



# Journal of Exercise Physiology **online** (JEP **online**)

Volume 11 Number 6 December 2008

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Official Research Journal of  
the American Society of  
Exercise Physiologists  
(ASEP)

ISSN 1097-9751

## Metabolic Responses to Exercise

### THE EFFECT OF DIFFERENT DOSAGES OF CAFFEINE ON ISOMETRIC STRENGTH AND ISOMETRIC ENDURANCE

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#### ABSTRACT

**Sharma Archna, Sandhu S Jaspal.** The effect of different dosages of caffeine on isometric strength and isometric endurance. *JEPonline* 2008;12(6):34-43. Caffeine has performance enhancing effects, some of which have been observed during submaximal isometric contractions. The purpose of the study was to investigate effect of different dosages of caffeine (0, 5, 9, and 13 mg/kg body weight) on neuromuscular variables such as isometric strength and endurance. Thirty-one healthy individuals participated in the double-blind repeated measure study. Caffeine capsules were administered randomly. One hour following capsule ingestion, subjects performed two isometric contractions: one of 10 seconds duration and the other of 60 seconds. Isometric angle specific peak force, average force and fatigue index of quadriceps in extension moment were measured. A significant increase ( $p < 0.01$ ) in all the above variables was found for all caffeine tests, compared to placebo. Significant ( $p < 0.05$ ) differences were found in isometric strength only for the highest dose of caffeine (13 mg/kg BW). A significant progressive increase in the isometric endurance with subsequent higher dose of caffeine from 5, 9, and 13 mg/kg BW was observed. A dose-response relation between caffeine and fatigue index was found for the dose range investigated. It is concluded that caffeine is an ergogenic aid, which stimulates both isometric strength and endurance. The results suggest that isometric endurance can be increased following low to moderate caffeine consumption whereas an increase in isometric endurance was observed following high caffeine consumption.

**Key Words:** Caffeine, Dose-Response, Force, Fatigue Index.

## INTRODUCTION

Caffeine (1,3,7-trimethylxanthine) is a plant alkaloid found in coffee, tea, chocolates and colas. It is similar in structure to several endogenous metabolites, following absorption it crosses the blood-brain-barrier and is distributed in intracellular fluid (1). These properties allow caffeine to affect many human tissues including central nervous system (CNS), cardio-vascular system (CVS) and both smooth and skeletal muscles (1). Caffeine has the potential to influence human neuromuscular performance through its effect on the central and peripheral events along the motor pathway.

Caffeine may increase the descending drive from the motor cortex by blocking the inhibitory effects of adenosine (2) thus both increasing a subject's ability to excite a motor unit pool by bringing the motor neuron closer to threshold and facilitating maximal activation. Caffeine also reverses central dopamine and cholinergic deficiencies and reducing the perception of effort and fatigue, thus increasing work output (3). On January 1, 2004, caffeine was removed from the World Anti-Doping Agency (WADA) list of prohibited substances because the ergogenic effects are said to be rather small, and realized that the vast majority of athletes use caffeine, and because it is not possible to distinguish social use from doping attempts (4).

Despite the evidence that caffeine may affect performance there is paucity of evidence investigating its effect on isometric endurance (5,6,7,8). Caffeine can initiate and potentiate twitch and tetanic tension in both *in vitro* & *in vivo* muscle contraction in numerous experimental conditions in different species (9).

For example, Kalmer and Cafarelli (6) found that fatigue was significantly delayed in submaximal contractions of quadriceps following caffeine (6 mg/kg) consumption and Palskette and Cafarelli (11) demonstrated that caffeine (6mg/kg) lead to a significant increase in isometric endurance of human quadriceps muscle. Other studies have found no such effects of caffeine on maximum voluntary contraction and muscular endurance following administration of caffeine (5,7,8). For example, Lopes et al. (7) found no significant effect of caffeine (500 mg) on the maximum voluntary contraction (MVC) of the adductor pollicis muscle.

