contracts it pulls the center of the muscle downwards decreasing intrapulmonary pressure and therefore increasing lung volume. Additional muscles that aid in inspiration include the external intercostals, which contract and rotate the ribs upward to help increase lung volume. The sternocleidomastoid and the scalene muscles also have an effect on inspiration in that they are attached to the

first two ribs and with contraction help to raise the rib cage. When all of these muscles contract there is an expansion of the chest cavity and pleural and intrapulmonary pressures become subatmospheric. This change in pressure also affects the alveoli which reach subatmospheric pressure as well. This change to atmospheric pressure creates a pressure gradient for airflow into the lungs from the atmosphere (12).

Expiration is the other half of the respiratory process. The muscles involved with expiration are the rectus abdominus, internal/external obliques and the transverse abdominus. During rest, expiration is achieved passively from the elastic recoil of the lung and chest wall. During exercise however, the muscles of expiration act to forcefully exhale air and return lung volume to normal resting values (19).

Respiratory Muscle Physiology During Exercise

The breathing pattern of the respiratory muscles (RM) are different at rest than during exercise. For this literature review we will be focusing on the physiology of the RM during exercise. The pattern of RM contractions during exercise produces changes in tidal volume (V_T), end-inspiratory and end-expiratory lung volumes, inspiratory and expiratory flow rates and respiratory timing. Increases in ventilation (V_E) during exercise are caused by increases in both V_T and breathing frequency (F_b). During higher intensity exercise additional increases in V_E are caused by increase in F_b while V_T changes little. V_T typically increases 3-5 fold from rest to maximal exercise and F_b increases 1-3 fold. The rise in V_T is caused by an increase in end-inspiratory lung volume and decrease in end-expiratory lung volume. Increases in the F_b are caused by a fall in both inspiratory time (T_I) and

expiratory time (T_E). During rest, V_E is approximately 6-8 L/min in trained individuals whereas untrained individuals can reach values as high as 130 L/min during strenuous exercise. Elite athletes can reach values that exceed 200 L/min. Breathing is primarily an inspiratory activity with little to no expiratory activity at rest (19,20). During exercise inspiration and expiration are active processes that require significant amounts of metabolic work (46).

To date, blood flow to RM during exercise has not been quantified directly in humans. However, a study performed on an equine model showed large increases in blood flow to both inspiratory and expiratory muscles that totaled about 16% of cardiac output at maximal exercise.

Animal studies have shown that the RM, especially the diaphragm, receives its share of blood flow. The locomotor muscles are also at work and need their share of cardiac output as well. A study by Harms et al. showed changes in leg blood flow with unloading of the RM via a pressure-assist ventilator indicating a competitive relationship between locomotor and RM for a limited cardiac output. However when this study was performed again at submaximal levels the changes in blood flow did not occur. It has been shown that fatigue of the diaphragm does not occur until exercise intensity reaches an excess of 80% VO_2 max and when this happens there is an increase in sympathetic activity and a decrease in resting leg blood flow (28,32).

Respiratory Muscle Fatigue

The diaphragm is just like any other skeletal muscle in the sense that it is capable of being fatigued. Even though the respiratory system can become fatigued

with exercise, it is not generally believed that it can limit exercise performance. A study by Boutlier and Piwko (10) showed differently. In their study, 4 sedentary male subjects went through breathing and cycle endurance tests as a baseline measurement and then performed respiratory training daily for 4 weeks by breathing 90 L/min for 30 minutes. After the four weeks the same breathing and endurance cycling tests were repeated. The respiratory training increased breathing endurance time from 4.2(SD 1.9) min to 15.3 (SD 3.8) min. Cycle endurance was improved from 26.8 (SD 5.9) min to 40.2 (SD 9.2) min. During the study it was found that the subjects increased ventilation continuously during the endurance cycling test in the untrained state but they were able to maintain a steady state of respiration in the trained state. These results support the hypothesis that the respiratory system can be an exercise-limiting factor when exercising at a constant submaximal intensity (64% VO₂ max) (10).

There have been several hypotheses made concerning inspiratory muscle fatigue (IMF) following heavy exercise. These include an accumulation of exercise-induced metabolites in the diaphragm (4,49), reductions in available energy substrate (28), and competition for blood flow between respiratory and locomotor muscles (4,28,33).

One theory about IMF centers on the fact that Ca⁺² is responsible for generating a muscle contraction at the sarcoplasmic reticulum (SR) and with prolonged endurance exercise the release of Ca⁺² can potentially become compromised. Ca⁺² within the terminal cisternae of the SR rises during fatigue, and when Ca⁺² release is inhibited there will be a decrease in the force of the muscle

contraction (25). One factor may be the increasing H^+ , which occurs largely from anaerobic metabolism aids in the generation of lactic acid. Elevated intracellular H^+ concentrations, within the range that is known to occur with fatigue cause an increase in Ca^{+2} binding to the SR and therefore inhibiting its release (40).

Adenosine tri-phosphate (ATP) is the useable form of energy that drives all of the bodily processes, especially muscle contraction. The body uses ATP to form the cross-bridge attachments that produce muscle contraction but does the muscle fatigue because of a lack of ATP? Even when performing exercise to fatigue, ATP is well preserved. Only small decreases have been shown with prolonged, exhaustive exercise (17,23). This is due to the fact that muscles store 4-6 times the amount of creatine phosphate (CrP), which can be used as an immediate source of ATP. CrP makes ATP available at the actin-myosin cross bridge site and helps prevent any diffusion that could occur between the contractile elements and the mitochondria (34). There is a common observation that ATP and force production during fatigue have no effect on each other so energy availability is generally believed not to be a limiting factor.

