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Original Research Article

Sublingual Caffeine Supplementation and Its Effects on Physical Performance Measures in Highly Fit United States Military Personnel

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ABSTRACT

Introduction: *Caffeine* is a common natural stimulant used to combat sleep deprivation and sustain performance in military personnel operating in extreme environments for extended periods. Although the mechanisms of actions of caffeine are well elucidated in the literature, caffeine-related human performance improvements are variable. The purposes of this study were to explore the effects of moderate doses of sublingual caffeine on physical performance measures and perceptions of fatigue in highly trained military personnel. **Methods:** Eleven highly trained, active-duty military male participants (mean ± SD: age, height, body mass, and VO_2max = 26.5 ± 5.0 yr, 179.0 ± 8.5 cm, 81.2 ± 10.2 kg, and VO_2max 52.5 ± 5.4 ml/kg/min, respectively) participated in this study. Participants consumed 6mg/kg of body mass of sublingual caffeine or placebo tablets sixty minutes before performing three sets of push-ups and pull-ups to exhaustion. They then completed a ten-mile ruck walk while wearing a forty-pound weighted vest, followed by three more sets of complete push-ups/pull-ups. Study investigators measured participants' exercise heart rate response, ratings of perceived exertion, and blood lactate levels during each exercise trial. **Results:** Repeated measures double-blinded placebo was applied in the current study and a linear mixed model (LMM) was employed to determine the mean differences in performance measures among three scenarios (baseline, placebo, treatment). The performance outcomes in the three scenarios showed minor differences in the fixed effects among baseline (p=0.3848), placebo (p=0.3736), and caffeine (p=0.3609). **Conclusions:** Findings from the study indicate there were no differences between sublingual caffeine and placebo effects on performance measures following exhaustive exercise. However, participants reported no adverse side effects of the sublingual caffeine during or following fatiguing muscle exercise. Future research may include using sublingual caffeine administered throughout training while comparing the effects of different doses (e.g., 3mg/kg, 6mg/kg) of sublingual caffeine on performance measures in a similar military cohort.

Key words: Caffeine, Exercise, Fatigue, Performance, Sleep deprivation.

Introduction

Highly trained military personnel such as infantry, Special Forces operators, and fighter pilots, routinely operate in extreme environments for extended durations and are rarely afforded ample recovery time before the next mission. For example, Sustained Operations (SUSOPS) are extended missions lasting up to 72 hours or longer. They can negatively impact the physical and cognitive performance of military personnel due to: (1) sleep deprivation, (2) heavy combat loads, (3) high caloric expenditures, (4) rapidity of movement, (5) severe energy deficits, and, (6) hot and humid environments[1-2]. Hence, these investigators chose to study the effects of sublingual caffeine supplementation in highly fit military personnel because frequently, they are required to conduct SUSOPS missions in austere environments for extended durations (e.g., 2 to 7 days) with minimal periods of respite occurring between repeated missions. Because little can be done to change the reality of SUSOPS missions, a proper ergogenic countermeasure, such as sublingual caffeine may help preserve physical and cognitive performance[1]. The feasibility and ease of dispensing sublingual caffeine during SUSOPS or extended training evolutions is essential due to constant movement under enemy fire and other environmental stressors.

Caffeine is a commonly used countermeasure to combat sleep deprivation and alleviate physiological and psychological performance degradations in highly trained military personnel operating for extended periods[3-5]. Although the mechanisms of action of caffeine are well elucidated in the literature, caffeine-related human performance improvements are variable. For example, caffeine's ergogenic effects depend on the person's nutritional status, sensitivity to caffeine, genetics, dose, timing, and overall physical condition[6]. Further, results vary regarding caffeine's effects on activities that require short bursts of high-intensity maximal efforts, especially in non-trained participants. Hence, there is a general need to explore the ergogenic effects of caffeine administered in an alternate form (e.g., sublingual) and dose on highly fit military personnel. The main aim of this investigation was to investigate its impact on mitigating the effects of fatigue on performance, as sustainability of performance is critical to overall mission success both in the tactical and battlefield arenas.

The ergogenic effects of caffeine delivered in alternate forms such as capsules, sports drinks, gum, aerosols, nasal sprays, mouth rinses, energy bars, and coffee on power athletes were reviewed by Wickham & Spriet[7] These alternate delivery methods had broad and varying physical and cognitive effects. Caffeine gum and mouth rinsing were the most studied delivery forms. They had distinct ergogenic effects on muscular endurance, sprint cycling, and power production. For example, they administered 200 mg or 3 mg/kg of caffeine gum with repeated doses, which delivered an earlier onset of therapeutic effects via a faster absorption rate through the oral mucosa and gut than pill form. However, the total absorption of caffeine over time was no different compared to the capsule delivery form[8].

Ergogenic doses of 100 mg of caffeine also supplied an ergogenic effect for improving performance in college athletes. Additionally, caffeine doses of 6mg/kg body mass (bm) have been reported to enhance performance in highly skilled athletes, especially those requiring team sports skills[9]. Additional exploration is needed to understand better how the administration of alternate forms of caffeine affects brain function, absorption rates, and performance in highly trained athletes and military personnel[8-9].

According to Yarnell & Deuster[6], studies focused on the effects of a moderate dose (6mg/kg bm) of caffeine are warranted better to understand an individual's sensitivity and metabolic activity. The optimal amount of caffeine needed to enhance performance and reduce health risk ranges from 2 to 6 mg/kg bm, and as a general rule, the absolute dose ranges from 100 mg up to 300 mg[6].