The differences in results are likely because of variability in methodology, subject selection, caffeine dosage, mode of caffeine administration and individual sensitivities to an acute dose of caffeine. The purpose of the experiment was to investigate whether caffeine exerts an ergogenic effect on maximal force production and endurance of human quadriceps muscle. Conflicting results of pervious studies with varying dosages necessitated incorporation of a wider dose range (5, 9, and 13 mg/kg BW) of caffeine to investigate the dose-response relation. Furthermore, the aforementioned dose range was also incorporated to evaluate the lowest dose at which the ergogenic effects are observed. The hypothesis was that there would be an increase in isometric strength (H1) and isometric endurance (H2) i.e., delayed development of fatigue of human quadriceps muscle following caffeine ingestion. The higher the caffeine dose, the stronger the dose response relation (H3).

## METHODS

### Subjects

Thirty-one (14 males and 17 females) healthy university students (mean weight  $63.0 \pm 2.9$  kg, mean age  $24.6 \pm 1.43$  yrs, and mean height  $166.80 \pm 9.84$  cm), participating in age specific sports activities and reporting a caffeine intake of  $\leq 200$ mg/wk (assessed via a standardized questionnaire) were studied. Prior caffeine habits were also taken into consideration, as acute and habitual intake of caffeine causes a diminished rise in epinephrine (11) and dampening of up regulation of adenosine receptors (12), respectively. However, these responses get potentiated after 4 days of withdrawal

(11). The experimental protocol and potential risks of the study were explained to each subject both verbally and in writing before their informed consent was obtained. The study was approved by the institutional ethical committee (IEC).

## **Procedures**

### ***Pre-experimental protocol***

Each subject visited the laboratory before the start of the study. Subjects performed maximum voluntary isometric contraction, on a HUR 5340 Leg Extension/Curl computer controlled isotonic/isometric dynamometer (University of Technology in Helsinki, Finland), to determine peak force (PF), average force (AVF) and fatigue index (FI) of the quadriceps femoris muscle of the dominant leg. The subjects performed a 10 second isometric contraction followed by a 60 second contraction (with a rest period of 2 minutes in between the two contractions) to familiarize themselves with the experimental protocol.

### ***Instructions to subjects***

The subjects were asked to refrain from any strenuous activity for 24 hours before the test. All subjects were provided with a list of caffeinated foods, drugs and beverages to be avoided for a minimum of 5 days before their first experimental session and throughout their participation in the study. A pre-structured standardized diet was given before each testing protocol to maintain almost identical glycogen concentration in muscles and liver cells (to minimize any variations in the results as a result of dietary intake & to maintain a standardized diet plan for each individual)

### ***Experimental protocol***

The study utilized a pre test/post test, repeated measure design, with experimental and placebo trials completed in a random order on 4 separate days with a constant time and day of the week for each individual. The tests differed only in the amount of caffeine ingested before the exercise. Besides a placebo (group P) that contained all-purpose flour and no caffeine (0mg/kg BW), the dosages of caffeine tested were 5, 9, and 13 mg/kg BW, constituting low, medium, and high dose, respectively. The standardized caffeine capsules were administered using a double blind procedure in which an individual who was unaffiliated with the study placed capsules of an appropriate dosage in code envelopes, which were identified by the subject's initials and the day the dosage were to be investigated. U.S. Pharmacopoeia grade caffeine (Sigma Aldrich, Saint Louis, USA) was used in the study.

Subjects were asked to consume food 2 hrs prior to the test. After capsule ingestion the subjects rested for one hour (13-15). Following a 5-minute warm-up (static stretching of quadriceps and hamstring muscle with 15 second hold, 4 times each followed by unloaded pedaling on cycle ergometer for 3 minutes) the PF, AVF and FI were measured at optimal standardized angle of the knee joint (60° of knee flexion; 0° implying full knee extension), the angle at which the quadriceps femoris muscle applies maximum force (16). The isometric test protocol was applied as per standardized procedure mentioned by HUR research line software user manual (Version 1.3).

