CAFFEINE IMPROVES NEUROMUSCULAR FUNCTION DURING MAXIMAL DYNAMIC EXERCISE

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ABSTRACT: Introduction: In this study we tested the hypothesis that caffeine supplementation improves neuromuscular function, which has both nutritional and clinical relevance. Methods: Fourteen male subjects (mean ± SD: 23.8 ± 2.8 years) volunteered in a double-blind, repeated-measures study with placebo (PLA) or caffeine (CAFF) (6 mg kg⁻¹). Maximal voluntary isometric contractions (MVCs), evoked maximal twitch, and maximal isokinetic contractions during elbow flexion were assessed. Mechanical and electromyographic (EMG) signals from the biceps brachii muscle were recorded, and muscle fiber conduction velocity (CV) was calculated to evaluate changes in the muscle force–velocity relationship and muscle fiber recruitment. Results: The torque–angular velocity curve was enhanced after CAFF supplementation. This was supported by a concomitant increase of CV values (8.7% higher in CAFF). Conclusions: Caffeine improves muscle performance during short-duration maximal dynamic contractions. The concomitant improvement of mean fiber CV supports the hypothesis of an effect of caffeine on motor unit recruitment.


Caffeine is the most commonly consumed drug in the world, as it is available in a variety of beverages, foods, and sports products. Caffeine supplementation has been used largely by athletes as an ergogenic aid in the belief it can increase exercise performance with minimal risks to health. Indeed, there is substantial evidence that caffeine enhances human performance, although the mechanisms of action are still unknown.¹,² In this regard, in vitro evidence suggests an increase in intracellular calcium concentration, which can be mediated by an enhancement of the release of calcium from the sarcoplasmic reticulum due to an interaction between caffeine and ryanodine receptors in the sarcoplasmic reticulum.² Potentially, caffeine can inhibit two isoforms. They are the adenosine receptors (A₁ and A₂), which, in turn, are located in the nervous system, liver, heart, adipose tissue, and muscles.³ Thus, the effect of caffeine is a combination of actions on various tissues.

Most of the studies of the potential of caffeine on human performance focused on endurance exercise and led to the notion that caffeine can be beneficial in these situations.¹⁻¹⁰ A number of studies have also examined the effects of caffeine on short-term intense exercise, but they report conflicting results.¹¹⁻¹⁵

The effect of caffeine on strength performance has been investigated infrequently.¹⁶⁻¹⁸ Findings have suggested direct effects on muscle excitation–contraction coupling and motor unit recruitment, which are independent from those related to metabolic efficiency.¹⁸⁻²⁰ Unfortunately, most of the aforementioned studies have focused on maximal isometric strength, whereas the effect of caffeine on neuromuscular function during dynamic contractions at different speeds has not been investigated thoroughly.

Since it has been shown that caffeine could potentially affect the central nervous system as well as skeletal muscle contractility, information extracted from surface electromyography (sEMG), which reflects both central and peripheral properties of the neuromuscular system, is of particular interest in both the clinical and sports context. Muscle fiber conduction velocity (CV), a basic parameter estimated from EMG, could add important information about changes in motor unit recruitment strategies, the changes in contractile properties, and the excitability of the sarcolemma.²¹,²² Consequently, caffeine supplementation has the potential to affect CV, but this has not been investigated.

Therefore, the purpose this study was combine mechanical and EMG parameters to investigate the effect of caffeine supplementation on neuromuscular activation of upper limb muscles during maximal isokinetic contractions conducted at different speeds in order to obtain a complete torque–velocity relationship. Moreover, electrically induced contractions (single twitch) were also assessed in the same subjects to discriminate between central and peripheral effects of caffeine supplementation on neuromuscular function.