Previously published studies examining the effects of caffeine on activities requiring repeated bursts, sprints, stop-and-go, and power-focused exercises reported mixed benefits of caffeine supplementation[9-10]. For example, Astorino et al[9] performed a systematic review on the benefits of acute caffeine ingestion for short-term high-intensity exercise such as resistance training, team sports, and sprinting. The results were mixed. For example, eleven of seventeen studies showed positive effects of caffeine ingestion on power output and sprint or power-based performance with caffeine doses ranging from 250 mg to 800 mg and from 100 mg/kg bm to 6 mg/kg bm. The remaining six studies showed no effect of caffeine administered in doses ranging from 5mg/kg bm to 6.2 mg/kg bm[9]. For studies exploring the effects of caffeine on improved strength measures (e.g., weight lifted), five of the eleven studies reported no effect of caffeine administered in doses ranging from 2.5 mg/kg bm to 6 mg/kg bm or 300 mg to 600 mg[9]. Although eleven of the seventeen studies that examined the effects of caffeine on power-based activities and team sports showed positive effects, most of these studies only included elite competitive athletes who did not routinely ingest caffeine. Further, six of the eleven studies that focused on the effects of caffeine on resistance training showed decreased performance with caffeine ingestion when repeated bouts of resistance exercises were completed. Lastly, the benefits of moderate to high doses of caffeine involving short burst, power, and resistance training remain equivocal, and the specific mechanisms of action of caffeine on participants performing these types of power-based activities are unknown[9-10].

Spriet et al.[10] found that as research advanced in this area, roughly 50% of published studies suggested that moderate doses of caffeine could benefit those activities that primarily elicit the use of the non-oxidative (anaerobic) energy system. These studies focused on power-based sports, repeated high-intensity intermittent bouts of exercise, resistance training models, and isometric and isokinetic muscle force production and endurance[10]. Further, dosages ranging from 5 mg/kg bm to 7 mg/kg bm improved muscular strength in highly resistance-trained males, enhanced participants' peak power output during a Wingate cycle test, and increased time to exhaustion during short-term high-intensity cycling[10]. However, we could not locate similar studies in highly fit military personnel. We were also interested in exploring the effects of rapidly absorbed (sublingual) caffeine on attenuating fatigue following exhaustive exercise in a highly fit United States military cohort.

Most researchers[4-5,11] who have studied the effects of caffeine in military personnel have reported its ergogenic benefits on physical and cognitive performance and marksmanship during sustained military and urban operations. For example, the Committee on Military Nutrition Research reported that absolute caffeine doses ranging from 100 mg to 600 mg sustain cognitive performance and improve vigilance in rested participants, with positive effects reported in sleep-deprived participants[11]. The ergogenic effects of caffeine on physical and cognitive performance largely depend on the modality of exercise, the dosage of caffeine ingested, and whether the participant is a regular caffeine user[11]. For this investigation, we chose to administer caffeine in relative doses based on the participant's body mass (bm) because relative doses based on bm can affect the bioavailability of caffeine and overall health safety of the participant. For example, 6 mg/kg bm of caffeine administered to a participant with a bm of 90 kg would require a higher dose of 540 mg, compared to a 70 kg participant who would need a lower dose of 420 mg of caffeine. Therefore, an underdose or overdose of caffeine relative to a participant's bm may affect caffeine's overall effectiveness on participant performance and health.

Caffeine has wide-ranging physiological effects on the organism that may or may not improve physical performance[12]. Studies showing the ergogenic benefits of caffeine on physical performance have primarily looked at highly trained athletes. The exercise tests often used to evaluate the effects of caffeine on performance have included running and cycling time to exhaustion with reported improvements of 25% to 35%[11]. Although elite competitive athletes may have similar physiological characteristics to highly trained military personnel, they do not routinely engage in extended, exhaustive missions that require high-intensity intermittent bouts of kinetic extended patrols while carrying heavy loads during periods of sleep deprivation.

Some researchers have reported an absolute dose of 200 milligrams (mg) of caffeine as optimal for producing an acute effect on marksmanship (e.g., skilled in precision shooting) in sleep-deprived United States Navy SEAL trainees (e.g., after 72 hours of U.S. Navy Hell Week), and 300 mg of caffeine as an effective performance enhancer for up to 8 hours[11]. For example, ingesting 200 mg of caffeine reduced sighting time to target, but not accuracy, in sleep-deprived United States Navy SEAL trainees after 72 hours of Hell Week[11].

Numerous investigators[13-15] have reported on the benefits and side effects of different doses of caffeine on heart rate (HR), blood pressure (BP), resting metabolic rate (RMR), and neuromuscular response[13-14]. For example, Ebrahimi et al.[15] examined the effect of two doses of caffeine capsules on heart rate, blood pressure, and shooting performance in eight elite male air pistols and rifle shooters under normal conditions versus sleep-deprived conditions using the double-blind method. They found that taking 3 mg/kg bm increased systolic blood pressure but had no effect on diastolic blood pressure, heart rate, or shooting performance. In contrast, taking 5 mg/kg, bm resulted in poor shooting performance, increased heart rate, and systolic and diastolic blood pressure[15]. Although the investigators reported poorer shooting performance in these participants after taking 5 mg/kg bm, they were not tested under sleep-deprived conditions. None of the participant's heart rate, systolic, or diastolic blood pressure was continuously monitored during the actual 30-minute shooting event. Instead, heart and blood pressure were measured five minutes after the shooting event. Interestingly, some elite shooters, such as those chosen to engage in this study, may experience a high sympathetic drive, resulting in increased heart rate and systolic blood pressure prior to the shooting event. However, once the actual shooting begins, these elite shooters can reduce heart rate and blood pressure immediately prior to pulling the trigger on the pistol. For example, Acikada et al.[16] examined the effect of heart rate on shooting performance in thirteen elite archers (6 male, 7 female) using telemetric heart rate monitors, which measured heart rate every five seconds during the event. They showed that in a simulated shooting environment, high heart rates did not negatively affect the shooting performance of elite archers. The investigators observed that elite archers, analogous to elite shooters, can lower their heart rates prior to shooting, whereby they perform the triggering phase of shooting (e.g., pull the trigger) during the diastolic phase of the cardiac cycle (e.g., relaxation phase of the myocardium) versus during the systolic phase of the cardiac cycle (e.g., contraction phase of the myocardium).

