

# Effects of caffeine on neuromuscular function

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**Kalmar, J. M., and E. Cafarelli.** Effects of caffeine on neuromuscular function. *J. Appl. Physiol.* 87(2): 801–808, 1999.—This double-blind, repeated-measures study examined the effects of caffeine on neuromuscular function. Eleven male volunteers [ $22.3 \pm 2.4$  (SD) yr] came to the laboratory for control, placebo, and caffeine (6 mg/kg dose) trials. Each trial consisted of  $10 \times 1$ -ms stimulation of the tibial nerve to elicit maximal H reflexes of the soleus, four attempts at a maximal voluntary contraction (MVC) of the right knee extensors, six brief submaximal contractions, and a 50% MVC held to fatigue. Isometric force and surface electromyographic signals were recorded continuously. The degree of maximal voluntary activation was assessed with the twitch-interpolation technique. Single-unit recordings were made with tungsten microelectrodes during the submaximal contractions. Voluntary activation at MVC increased by  $3.50 \pm 1.01$  (SE) % ( $P < 0.01$ ), but there was no change in H-reflex amplitude, suggesting that caffeine increases maximal voluntary activation at a supraspinal level. Neither the force-EMG relationship nor motor unit firing rates were altered by caffeine. Subjects were able to hold a 50% MVC for an average of 66.1 s in the absence of caffeine. Time to fatigue ( $T_{lim}$ ) increased by  $25.80 \pm 16.06\%$  after caffeine administration ( $P < 0.05$ ). There was no significant change in  $T_{lim}$  from pretest to posttest in the control or placebo trials. The increase in  $T_{lim}$  was associated with an attenuated decline in twitch amplitude, which would suggest that the mechanism is, at least in part, peripheral.

activation; contractile properties; ergogenic; fatigue; H reflex; motor unit excitability; motor unit firing rates

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CAFFEINE (1,3,7-trimethylxanthine) is the most ubiquitous member of a group of plant alkaloids found in coffee, tea, chocolate, soft drinks, and many over-the-counter medications. It is similar in structure to several endogenous metabolites, crosses the blood-brain barrier and the placenta, and is distributed in intracellular fluid (4). These properties allow caffeine to affect many human tissues, including the central nervous system, cardiovascular system, and smooth as well as skeletal muscle (4, 23).

Although the present understanding of caffeine's cellular mechanisms of action remains less than definitive, caffeine's physiological effects suggest that it may enhance human performance. This has been demonstrated in numerous studies, primarily with respect to endurance performance and exercise metabolism. These investigations report an increase in fat oxidation and muscle triglyceride use, a decrease in glycogen use, and an increase in time to exhaustion (14, 15, 19, 20, 36).

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Although caffeine's mechanisms of action would, in theory, affect human neuromuscular performance, little research has been done in this area. Although the potentiating effects of caffeine on twitch and tetanic tension are well established both in vitro as well as in vivo (28, 29, 37, 39), caffeine's ergogenic effects on voluntary neuromuscular performance are more ambiguous. The literature suggests that maximal voluntary contraction (MVC) and muscular endurance are not affected by the administration of caffeine (7, 28, 38); however, variability in experimental design, dosage, mode of administration, and subject selection makes interpretation of these results difficult.

It is clear that the effects of caffeine may be manifested in a number of locations along the human neuromuscular pathway from the motor cortex to the contractile apparatus. The present experiment uses several techniques to investigate some possible mechanisms. Caffeine may increase descending drive from the motor cortex by blocking the inhibitory effects of adenosine (16), thus increasing a subject's ability to excite a motor unit pool. This could increase synaptic input to the cell body of the  $\alpha$ -motoneuron, increasing its excitability, bringing the motoneuron closer to threshold, and facilitating maximal activation. We used the twitch-interpolation technique (2) to help clarify the effects of caffeine on maximal voluntary activation and a comparison of H reflexes (24) elicited before and after the administration of caffeine to help localize any changes in activation to spinal or supraspinal mechanisms. An increase in activation may represent an increase in motor unit recruitment or an increase in the discharge rates; thus single-motor-unit recordings were made during a series of voluntary contractions. Finally, caffeine may exert its effect on the neuromuscular system peripherally, by altering excitation-contraction coupling, as would be evidenced by changes in evoked twitches in fresh and fatigued muscle. Thus the purpose of this experiment was to determine whether caffeine exerts an ergogenic effect on maximal force production and endurance of human quadriceps muscle and to investigate the mechanisms that may be responsible for any effects that were observed.