We hypothesized that caffeine supplementation improves muscle performance for a wide spectrum of contraction speeds, possibly as reflection of an effect on muscle recruitment, and also evident as an enhancement of muscle fiber conduction velocity.
METHODS

Subjects. Fourteen moderately active men (age 23.8 ± 2.8 years of age, body mass 72.3 ± 5.6 kg, height 1.78 ± 0.05 m) were recruited to participate in this study. Subjects were fully informed of the experimental protocol and the possible risks and discomforts of the investigation before giving their informed written consent. All volunteers were non-smokers in order to exclude a pharmacokinetic interaction between caffeine and tobacco smoke. They were selected on the basis of their habitual caffeine consumption (<200 mg per week) as determined by questionnaire prior to participation in the study. In addition, subjects were asked to refrain from heavy exercise and alcohol for 48 h before experimental sessions and to abstain from consuming caffeine-containing foods and beverages for 4 days prior to, and throughout, the study. Exclusion criteria included history or signs of metabolic, renal, cardiac, or neurological diseases. The local ethics committee approved the study protocol.

Drug Administration. Caffeine (EP/USP caffeine anhydrous; Testa Industry, Savona, Italy) was administered in gelatin capsules (6 mg kg⁻¹ body mass). Placebo capsules were filled with all-purpose flour and had the same color as caffeine capsules. Treatment capsules were administered by a double-blind design in which an individual not involved in data recording and analysis placed the appropriate dose in coded envelopes. The order of capsule administration was randomly assigned, and each subject underwent all trials acting as his own control.

Overview of Study Protocol. Each subject visited the laboratory on three occasions. On the first visit, subjects were familiarized with the experimental procedures, and no treatment capsules were ingested. Participants then returned to the laboratory on 2 additional days separated by at least 1 week. In each session, subjects performed the experimental protocol before (pretest, PRE) and after (posttest, POST) ingesting caffeine or placebo, which were administered in a random order. The posttest commenced 1 hour after the ingestion of capsules to ensure an optimal caffeine plasma concentration.

Elbow flexion torque of the dominant limb was measured with an isokinetic dynamometer (KinCom, Chattanooga, Tennessee). Participants were seated comfortably in the dynanometric chair and were stabilized by chest and waist straps. The position of the upper arm was parallel to the trunk with the forearm halfway between pronation and supination. The wrist was secured in a cuff attached to the load cell. The center of rotation of the lever arm was aligned with the distal lateral epicondyle of the humerus. For detection of the evoked twitches, the cuff of the isokinetic dynamometer was substituted with a more rigid one especially made for this purpose.

The surface electromyographic signals (sEMGs) were recorded (sampling rate 2048 Hz) with a linear array of four electrodes (silver bars 5 mm long, 1 mm thick, and 10 mm apart; LISIN, Torino, Italy) from the biceps brachii (BB). After gentle skin abrasion and cleaning with ethyl alcohol, electrodes were attached to the skin over the BB along a line connecting the acromion to the cubital fossa. The optimal position and orientation of the electrodes were determined to be conveniently distant from the innervation zone and the tendon as previously described. A ground electrode was placed around the wrist of the contralateral limb. To ensure the same electrode placement throughout the two experimental sessions, individual maps of the upper arm were made on transparent plastic by marking the position of permanent skin blemishes with respect to the electrodes. Three sEMGs were detected in a single-differential mode. Two double-differentials were computed off-line and were used for further analysis. Signals were amplified (×1000), bandpass filtered (10 Hz to 450 Hz; EMG 16; LISIN), and sampled at 2048 Hz with 12-bit resolution (amplitude range ±10 V; DAQ Card AI-16XE-50; National Instruments, Austin, Texas), recorded, and stored on a personal computer.

Experimental Tests. During the test trial, the following parameters were evaluated: (1) maximal twitch; (2) maximal voluntary isometric contraction (MVC); and (3) maximal isokinetic contraction.

Maximal Twitch. After a period of standardized warm-up at submaximal intensity, the experimental trial started with determination of the motor point on the muscle belly using a constant current stimulator (DS7AH-HV; Digitimer, Ltd., Hertfordshire, UK). A stimulation pen was used, and the point that elicited the maximal response with the minimal stimulation amplitude was the motor point. A small round electrode was placed on the motor point (cathode) and a large rectangular electrode on the distal tendon (anode). Single impulses of 250-μs duration with a monophasic rectangular wave and constant envelope were delivered. Increments of 10-mA amplitude (separated by 30 s of rest) were delivered until the maximal mechanical response (maximal twitch) was obtained.
MVC. The joint angle was fixed at 90° (180°, full extension). The MVC task consisted of rapidly increasing the force exerted by elbow flexors to a maximum. Visual feedback was provided to the subjects by setting a target line on the computer screen at a value 20% higher than the best MVC. All subjects were verbally encouraged to exceed the target force, producing a maximal contraction “as hard as possible,” and to maintain it for at least 2–3 s before relaxing. A minimum of three maximal attempts were performed separated by 4 min to recover from fatigue. Participants were asked to perform further attempts if the MVC of their last trial exceeded the previous trials by at least 10%. However, in no instance did the number of MVC attempts exceed four per subject.