The primary purpose of this investigation was to explore the effects of a sublingual caffeine delivery system on physical performance and perception of fatigue in highly fit military personnel. For this investigation, fatigue is defined based on the concept known as the *task dependency of muscle fatigue*[17]. Task dependency of muscle fatigue is unrelated to a single cause of fatigue, but rather the dominant mechanism is specific to the physiological processes that are stressed during the fatiguing exercise. The task dependency of muscle fatigue is similar to the concept of the specificity of training principle that leads to specific muscle adaptations based on the imposed demand of a training stimulus on a biological system, which may occur after weeks or months of a specific type of physical training (e.g., running, cycling, resistance training)[17].

The secondary purpose of this research was to resolve if a moderate dose (6mg/kg bm) of sublingual caffeine negatively affected physical performance during and following extended, exhaustive exercise. It was hypothesized that rapidly absorbed (sublingual) caffeine tablets administered in moderate dose (6mg/kg bm) would: (1) not negatively affect physical performance; (2) augment bodyweight supported strength and endurance exercises (e.g., pull-ups/pull-ups), and (3) yield lower ratings of perceived exertion during exhaustive exercises.

Methods

Participants and recruitment

Fifteen male, highly trained, active-duty military service members aged 20-36 years volunteered to participate in the study. Four participants dropped out due to time constraints and unforeseen military travel requirements. Demographic and baseline measures for the eleven participants that completed the study are displayed in Table 1. Participants were recruited by a study advertisement flier posted in the military gymnasium and electronic announcements sent to all Wright Patterson Air Force Base squadron fitness program managers. Approval of the study was granted by the Air Force Research Laboratory Institutional Review Board, Wright Patterson Air Force Base, Ohio, under IRB-approved protocol FWR20150159H.

Inclusion and Exclusion Criteria

Participants were screened for inclusion and exclusion criteria. Inclusion criteria included participants whose predicted aerobic capacity (VO_2max) was ≥ 50 ml/kg/min for males and ≥ 43 ml/kg/min for females, which represents an aerobic capacity ≥ 90th percentile according to American College of Sports Medicine normative data for age and gender[18]. Additionally, U.S. Air Force personnel scored≥ 90/100 on their annual fitness test. U.S. Marines and Army had to score ≥ 270/300 on their annual fitness test, and all participants had to be physically able to ruck-walk for 10 miles (m) on a treadmill set at a zero percent grade while carrying 40 pounds (lb.) on their back.

Exclusion criteria included participants presenting with any one of the following 1) upper or lower body musculoskeletal injury in the past three months, 2) taking a beta-blocker medication, 3) uncontrolled hypertension, 4) routinely taking stimulants such as methylphenidate (e.g., ADD/ADHD medications), or 5) on military medical restrictions in any one of the following categories a) fitness testing; a) duty; or c) mobility deployment/assignment limitation code; d) on a military medical waiver.

Table 1. Participant's demographic and baseline measures (n=11).

Characteristic	Mean ± SD	Range
Age (yr)	26 ± 5.0	20-36
Height (cm)	179 ± 8.5	166.5-179.7
Mass (kg)	81.2 ± 10.2	65.1-89.0
Estimated VO_2 (ml/min/kg) [a]	52.9 ± 5.4	50.3-57.9
HR (b/min) [b]	78 ± 10.4	60.0-86.0
RPE[c]	6.3 ± 0.60	6.0-8.0
BLa[d]	3.3 ± 0.60	1.1-9.1

Abbreviations: HR= Heart Rate; RPE = Rating Perceived Exertion; BLa = Blood Lactate
[a] milliliters per minute, [b] beats per minute, [c] rating of perceived exertion,
[d] blood lactate concentration.

Design

A repeated measure double-blind placebo was applied in the current study. Subjects attended four testing sessions, separated by at least four days for a washout period. Each laboratory testing session lasted two to five hours in a temperature-controlled environment. All testing took place in the U.S. Air Force School of Aerospace Medicine's Satellite Human Performance Laboratory over six to eight months. The first meeting with potential volunteer participants was to determine if they met the age and annual military fitness testing score requirements for possible inclusion. Participants also completed a medical screening questionnaire during the first inclusion meeting, which the assigned medical monitor and primary investigator evaluated. After participants were provided explanations of all testing procedures for the study, potential participants reviewed and signed an informed consent document. Participants were then scheduled for their first formal inclusion physical testing session to determine their eligibility for participation in the study.

Except for inclusion meeting one, first formal inclusion testing session, and baseline testing two, all remaining testing sessions (e.g., 3-4) were under either placebo [PLA] or sublingual caffeine [SCA] condition in a randomized, double-blind scenario and followed the same testing sequence depicted in Table 2. Participants received instructions to refrain from consuming caffeine-containing substances (e.g., soft drinks, energy drinks, coffee, chocolate) 48 h before each testing session. Participants were informed to arrive in a hydrated state (≤ 12 h before testing) and refrain from high-intensity exercise 24 hours preceding all testing sessions. Before testing, a study investigator asked participants how much-estimated fluid they had consumed throughout the day. However, the precise value of fluid intake was not recorded. Lastly, the medical monitor assigned a unique alphanumeric identifier for testing sessions three and four to blind subjects and investigators. The study investigators only knew the subject's unique identifier after the statistician performed the final data analysis.

Experimental Procedures

Inclusion testing session one was performed with neither PLA nor SCA. Participants' height and body mass were measured using a stadiometer (Tanita WB-3000, Physician's scale). Each participant received instructions on the submaximal walking test procedures, followed by an explanation detailing the use of Borg's ratings of perceived exertion scale[19]. Finally, the laboratory technician fastened a heart rate monitor (POLAR® heart rate monitor system, Philips, Shevlin Corp, USA) around the participant's chest. Participants' aerobic capacity was assessed using a valid and reliable test to predict maximal oxidative capacity, known as the Ebbeling & Ward single-stage submaximal walking protocol[20]. If participants met established ACSM norms for aerobic fitness capacity, they were eligible for inclusion and scheduled accordingly[18].