RMF Testing

RMF has remained a controversial issue mainly due to the fact that the methods used to determine whether or not the phenomenon exists are indirect and not very reliable. Bi-lateral phrenic nerve stimulation (BPNS) has shown that the human diaphragm is capable of being fatigued during extended periods of loaded breathing (6,8). The BPNS method stimulates the phrenic nerve bilaterally by supramaximal shocks and the pressure changes in the diaphragm (Pdi) are recorded

at relaxation and voluntary contractions (27). It is currently regarded as being the most objective measure of diaphragmatic fatigue (44).

Another commonly used method is called maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP). It is a non-invasive technique in which pressure is recorded at the mouth during a short inspiratory breath usually at residual volume (RV) and total lung capacity (TLC) during an expiratory effort (9). A study by Larson et al. (37) examined the learning effect and fluctuations associated with technological errors and biological variability while performing MIP. The physical task to perform a MIP test is unique and for an accurate reading requires some practice.

Specific Training of RM

As discussed earlier, the RM are like any other muscle in the body, and just like the other muscles in the body they are capable of being exercised and trained. It is generally believed that RMF may limit exercise performance so if the RM can be trained, then there would be less of a decrease in athletic performance.

In a study by Inbar et al. (30) twenty well-trained endurance athletes were split into two groups of 10. One group received specific inspiratory muscle training (SIMT) while the other group was the control. The experimental group performed SIMT daily, 6 days a week for 30 minutes for a duration of 10 weeks. The subjects started out at a breathing resistance equal to 30% of their maximal pressure for the first week. Resistance was then increased by 5% each session until they reached 80% of their P_{imax} where they remained at that intensity for the rest of the

experiment. Results showed increases in inspiratory strength (P_{imax}) as well as respiratory muscle endurance measured in $P_{\text{m-peak}}$.

A different study by O'Kroy and Coast (43) examined the effects of resistive and flow type training and whether or not the two methods were better at improving both strength and endurance of the RM. 35 subjects (16 male; 19 female) were randomly assigned to 1 of 5 groups; a control, cycling exercise(E), inspiratory loading (IL), expiratory loading(EL) and hyperventilation group (H). Training took place for 4 weeks in each group. The IL group showed increases in both maximal inspiratory pressure (MIP) and time to fatigue. The EL group increased maximal expiratory pressure and had a slight increase in time to fatigue. The H group showed increases in MEP, maximal voluntary ventilation (MVV) maximal sustained voluntary ventilation (MSVV) as well as time to fatigue. The H group was the only group to show cross over effects from the resistive and flow training types (42).

There have been many studies performed analyzing the effects of RMT on athletic performance. A study by Williams et al. (50) analyzed the effects of inspiratory muscle training (IMT) on endurance exercise capacity in collegiate track athletes. The results showed improvements in MIP and breathing endurance time (BET) (31% and 128% respectively), however these improvements did not translate to an increased endurance exercise time. These results support prior studies that have shown improvements in ventilatory performance in terms of respiratory strength and endurance without an associated effect of markers of exercise performance such as $VO_{2\text{max}}$, V_{Emax} , arterial saturation or in the ventilatory equivalents for O_2 or C_{O_2} at peak exercise levels (14,30,43,45).

Caffeine as an Ergogenic Aid

There are many effects of caffeine ingestion that produce a wide range of physiological responses including stimulation of the central nervous system, adenosine receptor blockade, improved neuromuscular transmission, increased muscle contractility, and increased catecholamine levels (7).

Caffeine has been used in many studies where exercise followed ingestion. Most investigators have their participants ingest a dose an hour prior to performing exercise. This duration has been accepted because caffeine is rapidly absorbed and plasma concentrations will reach maximum level in approximately one hour. However caffeine is slowly catabolized (half life 4-6 hours) and individuals will maintain a concentration close to this level for 3-4 hours (26). It has been suggested that waiting 3 hours post-ingestion results in caffeine-induced lipolysis, which produces the highest levels of free fatty acids (FFA) (41,48).

The correct dosage to produce a desired effect also has various viewpoints. Doses as small as 3 mg/kg have been shown to increase endurance in long-term exercise (26). Another study found that when a smaller dose (2.1 mg/kg) ingested with a sports drink produced ergogenic effects but doses of 3.2-4.5 mg/kg had a greater effect (36). There is no definitive answer but it seems that doses ranging from 3-6mg/kg are most beneficial for producing ergogenic effects.

Caffeine and Respiratory Muscle Function

Caffeine is a well-known substance not only used for energy but to enhance athletic performance as well. It has many ergogenic properties, one of which being increasing muscle contractility (7). An increase in muscle contractility, especially in the diaphragm would have benefits for those who suffer from respiratory muscle fatigue. A study by Golgeli et al. (24) examined the effects of theophylline and caffeine on an isolated rat diaphragm. The results showed that caffeine was found to have a significantly greater effect on diaphragmatic muscle twitch tension than that of theophylline and also had a greater effect on diaphragmatic pressure (48). Another study by Supinski et al. (47) supports the results in the previous study that caffeine was more effective at increasing diaphragmatic contraction than theophylline. It was also reported that caffeine was less toxic on the cardiovascular system and central nervous system than theophylline.