## **Statistical Analyses**

**Isometric strength measurement:** The torque (Nm) was measured at 10 sec isometric contraction at 60° knee flexion for quadriceps. It was normalized to force (N) by dividing the torque (Nm) by lever arm length (m). Thereafter Peak Force (PF), highest force in 10 seconds and Average Force (AVF) for 10 sec, average force of 4 quarters; 1 quarter = 2.5 sec) were calculated.

**Isometric endurance measurement:** After a 2-minute rest, fatigue index (FI) was measured as an indicator of isometric endurance with the same seat position and knee angle as above. An isometric

contraction of 60 sec was performed to calculate isometric endurance (17). Torque in 1<sup>st</sup> sec ( $T_1$ ) and torque at 60th sec ( $T_{60}$ ) were observed. Torque  $T_1$  and  $T_{60}$  were normalized to force  $F_1$  and  $F_{60}$  respectively. Fatigue Index designed by Milner and Brown et al. <sup>(17)</sup> was calculated using the following formula:

$$\text{Fatigue - index} = F_1 - F_{60} \div F_1 \times 100 (\%)$$

To prevent any distractions, no visual or auditory cues were given to subjects during both strength & endurance measurements.

### Data Analysis

Data were presented as Mean  $\pm$  SD. The data were analyzed for statistical significance by using the statistical package for social sciences (SPSS 14.0) software. The dependent variables PF, AVF and FI were analyzed using one way analysis of variance (ANOVA) with repeated measurements for statistical analysis of the response differences between pairs of caffeine dosages. Since significant differences were found ( $p < 0.05$ ), a multiple comparison Bonferroni (Post Hoc Test) was applied to test for differences between pairs of dosages. Pearson coefficient of correlation was calculated to assess the relation between caffeine dosage and increase in performance variables (isometric strength and isometric endurance) post caffeine consumption.

## RESULTS

### Isometric strength

Peak force was examined by a 10 second isometric contraction of the dominant quadriceps femoris muscle. One Way ANOVA showed a significant increase in peak force ( $F=4.352$ ;  $p < 0.001$ ) with average increase of 40% in all the three caffeine-supplemented groups. When inter-group comparison was done, significant differences in peak force were found only in 13 mg/kg trial

**Table 1: Peak isometric Strength (N) with different caffeine dosages.**

Caffeine Dosage	Mean $\pm$ SD	P Value
Placebo (0mg/kg BW)	340.37 $\pm$ 146.06	NA
5 mg/kg BW	391.95 $\pm$ 175.45	1.00
9 mg/kg BW	465.50 $\pm$ 76.62	0.10
13 mg/kg BW	511.14 $\pm$ 76.32	0.013

(increase equal to 62.09%) compared to placebo, indicating that placebo may give a certain psychological benefit to the subject. On comparison with placebo group a non-significant increase in peak force was noted following consumption of 5mg/kg & 9mg/kg caffeine, as shown in Table 1 & Figure 1. There was a linear relationship with the amount of caffeine consumed & increase in peak force ( $r=0.45182$ ;  $p=0.809$ ) following 5mg/kg, ( $r=0.100539$ ;  $p=0.590$ ) following 9mg/kg & ( $r=0.21929$ ;  $p=0.236$ ) following 13mg/kg caffeine.

Similar are the findings when the average force (N) is taken into consideration with ( $F=3.783$ ;  $p=0.015$ ) with average increase 42% in all caffeine-supplemented groups. When inter-group comparison was done, this significance was observed only in the 13mg/kg dose with increase equal to 59%, compared to placebo. There was a non-significant increase in average force following consumption of 5mg/kg & 9mg/kg as compared with placebo group, demonstrated in

**Table 2: Average Isometric Strength (N) with different caffeine dosages.**

Caffeine Dosage	Mean $\pm$ SD	P Value
Placebo (0mg/kg BW)	300.38 $\pm$ 126.96	NA
5 mg/kg BW	359.95 $\pm$ 84.39	1.00
9 mg/kg BW	422.07 $\pm$ 80.27	0.10
13 mg/kg BW	444.23 $\pm$ 69.67	0.033

to 59%, compared to placebo. There was a non-significant increase in average force following consumption of 5mg/kg & 9mg/kg as compared with placebo group, demonstrated in

Table 2 & Figure 2. There was a linear relationship with the amount of caffeine consumed & increase in average force ( $r=0.10453$ ;  $p=0.576$ ) following 5mg/kg, ( $r=0.10893$ ;  $p=0.560$ ) following 9mg/kg & ( $r=0.29974$ ;  $p=0.101$ ) following 13mg/kg caffeine.