Baseline (controlled) testing session two was performed with neither PLA nor SCA. As depicted in Table 2, this testing session required participants to complete three consecutive sets of maximal push-ups, followed by three successive sets of maximal pull-ups. Participants then completed a 10-mile ruck-walk while walking at 3.5 mph on a treadmill, followed by an added three consecutive rounds of push-ups and pull-ups. Participants completed three rounds (sets) of push-ups and pull-ups for 60 consecutive seconds followed by 30 seconds of recovery between each round, or until they reached volitional (exertional) fatigue prior to completing the 60 second round (set). Immediately following three rounds (sets) of push-ups and pull-ups, participants were instructed to change into their Battlefield Dress Uniform (BDU). A POLAR® heart rate monitor strap (Philips Health care, Shevlin Corporate Park, Home Health Care Solutions, USA) and wristwatch were worn by participants along with a 40 pound (lb.) weighted vest and a military-issued camelback filled with 100 ounces of water. Participants were instructed to drink ad libitum during the 10- mile treadmill ruck-march. However, water consumption was not measured after each trial. The intensity of exercise was monitored at the end of every 2.5 miles using the Borg Rating of Perceived Exertion (RPE) scale (6-20), and 0.7 micromoles/liter (μL) of capillary blood was collected via a finger stick using a Softclix II (Sports Resource Group, Inc., USA) lancet at the end of every 2.5 miles. The Lactate Plus (Sports Resource Group, Inc., USA) was used to analyze the amount of lactate in each participant's blood.

Testing sessions three and four followed the same testing sequence depicted in Table 2. However, participants were provided with either a PLA or SCA. The PLA, supplied by the manufacturer (Zipp Tabs, LLC), was matched in taste, color, and texture to the caffeine tablet but contained no active caffeine ingredients. Each SCA tablet (Zipp Tabs, LLC, Myrtle Beach, SC) was fruit punch flavored, containing Vitamins B_6 B_{12}, and coated with natural sugar. According to the manufacturer's label, each tablet was 25 milligrams (mg). Thirty minutes before testing, participants were instructed to place 6mg/kg of body mass (bm) of either placebo PLA or SCA tablets under their tongues until they dissolved. An assigned investigator ensured that each tablet had adequately dissolved by visually checking under the participant's tongue. Participants were instructed to remain seated after the tablet had dissolved entirely for an additional 30 minutes before testing to allow for peak blood caffeine[11-12].

Table 2. Performance testing sequences.

Sequence 1	Weighted Vest Treadmill March (Sequence 2)					Sequence 3
1. Push-Ups 2. Pull-Ups	1. RPE 2. Lactate	1. RPE 2.Lactate	1.RPE 2. Lactate	1.RPE 2. Lactate	1.RPE 2. Lactate	1. Push-Ups 2. Pull-Ups
-30 minutes	0 miles	2.5 miles	5 miles	7.5 miles	10 miles	<30 minutes

Push-ups and Pull-ups

Push-ups were administered per U.S. Air Force standards[21]. Participants performed three sets of maximal push-ups with 30 seconds of recovery between each set. Participants were instructed to start with elbows fully extended, both hands on the floor with fingers facing straight ahead, and to lower their body to the ground until their upper arms were parallel to the floor (elbows bent at least 90° or less) before pushing back up to the starting position (chest could touch the floor). If the participant did not come down far enough, the push-up did not count. One full push-up was measured when the participant returned to the starting position with elbows fully extended. Participants were instructed that their body could not bow at the waist and had to remain rigid throughout the evaluation.

Pull-ups were measured per U.S Marine standards[22]. Participants performed three sets of maximal pull-ups with 30 seconds of recovery between each set. Participants assumed a grip with both palms facing the rear (supinated grip). The starting position began with arms full extended beneath the bar, with feet free from touching the ground or any bar mounting assist. The body remained motionless throughout, with legs in a bent knee position (not raised above the waist). One repetition consisted of raising the body with the arms until the chin was above the bar and then lowering until the arms were fully extended. Participants were instructed that they could not rest their chin on the bar. They could not use their body as a pendulum to enhance their ability to execute the pull-up.

Submaximal Aerobic Assessment

As previously described, participants predicted oxidative capacity was measured using a single-stage treadmill walking test[17]. Before the assessment, a heart rate monitor (POLAR® Heart rate monitor system, Philips, Shevlin Corp, USA) was fastened around the participant's chest.

Participants then warmed up for four minutes on a motorized treadmill at a 0% grade, and a walking speed was established between 2 to 4 miles per hour during the warm-up. The chosen walking speed had to elicit a heart rate range of 50% to 70% of age-predicted maximal heart rate (MHR= 220-age) and not exceed 85% of predicted MHR. If the participant's heart rate was not within this range after the first minute of the test, walking speed was increased to 3.4 to 4 miles per hour. Following the warm-up, participants walked at their established speed for an additional 4 minutes at a 5% incline. Exercise heart rate was recorded in the last 30 seconds of each minute for four minutes. If heart rate varied by more than five beats per minute (bpm) (e.g., steady-state) between the last two heart rates from minutes three and four, the test was extended an additional minute until the participant's heart rate reached a steady state. The final two heart rates were then recorded and entered into a regression equation to predict maximal oxidative capacity for each participant. The correlation between observed and estimated VO_2 max for the Ebbeling & Ward protocol is R2 = 0.92[19].

Statistical analyses

The data were entered in Microsoft Excel and converted to a comma-separated value (csv) format for analysis. The csv document was then transformed from wide to long format by stacking sessions two through four outcomes. Testing session two was baseline because no supplements (caffeine or caffeine placebo) were given to the participants. Participants in testing sessions three and four were either provided treatment placebo (PLA =1) or sublingual caffeine (SCA =2). A Linear Mixed Model (LMM) was applied to compare the three testing sessions' mean differences in performance measures. Fixed effects in the LMM were the treatment groups (baseline, session 3, and session 4), and the random effects accounted for the correlated errors. The physiological measures collected at miles (m)0 (pre), m5, and m10 represent the mean values for the treadmill exercise heart rate (10-mile ruck walk), treadmill exercise ratings of perceived exertion, and blood lactate levels.