Isokinetic Concentric Contractions. After the MVC task, the torque–velocity curve was assessed. Angular velocity values were fixed at 15°, 30°, 60°, 120°, 180°, and 250° s$^{-1}$, and subjects were requested to flex the elbow “as hard as possible.” The range of motion (ROM) was 120° starting from 150° to 30°, which included the angle at which the maximal torque at the elbow joint was reached. The order of the trials was randomized to minimize the effect of skill acquisition. Each contraction was followed by a 5-min rest to prevent cumulative fatigue.

In each trial strong verbal encouragement was given by the test leader.

Data Analysis. All data collected during the experiments were analyzed off-line (LabVIEW, version 8.0; National Instruments).

For the maximal twitch tasks, peak torque (PT), time to peak (TTP) (from the onset of force trace, defined as 1% of the twitch amplitude), and half-relaxation time (HRT; i.e., time to halve the peak torque) were calculated. In addition, in order to obtain an indication of the work done by the muscle, the area underneath the twitch between the two signals (i.e., the amount of time shift that must be applied to one signal to minimize the mean square error with the other). This time shift is the same, which maximizes the cross-correlation between the signals. Estimates of CV were accepted only when cross-correlation values were >0.8.

Trials chosen for CV estimation were selected on the basis of maximal force. During isokinetic contractions, maximal CV was estimated over 250-ms windows, and this windowing was applied over the 90°–120° range of motion where the ROM portion was more likely to reach the maximal value of torque. During maximal twitch, the CV window was selected manually in order to isolate the M-wave elicited during the twitch and to avoid stimulus artifacts.

Statistical Analysis. A repeated-measures analysis of variance (between factors: CAFF vs. PLA; within factors: PRE vs. POST) was used to compare the dependent variables (CV, TTP, HRT, and torque). A dependent-samples t-test was implemented when appropriate. Data are expressed as mean ± SD in the text and tables and as mean ± SE in the figures. Statistical significance was accepted at $P < 0.05$. Regression lines for individual data sets of torque vs. angular velocity were computed using the least-squares method.

RESULTS

Torque–Velocity Relationship. Figure 1 summarizes torque–velocity relationships for the caffeine (CAFF) and placebo (PLA) groups, obtained during the POST trials in the elbow flexors. Exponential regression lines were also fitted. After caffeine supplementation, maximal torque values increased significantly at all angular velocities ($P < 0.05$), whereas they remained unchanged or were even reduced at MVC after placebo (Table 1).
Mean fiber CV was significantly enhanced (15% on average) when subjects were supplemented with caffeine at all angular velocities ($P < 0.05$), except for MVC, whereas it remained unchanged in the PLA group (Fig. 2 and Table 1).

EMG root mean square (RMS) was similar between PRE and POST in the placebo trials. In contrast, after caffeine consumption, EMG RMS was significantly ($P < 0.05$) increased relative to the PRE conditions (Fig. 3).

Maximal Twitch. Figure 4 depicts PT, CV, HRT, TTP, and TA values for maximal twitch. We found a significant reduction of PT recorded in the POST trial when subjects consumed placebo ($P < 0.05$). Similarly, the area underneath the twitch between the onset and time of reaching PT was significantly reduced ($P > 0.05$) in the PLA but not the CAFF trial. On the other hand, there was no significant effect of caffeine supplementation on CV, TTP, and HRT.

**DISCUSSION**

In this study, we have reported that caffeine supplementation in humans enhances the mechanical and myoelectrical response of elbow flexor muscles for a wide spectrum of contraction speeds. Moreover, we found an improvement in some mechanical parameters of maximal twitch, supporting the hypothesis of a concomitant enhancement in muscle contractility.