Chapter III

Methodology

Subjects

13 recreationally active, healthy male subjects between the ages of 18-40 years were recruited to complete this study. The subjects were either caffeine naïve or had refrained from ingesting any caffeine 3 days prior to testing. Before being included in the study, subjects completed a health history questionnaire to determine that they are free from cardiopulmonary, metabolic or recent orthopedic medical conditions and gave informed consent, which was approved by the local institutional review board. Subjects were randomized into a caffeine or placebo treatment group in a double-blind cross-over fashion prior to the two testing sessions.

Procedures

Spirometry

To demonstrate normal lung function at rest, spirometry was performed in accordance with the American Thoracic Society Guidelines (41). MIP and MEP will be obtained according to the procedures of Black and Hyatt (9) to assess respiratory muscle strength. This method determines the maximal sustained mouth pressure

that can be generated from residual volume (RV) and acts as an index of global respiratory muscle fatigue (RMF). To ensure repeatable results and prevent testing-induced RMF, several trials will take place 30 seconds apart. The greatest pressure from three readings within 5% of each other was used for data analysis.

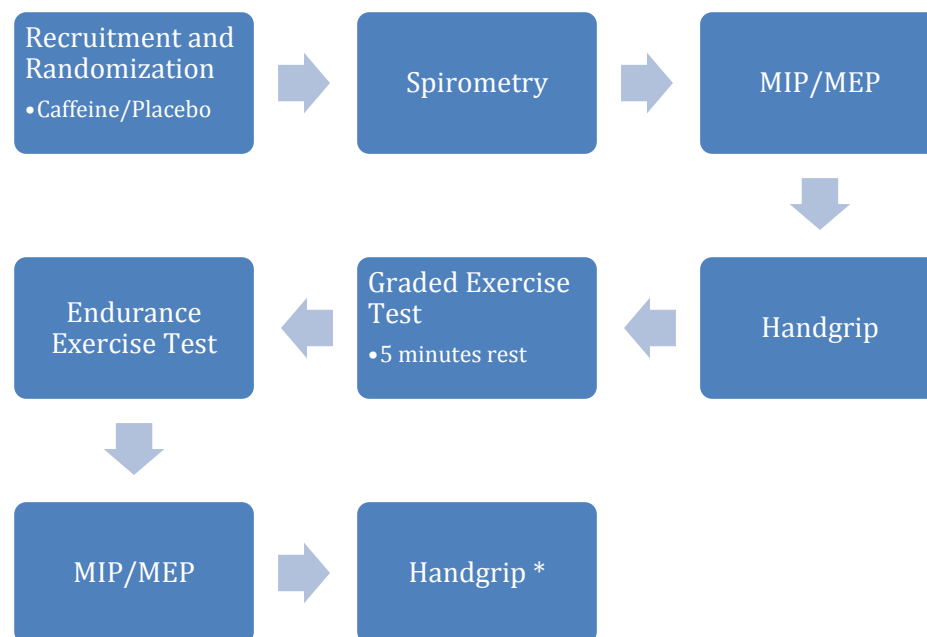
Fatigue Protocol

A graded exercise test (GXT) was performed next on an electronically braked cycle ergometer (Lode B.V., Zernikepark 16, 9747 AN Groningen, The Netherlands). The subjects performed a warm up at 50 watts for 5 minutes. After the warm up the workload was increased to 80 watts and increased in 30-watt increments every 2 minutes until volitional fatigue. During the GXT expired respiratory gases were collected to determine cardiorespiratory fitness (oxygen consumption, work rate maximum and other resultant variables) using a ParvoMedics TrueOne metabolic measurement cart (ParvoMedics, Sandy, Utah). Blood pressure was monitored via auscultation and heart rate and heart rhythm by electrocardiography. Following 5 minutes of rest after the GXT, subjects performed an endurance exercise test at 80% of their work rate maximum as determined from the GXT. As performed during the GXT, heart rate, heart rhythm, were assessed during the endurance exercise and MIP/MEP were assessed following the exercise bout using a MicroDirect respiratory pressure meter ([Micro Direct Inc. 803 Webster Street, Lewiston ME 04240 USA](#)). All testing was conducted in the same manner for both treatment groups with at least 72 hours of rest separating testing periods.

Caffeine/Placebo Administration

The study utilized a double-blind crossover design. A third party was used to randomize and blind the subjects caffeine/placebo supplements prior to each testing session. The caffeine treatment consisted of ingesting 6mg/kg of body weight of anhydrous caffeine in a gelatin capsule with water 1 hour prior to testing. This dosage has been shown to be safe and effective with regards to improvements in endurance performance (15). For the placebo treatment group, a nonnutritive gelatin capsule was ingested 1 hour prior to testing as well.

Testing Timeline



Data Analysis

Descriptive data were generated for subject anthropometrics. A paired t-test was used to determine baseline pulmonary function and selected graded exercise test results. A paired t-test was used to determine differences in time to exhaustion on the endurance exercise test. To determine the differences in respiratory muscle

strength (MIP/MEP) before and after the endurance exercise test, a repeated measures ANOVA (treatment x time) was used. All statistical analysis was conducted using SigmaStat for Windows. Results were presented as means (+/-SE) and a p-value of <0.05 was considered significant.