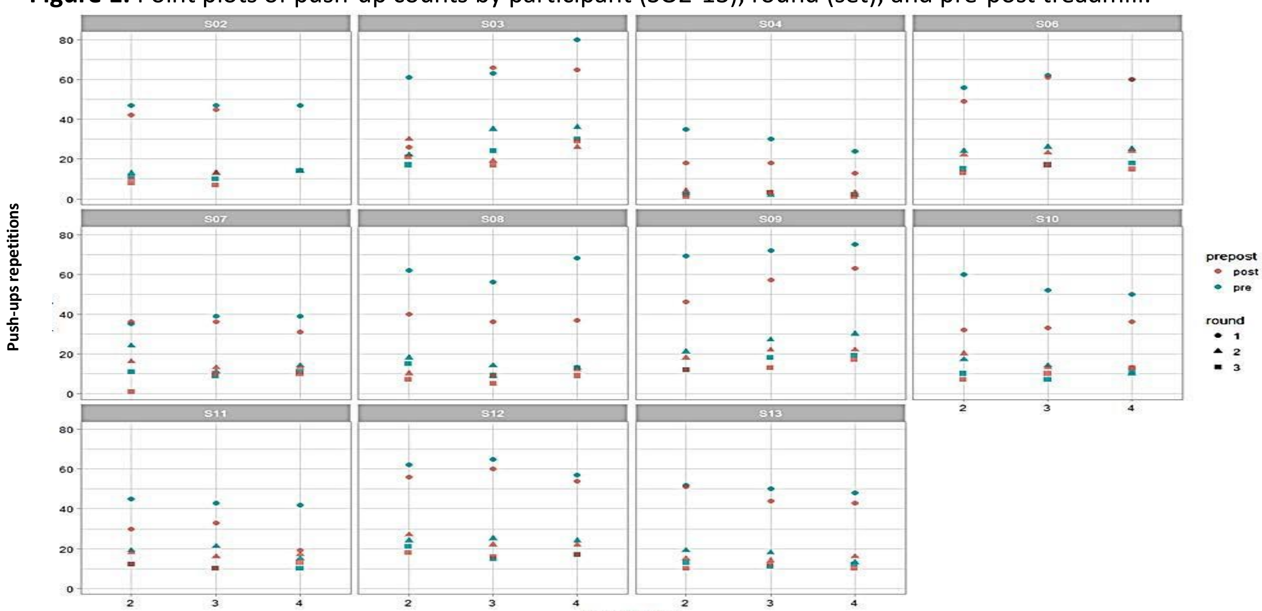
The software programs R version 3.3.2 and R Studio version 1.0.44 (R Core Team, Auckland, New Zealand) used the Defense Research and Engineering Network (DREN) for statistical analysis. The following packages were used: 1) dplyr[1] for data manipulation for faster performance, 2) ggplot2[2] for graphics to generate boxplots and dot plots, 3) lme4[3] to fit a linear mixed-effects model, 4) tidyr[4] to collapse columns that were not variables, and 5) tibble[5] to have better formatting and to add more columns[23-27].

Results

Physical Performance Outcomes

Results from the LMM comparing performance measures in three scenarios showed small differences in the fixed effects among baseline (p=0.38), PLA (p=0.37), and SCA (p=0.36). Participants showed consistent performance across all three conditions and had similar responses (e.g., pushups in round one was more remarkable than rounds (sets) two and three, both pre-and post- weighted vest treadmill walking) as depicted in Figure 1.

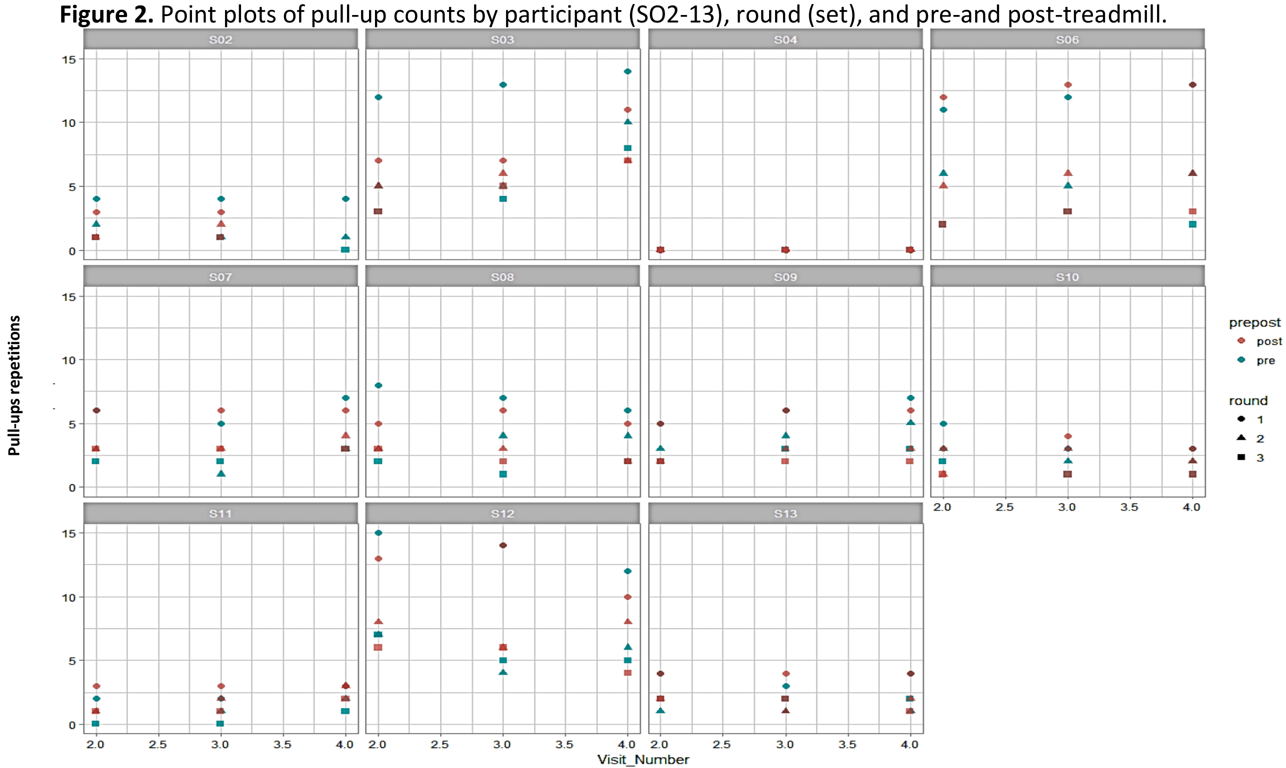
Figure 1. Point plots of push-up counts by participant (SO2-13), round (set), and pre-post treadmill.