## METHODS

### *Subjects*

Eleven nonsmoking men, aged  $22.3 \pm 2.4$  (SD) yr (weight =  $71.4 \pm 9.0$  kg), who reported minimal caffeine intake ( $<2$  cups of coffee or equivalent/wk) were recruited for the study. Each read and signed an informed consent document outlining the procedures and possible side effects of the protocol. The experiment was approved by the York University Human Participants Review Committee.

This sample population was selected to avoid some of the factors that are known to alter caffeine pharmacokinetics. We

selected male participants because caffeine elimination is slowed during the luteal phase of the menstrual cycle (27). In addition, oral contraceptives reduce the activity of the hepatic oxygenases that catalyze the breakdown of caffeine into paraxanthine and can double the plasma half-life of caffeine (1). Only nonsmoking subjects of average body mass were recruited to avoid the exacerbating effects of cigarette smoking and of obesity, which both increase the rate of caffeine degradation (26, 32). Prior caffeine habits were also taken into consideration in the selection of subjects. Some of caffeine's responses, such as a diminished rise in epinephrine with the acute administration of caffeine (5) and the upregulation of adenosine receptors (40), seem to be dampened by habitual intake. However, other effects of caffeine seem to be independent of habituation. Tarnopolsky et al. (37) reported no effects of chronic caffeine usage on 20-Hz stimulation after an acute administration (6 mg/kg). Thus applicants for the present study were only accepted if they reported a caffeine intake equal to or less than two servings per week (~200 mg). In addition, 4 days of withdrawal are sufficient to potentiate the effects of an acute administration of caffeine in habitual users (5). Therefore, as an additional precaution, subjects were asked to abstain from consuming caffeine-containing foods, beverages, and medications for 1 wk before and throughout the duration of the study.

#### Drug Administration

Six mg/kg of US Pharmacopoeia-grade caffeine (A&C American Chemicals, Montreal, PQ) were administered in gelatin capsules immediately after the pretest. In a dose-response trial using subjects with the same physical characteristics as those of our subjects, Graham and Spriet (20) measured a plasma caffeine concentration of ~45  $\mu$ M after a dosage of 6 mg/kg. This plasma caffeine concentration reached a plateau ~1 h after administration and remained stable for at least 50 min even during vigorous exercise, which increases the activity of hepatic oxygenases and decreases the half-life of caffeine (18). Thus we have followed the precedent of Jackman et al. (25) and not measured plasma caffeine levels.

Caffeine was administered by using a double-blind procedure in which an individual who was involved in neither data collection nor analysis placed capsules of an appropriate content and dosage in coded envelopes. The envelopes were identified by the subject's initials and the day the dosage was to be used. Placebo capsules were filled with all-purpose flour,

which has the same color and texture as caffeine. Control capsules were empty and were discarded by the subjects.

#### Protocol

The experiment utilized a pretest-posttest, repeated-measures design, with experimental, control, and placebo trials completed in random order on three separate days. In each trial, the posttest commenced 1 h after the ingestion of the capsules. The pretest and posttest protocols were identical and are illustrated in Fig. 1. This particular order was chosen to minimize factors that would have confounded the collection of the H-reflex data (22).

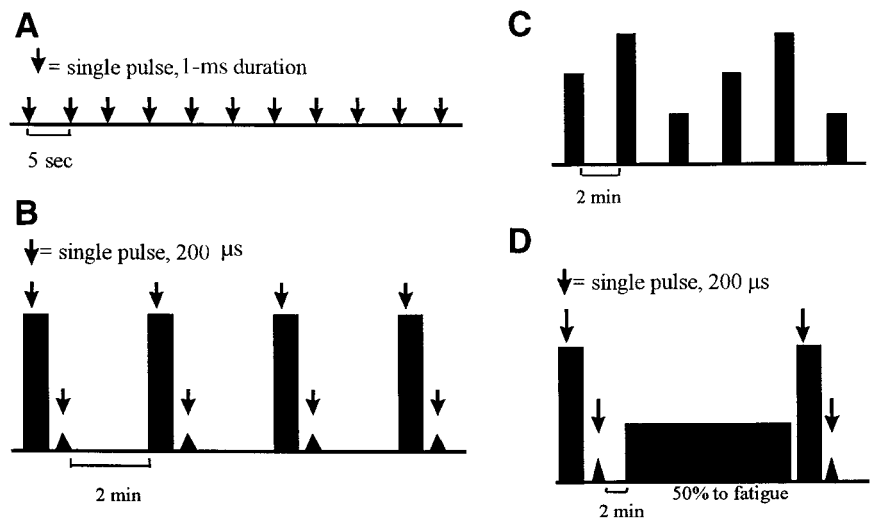
**Part A: H reflexes.** To determine the excitability of the motoneuron pool, H reflexes were recorded from the left soleus. This site was selected rather than the vastus lateralis because the longer latency facilitated recording and because this also eliminated local fatigue as a confounding factor in the experiment. A 5-cm<sup>2</sup> anode was placed immediately proximal to the superior border of the patella and a 1.5-cm<sup>2</sup> cathode in the popliteal fossa over the tibial nerve for the purpose of stimulation. These were secured for the duration of each experiment by using a Hypafix dressing-retention sheet. The recording electrode was placed just lateral to the middorsal line of the leg, slightly below the bifurcation of the medial and lateral heads of the gastrocnemius from the Achilles tendon.