Chapter IV

Manuscript

Key Words: Respiratory muscle fatigue, caffeine, respiratory muscles

Introduction

The respiratory muscles are very active during exercise and since they are just like any other muscle in the body, they are capable of being fatigued. Prolonged exercise at an intensity greater than 80% for 8-10 minutes has been shown to elicit respiratory muscle fatigue in most subjects, trained and untrained (5, 32). It is not generally believed however that respiratory muscle fatigue (RMF) can be an exercise limiting factor, but a study by Boutlier and Piwko (10) showed otherwise. This study had 4 sedentary males participate in breathing and cycle endurance tests as a baseline and then perform respiratory training for 4 weeks by breathing 90L/min for 30 minutes. The respiratory training increased the subjects breathing endurance time from 4.2 +/- 1.9 min to 15.3 +/- 3.8 min.8 and cycle endurance time was improved from 26.8 +/- 5.9 min to 40.2 +/- 9.2 min.

Caffeine is a well-known ergogenic aid and has many benefits including; improved neuromuscular transmission, CNS stimulation and muscle contractility (1,7,11). A study by Kassim et al. (35) investigated the effects that

caffeine had on respiratory muscle strength on mechanically ventilated infants. Results were positive and suggested that the use of caffeine can improve respiratory muscle strength and possibly attenuate respiratory muscle fatigue. Therefore, the purpose of this study was to investigate the effects of caffeine on respiratory muscle strength and endurance exercise capacity.

Methods

Subjects

Thirteen healthy and recreationally active males (22.85 ± 1.06 years, height $69.92 \pm .70$ in and weight 76.46 ± 2.55 kg)) participated in this investigation. The inclusion criteria consisted of males between the ages of 18 to 40 years old that were recreationally active which this study defined as participating in some type of exercise for at least three times a week for 45 minutes. Subjects had to be caffeine naïve (non caffeine users) and willing to refrain from ingesting caffeine for 3 days prior to testing and between test periods. All subjects completed an informed consent form (Appendix A), as well as a health history questionnaire (Appendix B) and had to be free from cardiopulmonary, metabolic and recent orthopedic medical conditions in order to participate in the study. Subjects were excluded from the study if their activity level was too advanced ($VO_2 > 50$ ml/kg/min) or did not meet any of the above requirements.

Instrumentation

A ParvoMedics-TrueOne (ParvoMedics, Sandy, Utah) metabolic measurement cart was used to collect expiratory gases during the graded exercise test (GXT) as well as forced expiratory volume (FEV) and maximum voluntary ventilations (MVV)

prior to the GXT. Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) were collected using Micro Direct Respiratory Pressure Meter ([Micro Direct Inc. 803 Webster Street, Lewiston ME 04240 USA](#)). Heart rate and rhythm (beats per minute) were monitored by electrocardiography. Blood pressure was collected prior to a following the GXT by auscultation. The GXT and endurance exercise test were performed on a Lode Corival electronically-braked cycle ergometer (Lode B.V., Zernikepark 16, 9747 AN Groningen, The Netherlands).

Procedures

A third party randomized and blinded each subjects caffeine/placebo supplements prior to testing. One hour prior to testing subjects orally ingested either a caffeine or placebo capsule (double blinded) filled with an amount based on the subjects weight (6mg/kg body weight). The primary investigator took a pre-test measurement of the subjects MIP and MEP. The greatest value of three readings within 5% of each other was recorded. Next, FEV and MVV were measured and are only done as a pre-test measurement. After these tests are performed the subject was fitted with electrodes so that heart rate can be monitored during the exercise portion of the test. The subject began the GXT with a 5-minute warm-up at 80W. After the 5 minute warm-up the wattage increased by 30W every two minutes until volitional fatigue. The max power output was recorded and 80% of that number was used as the constant power output for the endurance exercise portion of the test. During this portion of the test, the subject was instructed to ride for as long as possible at the given workload. After the endurance exercise ride the subject

received a two-minute break before MIP and MEP were measured along with blood pressure.

Statistical Analysis

Descriptive data were generated for subject anthropometrics, baseline pulmonary function (Table 1 and 2) and selected GXT results were analyzed with a paired t-test. A paired T-test was used to determine the differences in time to exhaustion on the endurance exercise test. A repeated measures ANOVA was used to determine the differences in MIP/MEP before and after the endurance exercise test (Figure 1 and 2). All statistical analysis was conducted using SigmaStat for Windows.

Results

General anthropometrics were completed on every subject prior to testing and consisted of age 22.85 ± 1.06 years, height $69.92 \pm .70$ in and weight 76.46 ± 2.55 kg.

Maximal Exercise Testing

Variables measured during the GXT and endurance test consisted of $\dot{V}O_2$ max (ml/kg/min), $\dot{V}E$ max (L/min), RER max, HR max (BPM), \dot{V}_t max (L/br), F_b max (br/min), SaO_2 max (%) and PO max (watts) (Table 1). Each subject participated in two double-blinded trials, one being caffeine and the other placebo. There were no significant differences ($p > 0.05$) between the two conditions for any of the variables listed above.

Table 1. Exercise Variables

Variable	Caffeine	Placebo
VO ₂ max (ml/kg/min)	42.93 ± 1.51	43.26 ± 1.77
VE max (L/min)	131.39 ± 4.91	129.12 ± 5.97
RER max	1.19 ± 0.02	1.21 ± 0.02
HR max (BPM)	185.53 ± 3.39	181.00 ± 3.50
V _t max (L/br)	10.67 ± 8.12	2.66 ± 0.12
F _b max (br/min)	49.15 ± 2.02	49.16 ± 2.25
SaO ₂ max %	98.09 ± 0.38	97.13 ± 1.11
PO max (watts)	239.23 ± 7.88	232.30 ± 8.63
Time to Exhaustion(sec)	405.69 ± 55.30	418.15 ± 49.08

Spirometry

Variables measured prior to the GXT and endurance test included FVC (L), %pred FVC, FEV₁ (L), %pred FEV₁, FEV₁/FVC and MVV (L/min) (Table 2). There were no significant differences ($p > 0.05$) between conditions for any of the variables except MVV. The difference between the two conditions in MVV suggests that supplementation of caffeine had a significant effect on the RM muscles via improved endurance.