Legend: Pre-post is pre-10-mile ruck walk push-ups and post 10-mile ruck walk pushups; Round 1-3 is sets of participant pull-ups; Visit_number 2.0= Baseline, 3.0= PLA or SCA, 4.0= SCA or PLA

Pull-ups had a higher variance than pushup counts, as depicted in Figure 2. Participants performed as expected, with the highest number of pull-ups in round one and decreased numbers in rounds two and three. Additionally, three of the participants were unable to complete any pull-ups in at least one testing round (set).

Figure 2. Point plots of pull-up counts by participant (SO2-13), round (set), and pre-and post-treadmill.

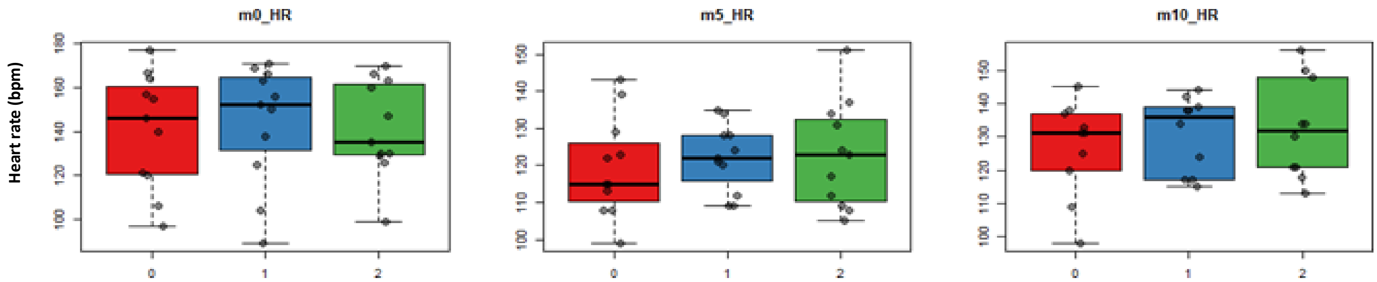


Legend: Pre-post is pre-10-mile ruck walk pull-ups and post 10-mile ruck walk pullups; Round 1-3 is sets of participant pull-ups; Visit_number 2.0= Baseline, 3.0= PLA or SCA, 4.0= SCA or PLA

Treadmill weighted vest ruck-march, heart rate, perceived exertion, and blood lactate

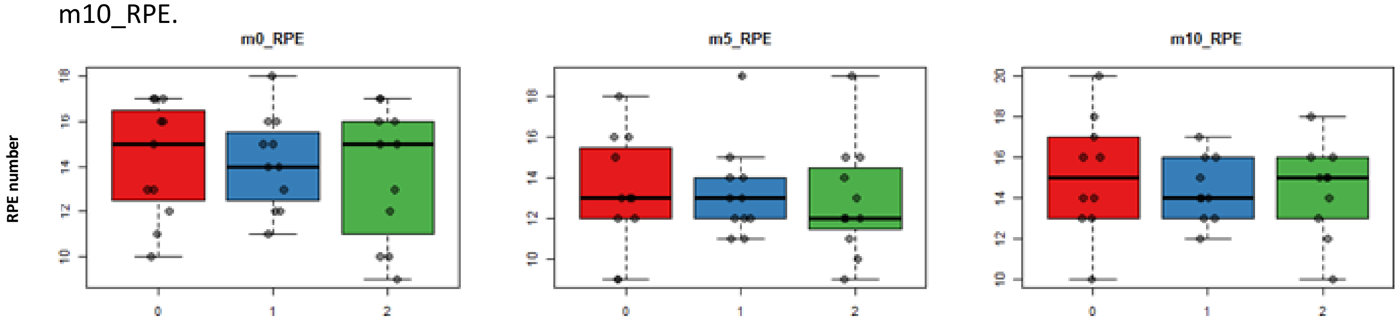
Overall, the boxplots show that the variance was similar, and minimal change occurred in the median in all groups, both pre-and post-treadmill exercises. Participants' exercise heart rate (HR), ratings of perceived exertion (RPE), and blood lactate (BLa) were measured during the treadmill weighted vest ruck-march at miles(m) m0 (pre), m5, and m10 (post). Participants HR, RPE, and BLa values were measured at m0 while standing on the treadmill directly following three pre rounds (sets) of pushups and pull-ups prior to starting the 10-mile weighted vest treadmill ruck march.

Figure 3. Treadmill exercise heart rate measures at m0, m5, and m10.



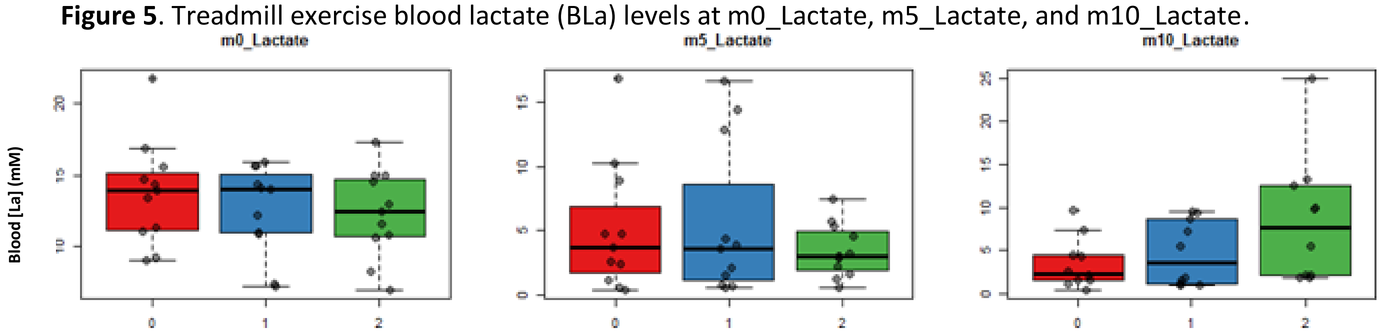
Legend: Baseline condition (Round "0"-Red), SCA condition (Round "1"-Blue), and PLA condition (Round "2"-Green)

Figure 4. Treadmill exercise ratings of perceived exertion (RPE) measures at m0_RPE, m5_RPE, and m10_RPE.