A single 1-ms pulse was delivered to the tibial nerve, and the voltage was increased until the H-reflex amplitude was maximal. Thereafter, 10 of these stimuli were applied at 5-s intervals, and each H reflex was normalized to the M wave evoked by the same stimulus. The average value of the 10 normalized H reflexes was used as an index of motoneuronal excitability. This average was compared pre- to posttest in the control, placebo, and caffeine trials.

**Part B: MVCs.** Superimposed twitches were used to assess the degree of voluntary activation during putative MVCs (2). Subjects were seated in the dynamometer, and a 4  $\times$  4-cm cathode-stimulating electrode was positioned in the femoral triangle over the femoral nerve. An anode (12.5  $\times$  7 cm) was positioned midway between the superior aspect of the greater trochanter and the inferior border of the iliac crest, with the hip flexed 90°.

During each MVC, two 200- $\mu$ s square waves were delivered to the nerve at a voltage 15% higher than that eliciting a maximal twitch. The first pulse was applied when the force reached a plateau, and a posttetanic potentiated twitch was

Fig. 1. Experimental protocol. Pretest and posttests were composed of 4 different segments, each investigating a different aspect of neuromuscular function. **A:** H-reflex protocol. Arrows indicate submaximal electrical stimulation of tibial nerve with leg relaxed. H responses were recorded from soleus muscle. **B:** superimposed and potentiated twitches were evoked during and immediately after a maximal effort. **C:** submaximal contractions, 25, 50, and 75% maximal voluntary contraction (MVC), each held for less than 15 s, during which single-unit recordings were made. **D:** fatigue protocol. 50% MVC was held to fatigue, preceded and followed by MVCs with superimposed and potentiated twitches. Arrows in **B-D** represent supramaximal electrical stimulation.



elicited when the force returned to baseline. All twitches in this experiment were potentiated to eliminate the within-subject variability in fresh muscle maximal twitch amplitude that would occur over the duration of the protocol. A segment of the force signal extending ~300 ms from the stimulus artifact was extracted, and the *y*-axis was expanded ~20 times. Any increase in force resulting from the superimposed stimulus, expressed as a fraction of the potentiated twitch, indicated the percentage of the motoneuron pool that was not maximally activated by the subject (2). Maximal values for attainable force, electromyographic (EMG), and contractile properties were also obtained.

*Part C: Brief submaximal contractions.* This part of the experiment examined the force-EMG relationship and single-motor-unit discharge rates. Forces equivalent to 25, 50, and 75% MVC were calculated from the peak force obtained in *part B* of the experiment. These values were marked with a horizontal cursor on a monitor visible to the subject and were used subsequently as a guide to produce each force twice in random order. Contractions were held ~10 s, with a 90-s rest period between contractions. Force, in addition to surface EMG and single-motor-unit recordings, was also obtained during these contractions.

*Part D: Sustained submaximal contraction.* This part of the experiment investigated the effects of caffeine on muscular endurance. After the collection of single-motor-unit recordings, subjects performed one additional MVC and then immediately commenced the fatigue protocol. The task was to hold a 50% MVC contraction to fatigue. Supramaximal shocks were administered every 10 s, and the time to fatigue ( $T_{lim}$ ) was the point at which force fell to <45% MVC for longer than 3 s. A final MVC and potentiated twitch were elicited on cessation of the contraction.

#### Data Acquisition

*Dynamometry.* Isometric torque of the quadriceps femoris was measured in a dynamometer as described by Psek and Cafarelli (35). Subjects were seated in the apparatus with the hip and knee joints at 90° of flexion. A transducer measuring the force of isometric knee extension was clamped onto the subject's right leg, ~2.5 cm above the lateral malleolus. The electrical signal from the transducer was amplified  $\times 10$  and stored on cassette tape.