### Isometric endurance

Fatigue index (%) was significantly decreased following caffeine consumption ( $F=7.539$ ;  $p=0.00$ ) with average decrease of 60% for the 3 caffeine supplemented groups compared to placebo. The inter-group comparison demonstrated significant decrease in fatigue Index across all trials, and percentage decrease 42%, 66% and 71% 5 mg/kg

**Table 3: Isometric Endurance (Fatigue Index, %) with different caffeine dosages**

Caffeine Dosage	Mean $\pm$ SD	P Value
Placebo (0mg/kg BW)	37.73 $\pm$ 23.39	NA
5 mg/kg BW	23.66 $\pm$ 10.81	0.044
9 mg/kg BW	13.61 $\pm$ 8.35	0.001
13 mg/kg BW	11.81 $\pm$ 2.27	0.004

respectively, with 5mg/kg trial, 9 mg/kg trial and 13 mg/kg trial, when compared with placebo, as shown in shown in Table 3 and Figure 3. There was a

significant linear relationship with the amount of caffeine consumed & increase in fatigue index ( $r=0.34515$ ;  $p=0.576$ ) following 5mg/kg, ( $r= -0.23275$ ;  $p=0.0408$ ) following 9mg/kg & ( $r= -0.37712$ ;  $p=0.036$ ) following 13mg/kg caffeine.

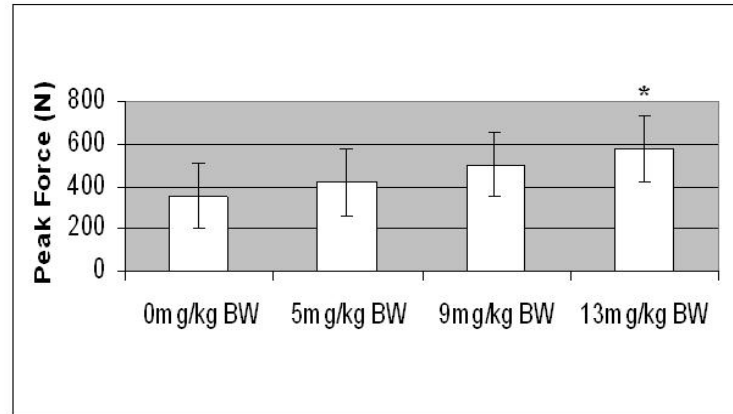
## DISCUSSION

In the present study the effect of caffeine on maximum voluntary contraction of the dominant knee extensor were measured in isometric mode rather than on either isotonic or isokinetic modes, because studies have demonstrated that high correlations exists among the three testing modes (when tested at joint angles of peak isometric torque)(18). A dosage of caffeine as high as 13mg/kg was included in the study as it is reported that some cyclists consumed such high caffeine dosages in competition (19), furthermore, to observe the effect of 13mg/kg dosage on isometric strength & isometric endurance, this high dosage was investigated.