Legend: Baseline condition (Round "0"-Red), SCA condition (Round "1"-Blue), and PLA condition (Round "2"-Green)

Figure 5. Treadmill exercise blood lactate (BLa) levels at m0_Lactate, m5_Lactate, and m10_Lactate.



Legend: Baseline condition (Round "0"-Red), SCA condition (Round "1"-Blue), and PLA condition (Round 2-Green)

Treatment effects

The treatment effects (PLA or SCA) were measured to determine the difference in outcomes when participants were given either the SCA or PLA. The effects of caffeine (treatment) compared to placebo showed little difference, with most of the results bordering zero. Additionally, there was minimal change in treatment effects when comparing baseline, SCA, and PLA groups and no linear relationship was found. Thus, the SCA supplement cannot be used to explain the outcomes.

Discussion

The overarching hypothesis for this investigation was that a moderate dose of caffeine administered sublingually (SCA) to a cohort of highly fit military personnel would increase performance measures, reduce perceptions of fatigue, and not produce adverse side effects. Specialized military populations, such as Special Forces operators, fighter pilots, and Infantry soldiers, must sustain physical and cognitive performance under harsh conditions that may result in physical and psychological exhaustion[1]. Hence, more research is needed that examines the effects of alternate fast-acting caffeine delivery systems on sustaining performance and cognition in specialized military cohorts. Exploring the effectiveness of alternate caffeine delivery systems could potentially save the lives of military personnel working under extreme fatigue and further enhance their ability to complete their mission aims. To study the efficacy of SCA, we included similar exhaustive exercises, such as the 10-mile weighted ruck walk, that specially trained military personnel routinely perform in the field. Hence, we recruited similarly highly fit military personnel who could withstand the rigors of the experimental activities that were employed to induce muscular exhaustion. Additionally, we selected an alternate caffeine delivery system (e.g., SCA tablets) that military personnel could easily consume during an extended military mission where time is limited and of the essence.

The findings of this study show that a moderate dose of SCA did not attenuate perceived fatigue, nor did it enhance bodyweight supported muscular strength or endurance exercises (e.g., push-up, pull-up) following exhaustive exercise in our military cohort. However, a moderate dose of SCA did not negatively affect performance measures due to adverse side effects, such as gastrointestinal issues, high heart rate, or headaches during or following the caffeine testing sessions. Although our results do not support our hypothesis, the novelty of the chosen caffeine delivery system used in this investigation was subjectively reported by the participants as having a favorable taste, did not cause irritability, restlessness, nervousness, or jitters, and there were no reported muscle tremors, or fast irregular heartbeats during or following testing. To our knowledge, this was the first attempt for testing a quick dissolve sublingual tablet in U.S. military personnel.

Although the participants who completed this study were not Special Forces operators or elite U.S. military fighter pilots, their physical characteristics and physical conditioning status were similar. Unfortunately, based on the study location, we could not recruit a homogenous group of military forces operators or elite fighter pilots for this study. Future investigators should consider conducting similar caffeine studies on elite military personnel in a field training environment using an alternate form of caffeine delivery, such as the one used in this investigation. For example, Lieberman et al.[11] explored the dose-response effects of 100 mg, 200 mg, or 300 mg of caffeine on visual vigilance, choice reaction time, tests of learning and working memory, and self-reported measures of fatigue on U.S. Navy SEALs during 'Hell Week,' which is considered the most stressful week of training. The 300 mg group of trainees showed marked improvements in cognitive performance compared to placebo, 100 mg, and 200 mg groups. Although the participants who completed this study were highly fit military personnel, we did not measure the effects of a moderate dose of SCA on visual vigilance, choice reaction time, or tests of learning and working memory after performing exhaustive exercises, nor were our participants sleep-deprived, which could have affected our outcomes. Like the Lieberman study, future investigators who replicate these investigators study should consider specific tasks that measure reaction time, visual vigilance, and working memory.

In a similar study, Stein et al.[5] explored the effects of 4mg/kg of military energy gum (MEG) on 39 highly fit male and female ROTC students, veterans, and civilians in a non-sleep-deprived state. Results showed no differences between placebo or caffeine conditions on mental performance, marksmanship, or reaction times. The dose of caffeine administered in the Stein et al. study was slightly lower than the dose administered in this investigation; however, the delivery system they used was analogous to ours, and the participants were likewise not sleep deprived. The researchers who conducted this study concluded that they "could not discount the possibility of improvements in performance from caffeine after sleep deprivation." [5, p.90]

Although we chose exercise modalities commonly performed by an elite military population, several of our participants reported that they did not routinely perform maximal pull-ups, which could explain why the highest number of pull-ups occurred in the round (set) one and decreased in rounds two and three. Unlike push-ups, which is a component of the U.S. Air Force (USAF) annual fitness assessment, pull-ups are not, which may explain why three participants could not complete any pull-ups in at least one pull-up round. Currently, only the U.S. Marines and the U.S Army include pull-ups as a component of their annual fitness assessment. The participants enrolled in this study consisted of only highly fit USAF military personnel.