Table 2. Spirometry Variables

Variable	Caffeine	Placebo
FVC (L)	6.29 ± 1.02	5.98 ± 0.22
%pred FVC	113.92 ± 19.29	108.15 ± 3.85
FEV ₁ (L)	5.21 ± 0.85	4.96 ± 0.19
%pred FEV ₁	112.61 ± 17.45	107.2 ± 3.22
FEV ₁ /FVC	82.96 ± 6.31	83.20 ± 1.82
MVV (L/min)	* 216.74 ± 50.72	187.07 ± 7.10

*Significantly different from placebo

Maximal Inspiratory/Expiratory Pressure

MIP and MEP were measured in a pre-post fashion for each testing condition. No significant differences ($p > 0.05$) were detected between conditions for the pre

MIP measurements. There was a significant change ($p < 0.05$) from the pre MIP caffeine condition compared to post ($124.9 \pm 7.05 - 114.77 \pm 6.03$) however there was no significant difference ($p > 0.05$) between the caffeine and placebo conditions which suggests that caffeine had no physiological effect on inspiratory muscle strength when compared with placebo (Figure 1).

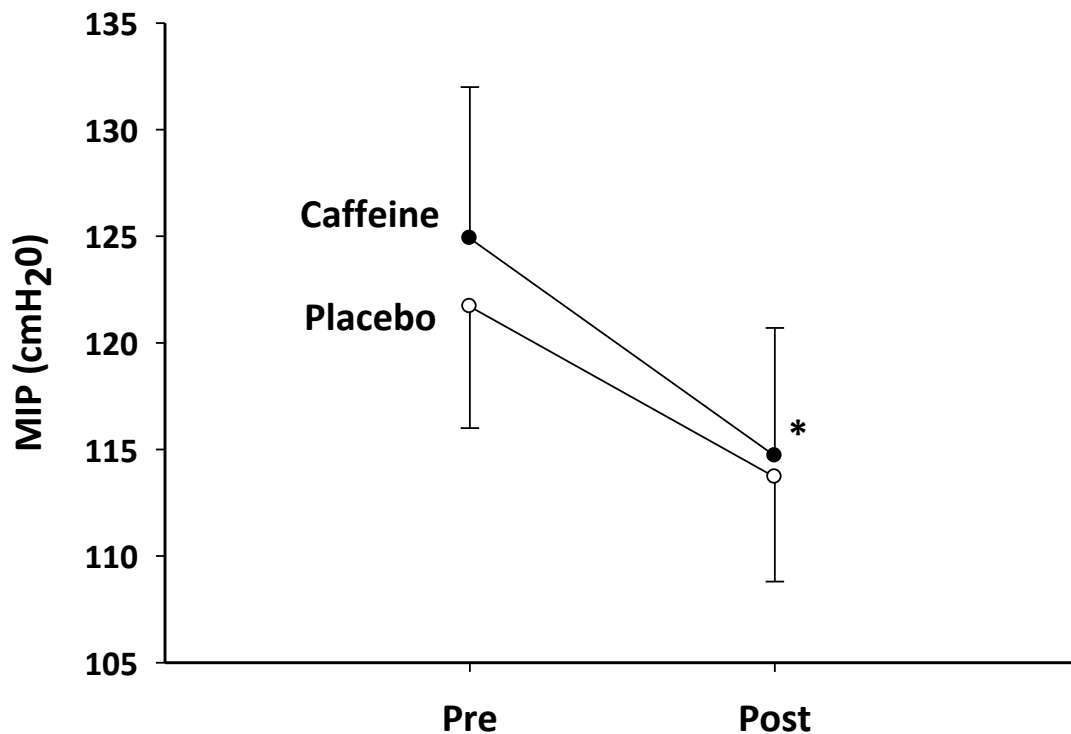


Figure 1. Maximal inspiratory pressure (MIP) generated at the mouth pre and post exercise. * significantly different from pre caffeine condition. Values are means \pm SE.

No significant differences ($p > 0.05$) were found between conditions for the pre MEP measurements (Figure 2). A significant difference in MEP was found for both post conditions (Figure 2). The pre value for the caffeine condition (159.77 ± 10.25) was significantly different from the post value (134.69 ± 9.44)

suggesting that there is only a significant difference within the caffeine condition. The placebo condition follows the same trend, significant differences were found pre-post ($153.77 \pm 10.65 - 139.92 \pm 9.68$). These results reflect that there are significant differences within conditions (pre-post) but not between.