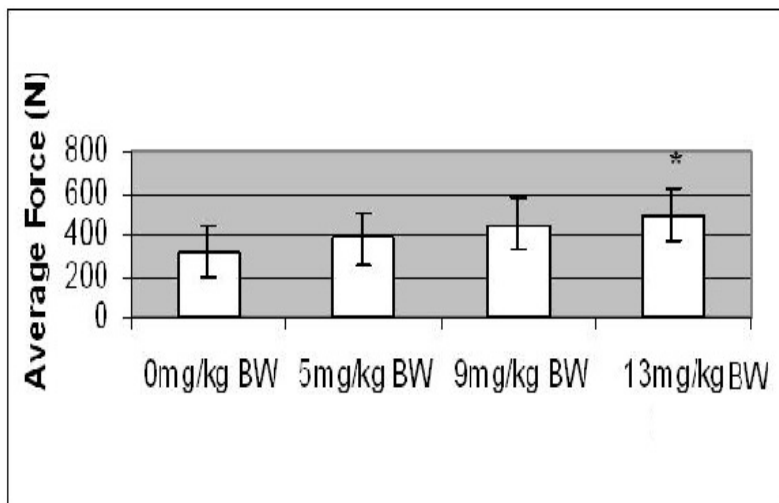
The effect of caffeine on exercise performance has been extensively explored, and results, especially for short-term high intensity exercise are equivocal. Studies have demonstrated that caffeine has an ergogenic effect on peak force generation and muscular endurance (6,10,20,21). Caffeine ingestion reduces rate of perceived exertion and improves exercise performance (22). However, other investigators did not find any significant difference in measures of peak torque, power and fatigue index following caffeine ingestion (23,24,25).

### Dose response and Isometric strength

Results indicate that 5 and 9 mg/kg BW doses of caffeine increased peak force and average force by 18% and 21%, 41% and 44%, respectively, as compared with placebo, but these were not statistically significant. Only the highest dose of caffeine (13mg/kg BW) significantly increased both peak force and average force by 62% and 58%, respectively, as compared with placebo. This is consistent with the findings of James et al. (24) and Williams et al. (25) who demonstrated non-significant effects of medium doses of caffeine on force output. Their findings may be attributed to a small sample size, in combination with small effect size, resulting in low statistical power.



**Figure 1: Effect of different dosages of caffeine on peak force (N). Values are mean  $\pm$  SD\*;  $p < 0.05$ .**



**Figure 2: Effect of different dosages of caffeine on average force (N). Values are mean  $\pm$  SD. \*;  $p < 0.05$ .**

Thus beneficial effects of caffeine on isometric strength were evident only after high dose of caffeine and not following low to moderate caffeine consumption. However, the findings of Plaskett and Cafarelli (10) reported a significant increase in force output following ingestion of moderate dose of caffeine (6mg/kg BW). Thus our results do deviate from previously published data, however, this discrepancy may be due to differences in muscle groups selected for the study or the larger sample size. Moreover, physiological lifestyle and dietary factors can alter caffeine absorption, distribution, elimination, and habituation (1).

Caffeine mobilizes and increases release of intracellular  $\text{Ca}^{2+}$  from sarcoplasmic reticulum (26). Caffeine also increases sensitivity of myofibrils to calcium & inhibition of phosphodiesterases leading to a subsequent increase in cyclic-3',5'-adenosine monophosphate (cAMP) in the various body tissues, including skeletal muscles in high doses (27). The third main mechanism of action of caffeine is linked to the antagonism of caffeine at adenosine receptors, mainly in the CNS (28). Direct effects

of caffeine on muscle include potentiating the tension of isolated muscle contraction by direct stimulation, both at rest and after fatigue (29).

### Isometric Endurance

The study investigated the effects of caffeine on isometric endurance, and demonstrated statistically significant effects on fatigue index for all the caffeine dosages examined. Fatigue index decreased by 42%, 66% and 71% for 5, 9, and 13mg/kg BW caffeine dosages respectively, (average 59.5%), compared to placebo. Thus a beneficial effect of caffeine on fatigue was evident with the lowest dose of caffeine. Other investigators have also demonstrated similar findings (10,30).

For example, Kalmer and Cafarelli (6) demonstrated that caffeine had an ergogenic effect on peak force generation and muscle endurance; citing efficient activation of motor unit pool at the supra spinal level, as a probable explanation. They also suggested that caffeine ingestion might enhance endurance performance by inhibiting pain sensation associated with sustained isometric muscle contraction. Plaskett and Cafarelli (10) suggested that caffeine (6 mg/kg) induced an increase in endurance performance resulting from alteration in muscle sensory processes, implying that the mechanism may be neural.