*Surface EMG.* Surface EMG signals were recorded from the right vastus lateralis, ~10 cm proximal to the superior border of the patella, by using bipolar silver-silver chloride electrodes (EQ, Plymouth Meeting, PA). The EMG signals were preamplified  $\times 35$  at the electrode and passed through a second-stage, variable-gain amplifier with a frequency response that was almost flat from 0 to 1,000 Hz, before being stored on cassette tape.

*Intramuscular EMG.* Average motor unit firing rates were obtained by recording single-unit trains with tungsten microelectrodes (FHC, Bowdoinham, ME; Howarth Instruments, Cornwall, UK). The skin was prepared by shaving and then by swabbing of the area with a 70% ethyl alcohol solution. A 25-gauge hypodermic needle was used to first puncture the skin and fascia over the midbelly of the vastus lateralis and facilitate the insertion of the microelectrode. The recording electrode was then inserted into the muscle at right angles to its long axis and advanced manually at 0.5 mm/s to record from as many motor units as possible. A reference electrode was inserted into the subcutaneous fat ~2 cm proximal to the patella. All microelectrodes were sterilized in an autoclave at 200°C for 20 min before each experiment and were reserved for the use of only one subject. A water-soaked strap electrode was wrapped around the upper thigh to serve as a ground.

#### Data Processing

*Torque.* Torque records were digitized at an acquisition rate of 1,000 Hz and smoothed by calculating a moving average for every 15 points by using the Spike2 for Windows, version 2, software package (Cambridge Electronic Design). Force values were expressed in newtons by using a regression equation for the voltage-force relationship or as a percentage of the voltage of a MVC.

*Surface EMG.* Surface signals were digitized off-line at an acquisition rate of 5,000 Hz and band passed at 15–2,500 Hz. The filtered EMG signal was quantified by obtaining the root mean square (RMS) of a 1-s sample (500 ms for MVCs). H-reflex and M-wave amplitude were calculated by using algorithms resident in Spike2.

*Intramuscular EMG.* The signals from the microelectrodes were preamplified near the source, band-pass filtered between 1 and 5 kHz (Neurolog, Digitimer, Medical Systems, Greenvale, NY), and stored on cassette tape. Intramuscular signals were digitized at an acquisition rate of 25 kHz. Spikes were categorized manually, first on the basis of differences in amplitude and then by shape and interspike interval (see Fig. 2). Once categorized, the mean frequency, mean interspike interval (ISI), and the ISI coefficient of variation were determined for each motor unit. Only spike trains consisting of a minimum of four spikes with an ISI coefficient of variation <20% were used to calculate average motor unit firing rates.

*Contractile properties.* Twitch amplitude, time to peak tension (TPT), and half relaxation time,  $+dF/dt$ , and  $-dF/dt$  of the potentiated twitches were measured from the smoothed force record.

#### Statistical Analysis

Data collected from *parts A* and *B*, and the  $T_{lim}$  data from *part D*, were expressed as percent change from pretest to posttest (indicated in all cases by  $\Delta$ ) in the control, placebo, and caffeine trials. In each case, these values were compared by using a two-way (drug  $\times$  pre-/posttrial) repeated-measures ANOVA design on Statistica (release 5.1, Statsoft, Tulsa, OK).  $\Delta$ EMG for the submaximal contractions in *part C* were compared by using a two-way (drug  $\times$  %MVC) repeated-measures ANOVA. The firing rates from *part C* were compared in a three-way (drug  $\times$  %MVC  $\times$  pre-/posttrial) ANOVA, and the data were treated as separate groups to deal most effectively with missing data from the 75% MVCs. The decline in twitch amplitude after the 50% MVC was compared from pretest to posttest by using a two-way repeated-measures ANOVA (drug  $\times$  pre-/posttrial). Individual and group data are expressed as means  $\pm$  SD and means  $\pm$  SE, respectively.