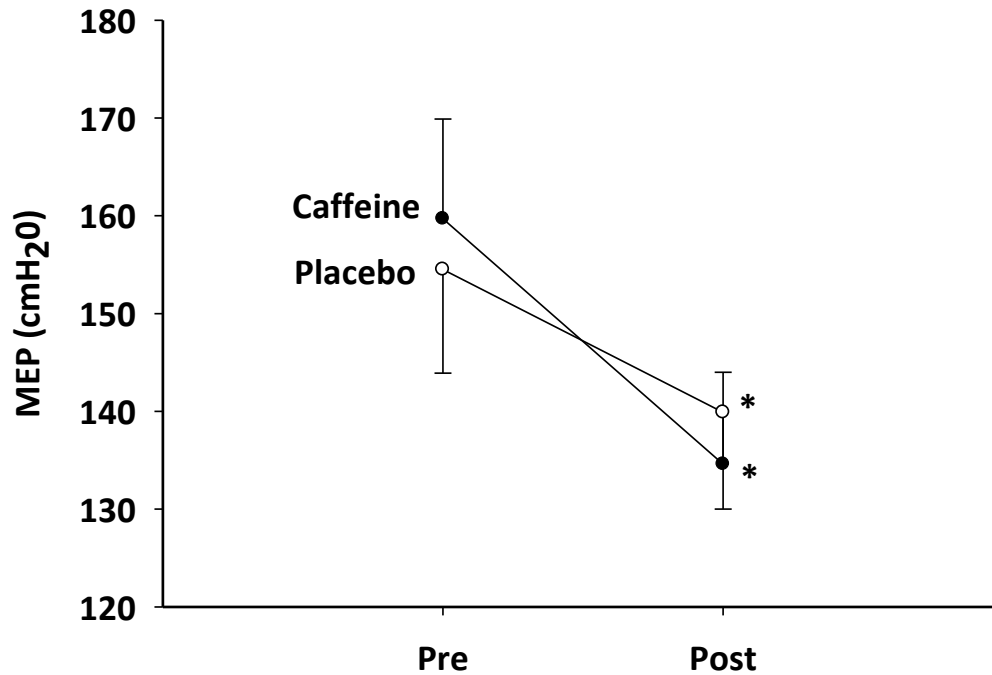


Figure 2. Maximal expiratory pressure (MEP) generated at the mouth pre and post exercise. * significantly different from pre values for both conditions ($p < 0.05$). Values are means \pm SE.

Analysis of the hand grip data demonstrated no significant differences ($p > 0.05$) within or between conditions pre to post exercise. This finding suggests a similar degree of effort was provided for both conditions during the MIP/MEP testing.

Discussion

The purpose of this study was to investigate the effects of caffeine supplementation on respiratory muscle strength before and after endurance exercise. It was hypothesized that caffeine supplementation would attenuate fatigue of the respiratory muscles when compared with placebo and would enhance endurance exercise performance. Results of the study suggest that caffeine did not provide enhancement of respiratory muscle strength or endurance exercise time compared to placebo.

Caffeine is a well-established ergogenic aid and has been shown to prolong time to exhaustion during exercise (1,7,11). The amount of literature is small however concerning the effects of caffeine on attenuating RMF. Kassim et al. (35) investigated the effect of caffeine on respiratory muscle strength in prematurely born, ventilated infants. Results suggested that caffeine supplementation improved respiratory muscle strength enough so that the prematurely born infants could be weaned of mechanical ventilation. A study by Supinski et al. (47) investigated the effects that caffeine had on diaphragm contractility. The results reported improved inspiratory muscle endurance in normal subjects when supplemented with caffeine.. Since the results suggested that caffeine showed improvements in respiratory muscle strength and endurance, the goal of the current study was to investigate these effects with an exercise protocol. This study however reported no significant effects with MIP/MEP between the caffeine and placebo conditions. This is consistent with a study by DeKhuijzen et al. (18), which reported no effects of caffeine supplementation on resting values of MIP/MEP in healthy subjects.

The present study showed no significant effect on FVC or FEV₁ but did however show a positive significant effect on MVV between caffeine (216.75±14.07l/min) and placebo (187.08±7.10l/min). The lack of significant difference in FVC and FEV₁ could be due to the fact that flow rates and capacities are more a function of airway mechanics and less dependent on RM strength. Caffeine had a positive effect on the improved endurance of the RM. The positive effect on MVV reflects improved function of the RM which are very dependent on RM strength/endurance capacity.

Caffeine showed no significant effect on VO₂ max, VE_{max}, VT_{max}, F_bmax or HR_{max} in this study. Similar results were reported in studies by Ahrens et al. (2), and McClaran et al. (38) where there were no significant differences in the above parameters between caffeine and placebo trials. Other studies are variable however reporting increases in VE when supplemented with caffeine (13). The difference between these studies could be related to caffeine dosage and testing procedures.

This is the first study to determine the effects of caffeine supplementation on exercise-induced respiratory muscle strength (MIP/MEP). The proposed hypothesis that caffeine would attenuate fatigue and allow for improved endurance exercise time was not met in this study. It is possible that respiratory muscle endurance was improved (MVV), however this did not carry-over to an improvement in endurance exercise capacity. These findings are similar to other studies that showed enhanced RM strength/endurance, and breathing endurance time but showed no correlation with an increase in endurance exercise time (50).

The results of this study showed that caffeine had no positive effects on endurance exercise performance. However there are mixed results concerning this aspect in the literature. A study by Desbrow et al. (21) investigated the effects of caffeine using 16 well-trained male cyclists. Subjects participated in 3 trials, which consisted of ingesting caffeine in 3mg/kg body mass, 6mg/kg body mass, or placebo and completed a 60 minute timed trial. Results showed improved time trial times when the subjects were supplemented with caffeine (4.2% with 3mg/kg body mass and 2.9% with 6mg/kg body mass). These results are inconsistent with a study by Acker-Hewitt et al. (1) that showed no effect on time trial performance with solely caffeine supplementation, but did show improved performance when supplemented with a combination of caffeine and carbohydrate. The type of endurance test used to determine the effects of caffeine on exercise performance plays a role in the outcome of the results. The two common trial types are a open-ended and close-ended trial. Burke et al. suggests that the use of a time-to-exhaustion protocol better serves as a measure of exercise capacity rather than absolute performance (11), which is what this study employed. This is different from time-trials however, which have greater ecological validity and appear to be more highly reproducible (16,31).