For this investigation, we intended to simulate exhaustive physical modes of activity analogous to what highly trained military personnel may experience during tactical training evolutions and on the battlefield. Unfortunately, we could not incorporate any simulated shooting scenarios to assess the effects of marksmanship after performing exhaustive exercises due to space and budgetary limitations. However, future investigators may incorporate similar exhaustive exercise modalities used in our study but should also consider adding a cognitive simulated shooting component to assess the effects of caffeine on reaction time, decision-making, and marksmanship.

There were three significant outliers for blood lactate at the five-mile marker, exceeding fifteen millimoles (mm) and dropping to ten (mm) at the ten-mile marker for several participants. The lower lactate values at the ten-mile mark may be attributed to these participants achieving a steady-state heart rate as the test progressed, as walking speed and incline were not increased throughout the 10-mile walk. Another physiological explanation may be related to the participant's ability to oxidize lactate in the mitochondria at a rate exceeding pyruvate, known as the intracellular lactate shuttle mechanism, whereby the mitochondrion inside the working skeletal muscle rapidly oxidizes lactate through monocarboxylate transporters[28]. Simply, the participant's skeletal muscle make-up (slow vs. fast twitch), type of training adaptation, and ability to shuttle lactate at faster rates out of the working skeletal muscle to be oxidized may have resulted in lower lactate values at the ten-mile mark. Nonetheless, considerable outliers for several participant’s during the ten-mile walking test may have partially contributed to our non-significant findings.

For this study, it was unknown how much caffeine the participants regularly consumed, even though we provided specific pre-testing guidelines before testing trials and asked participants how much caffeine they had consumed before each testing session. Therefore, participants' sensitivity to caffeine after a brief restriction period may have affected the results. Similarly, the recovery time for each participant varied due to unexpected official military travel and other military duties. Since the time interval between participants' visits was not constant, some participants had more recovery time than others. This inconsistency in recovery time may have resulted in fewer changes in participants' blood lactate, ratings of perceived exertion, and exercise heart rate response during exercise.

Our study participants received SCA at a one-time point prior to testing for this study. However, in a similar study conducted by McClellan and colleagues[4], sixteen highly trained military participants completed a double-blind placebo and caffeine trial that included a control day and period of sleep, followed by 28 hours of sleep deprivation. For example, prior to the exhaustive performance trials, participants first consumed a 400 mg dose of caffeine, and 5.5 and 7.5 hours later, participants received a 100 mg dose of caffeine. Participants in this study completed a 2-hour forced ruck-march, a sandbag piling task, and a treadmill run to exhaustion at 85% of their maximal oxidative power. Results showed that caffeine did not affect the oxidative measures; however, RPE (subjective fatigue) levels were lowered. Caffeine was shown to be beneficial for military personnel who are doing sustained missions while in a sleep-deprived state. However, unlike our study, which administered only one moderate dose of SCA prior to the testing activity, caffeine was administered at various time points throughout each trial in the McClellan study, which may have contributed to the noted improvements in run time to exhaustion and the preservation of performance at control levels for their study participants[4].

The pharmacokinetics of the SCA tablet administered to participants in our investigation is similar to military energy gum (MEG). However, a piece of MEG delivers 100 mg of caffeine, while each SCA tablet used for our study delivered 25 mg of caffeine per tablet. The lower dose may have presented a problem in absorption rate efficacy in some of our study participants. For example, considering that the mean body-mass of a United States male is roughly 79.5 (kg), he would need to chew 4.5 pieces of "Military Energy" caffeine gum (e.g., 100 mg caffeine per piece) compared to 19 sublingual tablets to receive an equal amount of caffeine at an equivalent body mass. Because the tablet was sublingual, we could only administer roughly one bolus at a time, which consisted of five tablets. The five-tablet bolus was administered in this manner until a 6mg/kg dose was achieved for each participant. The five-tablet bolus may have contributed to varying absorption rates in study participants and affected the results. Future investigators should consider using a similar military cohort but administer higher-dosed sublingual tablets before and throughout the testing trials. Although MEG is considered an effective delivery system that enhances absorption rates through the oral mucosa, some military personnel may prefer alternate delivery systems other than caffeinated gum, which can begin to taste bitter to chewing time.

For our study, we were conservative in using SCA in one dose (6 mg/kg bm) administered to our participants sixty minutes before each testing session while only focusing on the effects of SCA mitigating fatigue and enhancing gross motor activities. However, Van Handel[25] concluded that caffeine does help improve reaction time, increase alertness, and heighten individuals' sense of well-being. Van Handel stressed that caffeine might be of particular benefit in such sports as shooting and archery. However, the effects appear to be dose-related and largely depend on the participants' habituation level (e.g., the average caffeine intake of the subjects)[29]. Consistent with the previous investigation, future research may include using SCA administered throughout exhaustive activity sessions to explore the effects of varying doses of caffeine (e.g., 3mg/kg bm, 6 mg/kg bm) on physical performance[6,13,30]. Future investigators may also benefit from adding more participants, controlling for fitness, ensuring that participants are pre-hydrated before testing trials, and maintaining a consistent time interval between participants' testing sessions. Lastly, and perhaps more importantly, future researchers should consider performing field-based testing using a similar caffeine delivery system like ours and recruiting elite military personnel, such as Special Forces operators and fighter pilots, to take part.

Conclusion

Further research in formulating and exploring alternate caffeine delivery systems is necessary, especially for specialized military personnel who must perform long, arduous missions, which require physical and cognitive sustainment. Delivery system choice should include tactical combat environmental usage factors to minimize noise and motion and maximize rapidity between a decision to use the administration of the substance and the onset of action. For example, noise from unwrapping, spraying, or chewing may result in an adversary detecting one's location. Lastly, future exploration in the domain of caffeine's effects on performance during sleep deprivation using an alternate caffeine delivery system, such as SCA, is warranted, as reported by the International Society of Sports Nutrition's Position Stand on caffeine and performance, "During periods of sleep deprivation, caffeine can act to enhance alertness and vigilance, which is an effective aid for special operations military, as well as athletes during times of exhaustive exercise that requires sustained performance and vigilance". [12 p.12]

Disclaimer

The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Army, the Department of the Air Force, or the Department of Defense or the U.S. Government."

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