The effect of caffeine on muscle strength has been investigated by several investigators using a variety of protocols. Most of them have used isometric contractions to assess the maximal force, and no effect after caffeine loading has been reported.$^{19,31-33}$ Isokinetic strength has been poorly investigated, and the findings from those studies are controversial. Bond and colleagues,$^{16}$ for example, did not find any effects on strength and power during low, moderate, and high contraction speeds in track sprinters who consumed 5 mg kg$^{-1}$ of caffeine. The same protocol was repeated by Jacobson and colleagues$^{17}$ on resistance-trained athletes, but they concluded that caffeine can improve maximal isokinetic torque. In our study, subjects were asked to perform maximal isokinetic elbow flexions at six different contraction speeds in order to draw a complete torque–velocity curve.

### Table 1. Torque and CV raw data.

<table>
<thead>
<tr>
<th>Angular velocity (deg s$^{-1}$)</th>
<th>CV (ms$^{-1}$)</th>
<th>Torque (Nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Caffeine</td>
</tr>
<tr>
<td></td>
<td>PRE</td>
<td>POST</td>
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</tbody>
</table>
| 0                             | 4.82 ± 0.38  | 4.67 ± 0.44 | 4.63 ± 0.33  | 4.72 ± 0.49 | 98.50 ± 21.11 | 88.76 ± 20.22$^*$ | 95.64 ± 19.93 | 95.41 ± 20.43
| 30                            | 4.72 ± 0.42  | 4.54 ± 0.30 | 4.54 ± 0.39  | 4.70 ± 0.59 | 72.06 ± 11.90 | 65.09 ± 10.41 | 71.42 ± 14.87 | 74.72 ± 13.30
| 60                            | 4.74 ± 0.37  | 4.48 ± 0.28 | 4.58 ± 0.35  | 4.81 ± 0.67$^*$ | 69.29 ± 13.35 | 63.66 ± 12.10 | 65.71 ± 12.16 | 67.69 ± 12.51
| 120                           | 4.83 ± 0.47  | 4.54 ± 0.28 | 4.55 ± 0.43  | 4.77 ± 0.56$^*$ | 62.46 ± 12.44 | 59.04 ± 11.63 | 59.44 ± 12.29 | 62.44 ± 11.72
| 180                           | 4.74 ± 0.35  | 4.52 ± 0.36 | 4.57 ± 0.40  | 4.77 ± 0.52$^*$ | 57.13 ± 12.85 | 54.62 ± 12.04 | 55.84 ± 12.24 | 58.51 ± 10.96
| 250                           | 4.72 ± 0.44  | 4.47 ± 0.24 | 4.49 ± 0.25  | 4.74 ± 0.48$^*$ | 51.17 ± 10.44 | 49.33 ± 9.88  | 49.46 ± 9.31  | 55.01 ± 11.74

CV, conduction velocity.

$^*$ $P < 0.05$. 

**FIGURE 2.** CV values in CAFF (open circles) and PLA (filled circles) during the POST supplementation. Data are expressed as percentage of the values recorded during the PRE trial (mean ± SE). $P < 0.05$ for PLA vs. CAFF.

**FIGURE 3.** EMG RMS in CAFF (white bars) and PLA (black bars) during the POST supplementation. Data expressed as percentage of the values recorded during the PRE trial (mean ± SE). $P < 0.05$ for PLA vs. CAFF.
Caffeine and Neuromuscular Function

The findings are noteworthy because caffeine seems to positively affect this relationship. In particular, when comparing maximal torque exerted during the POST sessions, we found significant enhancement at any speed when subjects ingested caffeine as compared with placebo. Of note, subjects who ingested caffeine during the POST sessions were able to maintain maximal isometric torque or even increase torque at the highest contraction velocities compared with the PRE trial, whereas the MVC of the POST session was significantly reduced in the placebo group. It is possible that subjects were fatigued after the PRE session and caffeine consumption reduced the perception of fatigue, so they were able to exert the same maximal force as in the first session.