Regarding the effects of caffeine on short-term high intensity exercise, a systematic review by Astorino et al. (3) showed no positive effects. Possible reasons for the inefficacy of caffeine to produce desired effects could be due to discrepancies in the exercise protocols, amount of caffeine given to subjects, training status and inclusion of habitual caffeine users.

Another possible explanation for the lack of proposed effects of caffeine is the coincidental sampling of non-responders to caffeine. Doherty and McLellan (22, 39) report that approximately one third of subjects included in a study do not benefit from caffeine ingestion (non-responders). This may explain the failure of this study to meet its proposed hypothesis regarding the effects of caffeine on attenuating RMF and enhancing endurance exercise performance.

Chapter V

Conclusion, Applications And Recommendations

Conclusion

Caffeine supplementation did not attenuate fatigue of the RM when induced with an exercise protocol. Mean post MIP values and endurance exercise time were lower for the caffeine condition when compared with placebo even though an increase in RM endurance was noted. It has been concluded that caffeine supplementation has no effect on endurance exercise performance or RMF but significant results were reported for increases in MVV and possibly RM endurance. Further investigations should analyze the effects of caffeine on endurance exercise performance using highly trained athletes.

Applications

The following study investigated the effects of caffeine supplementation on respiratory muscle strength and endurance exercise capacity. It was concluded that there was no significant difference between the caffeine and placebo conditions during the exercise protocol. Research has shown that caffeine is a well-established ergogenic aid and has been shown to prolong time to exhaustion during exercise (4). Healthcare providers should not discount the ergogenic effects of caffeine based on

this study. There are still many applications available to a non-athletic population.

Recommendations

The data collection of this study encountered some limitations due to user error when performing the spirometry techniques (MIP/MEP). After the endurance exercise test the subjects are given two minutes to regain their breath and let their heart rate slow down before the post spirometry measurements are recorded. There were two instances where the subjects felt nauseous after the endurance exercise test and 5 minutes passed before any measurements were recorded which would have allowed the subjects RM to rest more so than the others. The lack of an increase in endurance exercise capacity in the caffeine condition could have been due to a learning effect where no matter what condition the subject was given on the first trial, the second trial tended to show a longer endurance exercise time, which is contrary to our research hypothesis. Further studies should have the subjects become familiar with the exercise testing protocol prior to data collection so that any learning effect will be eliminated. And lastly, since this is an effort dependent study it cannot be assumed that every subject gave their best effort for both trials.

Appendix A

Health History Questionnaire

Demographic Information

Last Name _____

First Name _____

Middle Initial _____

Date of Birth _____

Sex _____

Home Phone _____

Address _____

City _____

State _____

Zip Code _____

Work Phone _____

Family Physician _____

Section A

1. When was the last time you had a physical examination?
2. If you are allergic to any medications, foods, or other substances, please name them.
3. If you have been told that you have any chronic or serious illnesses, please list them.

4. Give the following information pertaining to the last three times you have been hospitalized.

Note: Women, do not list normal pregnancies.

	Hospitalization 1	Hospitalization 2	Hospitalization 3
Reason for hospitalization			
Month and year of hospitalization			
Hospital			
City and State			

5. Are you color blind?

6. Are you affected with hemophilia?

Section B

During the past 12 months...

1. Has a physician prescribed any form of medication for you? Yes__No__

2. Has your weight fluctuated more than a few pounds? Yes__No__

3. If yes, did you attempt to bring about this weight change through diet or exercise?

Yes__No__

4. Have you experienced any faintness, light-headedness, or blackouts? Yes__No__

5. Have you occasionally had trouble sleeping? Yes__No__

6. Have you experienced any blurred vision? Yes__No__

7. Have you had any severe headaches? Yes__No__

8. Have you experienced chronic morning cough? Yes__No__

9. Have you experienced any temporary change in your speech pattern, such as slurring or loss of speech? Yes__No__

10. Have you felt unusually nervous or anxious for no apparent reason? Yes__No__

11. Have you experienced unusual heartbeats such as skipped beats
or palpitations? Yes__No__

12. Have you experienced periods in which your heart felt as though it were
racing for no apparent reason? Yes__No__
of breath while walking with others

At present...

1. Do you experience shortness or loss of breath while walking with others
your own age? Yes__No__

2. Do you experience sudden tingling, numbness, or loss of feeling in your
arms, hands, legs, feet, or face? Yes__No__

3. Have you ever noticed that your hands or feet sometimes feel cooler than
other parts of your body? Yes__No__

4. Do you experience swelling of your feet and ankles? Yes__No__

5. Do you get pains or cramps in your legs? Yes__No__

6. Do you experience any pain or discomfort in your chest? Yes__No__

7. Do you experience any pressure or heaviness in your chest? Yes__No__

8. Have you ever been told that your blood pressure was abnormal? Yes__No__

9. Have you ever been told that your serum cholesterol or triglyceride level
was high? Yes__No__

10. Do you have diabetes? Yes__No__

If yes, how is it controlled? (Check One)

_Dietary means _Insulin injection _Oral medication _Uncontrolled

11. How often would you characterize your stress level as being high? (Check One)

Occasionally Frequently Constantly

12. Have you ever been told that you have any of the following illnesses? Yes__No__

Myocardial infarction Arteriosclerosis Heart disease

Coronary thrombosis Rheumatic heart Heart Attack

Coronary occlusion Heart failure Heart murmur

Heart block Aneurysm Angina

Heart arrhythmia

Section C

1. Participants must be physically active healthy men and women between 18 and 35 years of age. Do you meet these study inclusion criteria? Yes__No__

2. If not, which criteria in #1, above, does not apply to you: _____

3. Individuals who currently smoke, are pregnant, are overtly obese, have a history of known cardiac, respiratory or metabolic disease or musculoskeletal disease that would limit exercise participation, are currently experiencing a major physical or mental illness, or are currently

taking medication for a major physical or mental ailment will be excluded from participating.