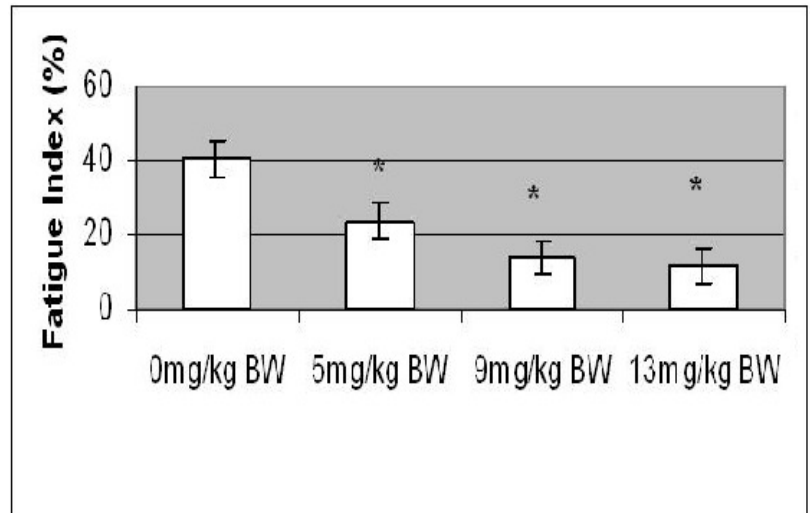
However, some investigators did not find any significant difference in measure of fatigue index following caffeine ingestion (23,24,25). The latter could be attributed to methodology (force-EMG relationship) used for interpretation of the results; because it represents a summation of both motor unit recruitment as well as discharge rate, surface EMG may not be a correct procedure to measure the effects of caffeine on excitation contraction efficacy during sub-maximal contractions (10).

Potential mechanisms for increased isometric endurance following caffeine ingestion include release of  $\text{Ca}^{2+}$  from sarcoplasmic reticulum (26). The performance enhancing properties of caffeine during aerobic activities have been associated with an attenuation of exercise sensory processes (31). A hypoalgesic effect of caffeine has been observed during ischemic muscle contraction (21). This too may contribute to delay of fatigue (perception of discomfort during fatigue). These mechanisms are mediated by altering the chemical composition of muscle environment.

It is also likely that feedback mechanoreceptors, such as Golgi tendon organs (31) and class III/IV muscle afferents (32,33) that are sensitive to increases in tension/pressure, are influenced by caffeine. Caffeine may alter feedforward information and may alter how information from either feedforward/feedbackward mechanism is processed centrally (10). Caffeine could mask fatigue, thus allowing individuals to feel better and to increase arousal and capacity to sustain effort (5).

### Side effects of caffeine

Although moderate doses of caffeine (200-300mg) can elevate mood and improve psychomotor and intellectual performance, larger doses can be anxiogenic, producing symptoms such as insomnia,



**Figure 3: Effect of different dosages of caffeine on Fatigue Index (%). Values are mean  $\pm$  SD. \*,  $p < 0.05$ .**



headache, irritability, tremor, nausea, and diarrhea depending upon individual tolerance, rate of absorption, metabolism and age (19). Symptoms including dizziness, headache, tremor, hunger sensations, and insomnia were reported during and after ingestion of 9mg/kg and 13 mg/kg doses in the current study, but disappeared within a few hours.

### Limitation of the study

In the present study, the urinary concentration of caffeine, rate of perceived exertion (RPE), anaerobic/lactate threshold (LT) for the various dosages (5, 9, and 13 mg/kg body weight) of caffeine were not determined.

### CONCLUSION

In conclusion, an ergogenic effect of caffeine was found for all caffeine doses examined. The peak force, average force significantly increased (average  $40\pm 22\%$  and  $41\pm 19\%$ , respectively) and fatigue index significantly decreased (average  $60\pm 16\%$ ) for all the caffeine dosages. In the dose range investigated a significant dose response relationship was observed only for isometric endurance, following caffeine consumption. Hence, it can be implied that caffeine can be used as an ergogenic aid in endurance events even at low doses but not in short duration, high intensity events, to enhance performance.

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