When subjects consumed caffeine they were able to maintain maximal strength and even improve the force–velocity relationship, as indicated by the shift of the right portion of the curve toward higher values. This can be explained by several mechanisms that involve both central and peripheral sites. First, our findings are in line with the central fatigue hypothesis, which states that caffeine can alter central nervous system transmission and lead to a decrease in the sensation of effort and pain.34 Caffeine, in fact, has been reported to be an antagonist of A1 adenosine receptors. Inhibition of these receptors, in turn, facilitates the release of neurotransmitters, including dopamine and serotonin.10,35 Moreover, the ability to generate greater force could be explained by an increase in motor unit activation. The increase in maximal activation was suggested by Kalmar and Cafarelli, who found an increase in the ability to fully activate the muscle during MVC of the knee extensors.18 They also suggested that factors involved in this enhanced activation should be supraspinal, because the amplitude of the H-reflex did not change after caffeine supplementation. Furthermore, it has been shown that the antagonist effects of methylxanthines on adenosine and the adenosine nucleotides enhance the spontaneous firing rate of cerebral cortical neurons.36 Some studies, however, failed to find a different percentage of motor unit activation after caffeine ingestion.19,37,38 All of these studies used the interpolated twitch technique to calculate muscle activation (i.e., the ability of a superimposed twitch to enhance force during an MVC). The effect of caffeine on the torque–velocity relationship in our study was also associated with a significant increase in mean fiber CV. Our findings are in line with the hypothesis of an increased capacity to fully recruit motor units mediated by caffeine consumption. In addition, in light of the proposed relationship between CV and sarcolemmal excitability,22 our data could indicate that the latter may be enhanced by caffeine supplementation. Moreover, increased excitability of the fast motor units is also in line with the higher EMG RMS recorded after caffeine, but not placebo, consumption.

We cannot exclude that peripheral factors are also involved in the ergogenic effect of caffeine we found in this investigation. Calcium release from the sarcoplasmic reticulum, for example, is influenced by caffeine because administration of repetitive applications of caffeine has been shown to produce characteristic all-or-none rises in intracellular calcium mediated by the ryanodine receptors.2,39,40 Moreover, it has been suggested that this greater mobilization of calcium from sarcoplasmic reticulum induced by caffeine is also associated with an increased sensitivity of myofibrils to calcium.1 All the aforementioned mechanisms could positively affect muscle strength both during voluntary and stimulated muscle contractions. For this reason we also investigated the effect of caffeine on maximal twitch. Our findings showed an increase in peak torque when subjects consumed caffeine as compared with placebo. Time to peak and half-relaxation time did not change significantly, but this can be explained by the fact that if the twitch were higher and both the time to reach and to halve the peak torque were the same, then the rate of force development and recovery should be greater. Indeed, the effect on maximal twitch is evident when comparing the tension–time area, which was significantly higher after caffeine than after placebo, suggesting greater work performed by the muscle. These findings are supported by the fact that more calcium is released by the sarcoplasmic reticulum and that there is an increase in calcium sensitivity. It has also been suggested that caffeine

![Graph](image)

**FIGURE 4.** Peak torque (PT), mean fiber conduction velocity (CV), time to peak (TTP), half-relaxation time (HRT), and area underneath the curve (TA) of the maximal twitch elicited in CAFF and PLA groups. The values are expressed as a percentage of the value recorded during the PRE trial (mean ± SE). *P < 0.05 for PLA vs. CAFF.
would slow calcium reuptake by the reticulum, increasing calcium availability.\textsuperscript{1} Mean muscle fiber CV can also be affected by peripheral factors such as the conduction of action potentials mediated by ions. Nevertheless, in this study, the CV increased significantly during voluntary contractions, whereas the increase during the twitch did not reach statistical significance.

In conclusion, this study has shown that caffeine supplementation improves muscle performance during short-duration maximal dynamic contractions of the elbow flexor muscles. This was coupled with enhanced action potential velocity of propagation along the muscle fibers, which supports the hypothesis of an effect of caffeine on muscle recruitment. These findings, together with the improved electrically induced twitch contractions, strengthen the notion that the effect of caffeine is both central and peripheral in origin.

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REFERENCES