Do any of the criteria in the list apply to you? Yes__No__

4. If yes, please specify which criteria in #3, above: _____

From Vivian H. Heyward, 2002, Advanced Fitness Assessment and Exercise

Prescription,

4. ed. (Champaign, IL: Human Kinetics)

Appendix B

Effects of Caffeine Supplementation on Respiratory Muscle

Project Title: Function

IRB Number: 2011B8863

Principal Investigator: James S. Williams, 512-245-1970, jw88@txstate.edu

Investigator:

Funding

Faculty Pilot Research Grant-COE

Source:

INTRODUCTION. You are asked to take part in a research study designed to determine the effects of caffeine on lung and respiratory muscle function before and after intense exercise. Your participation is requested because you are a healthy male between the ages of 18-40 yrs that is active but not engaged in competitive sports. The study is being conducted by a professor (Jim Williams, PhD) and graduate students (Matt Pennucci, Russell Rajnoch) at Texas State University-San Marcos. Your participation is voluntary. Read this form and ask questions about anything you do not understand before you decide if you want to participate.

PURPOSE OF THIS RESEARCH STUDY. The purpose of this research is to determine how caffeine effects fatigue of your respiratory muscle following exhaustive exercise.

PROCEDURES. If you agree to participate in this study, you will be expected to meet with the researchers on 3 different occasions.

During your first visit you will fill out a form asking you some questions about your health and exercise habits and then perform a practice session on all of the testing equipment. On the second and third visits you will complete a battery of tests assessing your lung/respiratory muscle function and aerobic capacity after ingesting a safe dose of caffeine or a nonnutritive placebo. The aerobic capacity assessment will include a graded exercise test to your maximal capacity followed by (5 min rest period) an endurance exercise test that will last from 8-12 minutes that is designed to fatigue your respiratory muscles. The lung function/respiratory muscle testing will be repeated following the endurance test. All testing sessions will be performed in the Exercise Physiology Research Laboratory, Jowers Center on the campus at Texas State University. The testing sessions will require about 1.5 hours of your time. If you decide to participate, you will be asked to forgo strenuous exercise for at least 48 hours and abstain from caffeine containing products for 3 days prior to the exercise testing sessions.

POTENTIAL RISKS OR DISCOMFORTS. There are no known risks associated with the lung function/respiratory muscle strength testing procedures. Injuries to young healthy subjects during exercise testing are uncommon. However, the chance for injury is acknowledged and precautions will be taken to prevent injuries. There exists the possibility of adverse changes during the exercise testing. These changes could include abnormal blood pressure, fainting, disorders of heart rhythm, stroke, and very rare instances of heart attack or even death. There is the possibility of dizziness and nausea immediately following the exercise performances. Also, there is the possibility of muscle strain and muscle soreness may be present for 24-48 hours following the exercise performances. Please note that you are responsible for paying your own medical bills if you seek/receive medical health services due to a complication associated with your participation in this research study.

POSSIBLE BENEFITS. You will gain knowledge of your exercise capacity in relation to the general population and a better understanding of your level of fitness for certain sports and recreational activities. This knowledge may aid you in planning a future physical conditioning program or in evaluating the effects of recent physical activity habits.

AVAILABLE TREATMENT ALTERNATIVES. There are other facilities in town where your exercise capacity can be assessed. For instance, your health care provider and local gyms can assess your aerobic and strength capacity.

COMPENSATION / INCENTIVES. Knowledge of your exercise capacity in relation to the general population.

CONFIDENTIALITY. Your personal information will be kept private. Your file will be kept in a locked cabinet for five years, after which, it will be destroyed. The researchers will use this information for analysis, but your name will not be given out in any reports. The information gathered will never be revealed to anyone other than the researchers and will only be reported in aggregate, that is, on average.

TERMINATION OF RESEARCH STUDY. You are free to decide if you would like to take part in this study. You may decide to stop participating in the study at any time. If you decide to stop participating in the study, please notify the researchers of your decision. In addition, the researchers may end your participation in the study without your consent if they believe that you may be in danger. For questions you may have about your rights as a research subject call:

Institutional Review Board Chair: Dr. Jon Lasser

Phone Number: 512-245-3413

Compliance Specialist: Ms. Becky Northcut

Phone Number: 512-245-2102

AUTHORIZATION. "I have read and understand this consent form, and I agree to participate in this research study. I understand that I will receive a copy of this form. I voluntarily choose to participate, but I understand that my consent does not take away any legal rights in the case of negligence or other legal fault of anyone who is involved in this study. I further understand that nothing in this consent form is intended to replace any applicable Federal, state, or local laws. I also understand that I may withdraw from this study at any time without penalty."

Participant Name (Printed): _____

Participant Signature: _____

Date: _____

Person Obtaining Consent (Signature):

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