## RESULTS

### Part A: $\alpha$ -Motoneuron Excitability

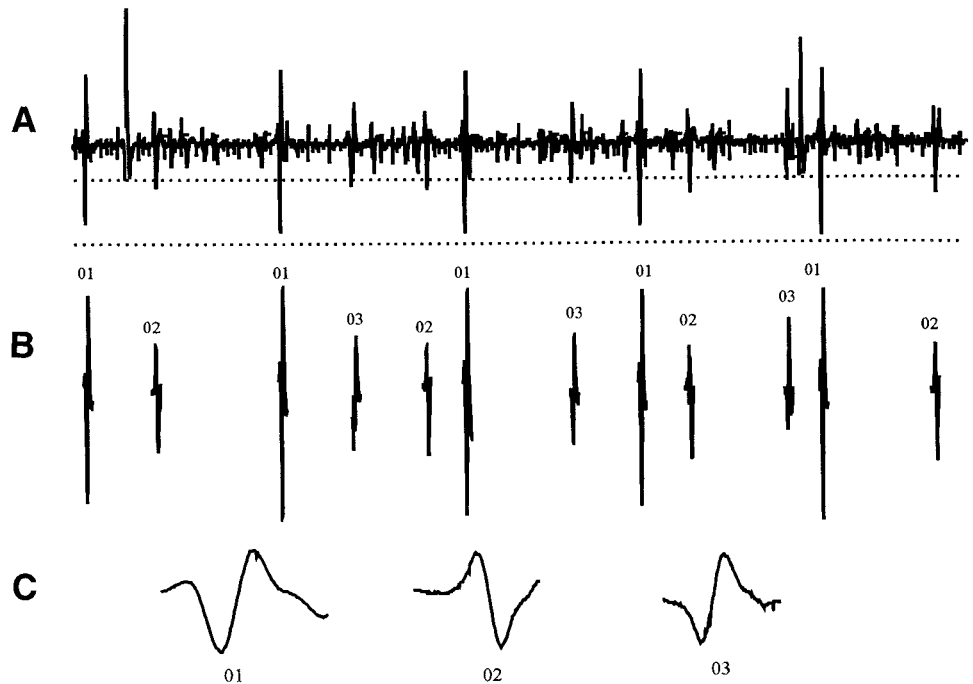
In *part A* of the protocol, the effects of caffeine on  $\alpha$ -motoneuron excitability were examined by eliciting H reflexes in the left soleus. There was no change in H-reflex amplitude from pre- to posttest in any trial. This suggests that caffeine has no effect on excitability at the level of the spinal cord.

### Part B: MVCs

Maximal voluntary activation, MVC, and surface EMG decreased in the posttest of the control and placebo conditions, resulting in negative  $\% \Delta$  values. In



Fig. 2. Illustration of spike recognition technique used to determine motor unit firing rates during *part C* of protocol. *A*: intramuscular recording (500 ms) obtained from vastus lateralis during a 50% MVC. A window discriminator (dotted horizontal lines) is used to select spikes. *B*: signals that fall within window are extracted from recording and sorted manually according to shape. This allows for changes in amplitude as needle is advanced past muscle cell. *C*: examples of 3 different motor units (01–03). In short time frame shown, only units 01 and 02 would have met requirements of a minimum of 4 spikes. Unit 01 discharged at 9.8 Hz and unit 02 at 10.7 Hz. During data collection, ~1 ms would be viewed.



each case, caffeine reversed the direction of this change; however, the magnitude of this effect varied (Fig. 3).

Subjects were able to achieve an average of 94% of optimal vastus lateralis motor unit activation in control contractions. Among subjects, the ability to activate motor units varied considerably, and some subjects demonstrated a greater variability between attempts than others (mean activation =  $94.5 \pm 1.4\%$ , range = 81.1–99.5%). These results are similar to those of a previous investigation (2). Only two of our subjects were able to optimally activate 100% of the motor unit pool voluntarily, and only in the posttest of the caffeine trial. Caffeine ingestion was associated with an increased ability to activate the total vastus lateralis motor unit pool ( $P < 0.01$ ). MVC was also significantly increased in the posttest of the caffeine trial ( $P < 0.05$ ), but  $\Delta$ EMG was not significantly different among trials.

The  $\Delta$ M-wave amplitude did not change significantly in any trial, suggesting that caffeine did not exert a measurable effect at the neuromuscular junction or along the sarcolemma. Similarly, caffeine did not alter the contractile properties of the vastus lateralis, as  $\Delta$ twitch amplitude,  $\Delta$ TPT,  $\Delta +dF/dt_{\max}$ , and  $\Delta -dF/dt_{\max}$  were the same in all trials.

#### Part C: Submaximal Contractions

The  $\Delta$ EMGs for each submaximal contraction were compared with a two-way ANOVA, which determined that the relationship between force and surface EMG during submaximal contractions was not altered by caffeine (Fig. 4). Intramuscular recordings from 883 motor units were made during these same submaximal contractions. The actual mean force output for attempts of 25, 50, and 75% were  $24.05 \pm 0.47$ ,  $48.75 \pm 0.78$ , and  $71.90 \pm 0.97$  %MVC, respectively. The average firing rates of units recruited during these contrac-

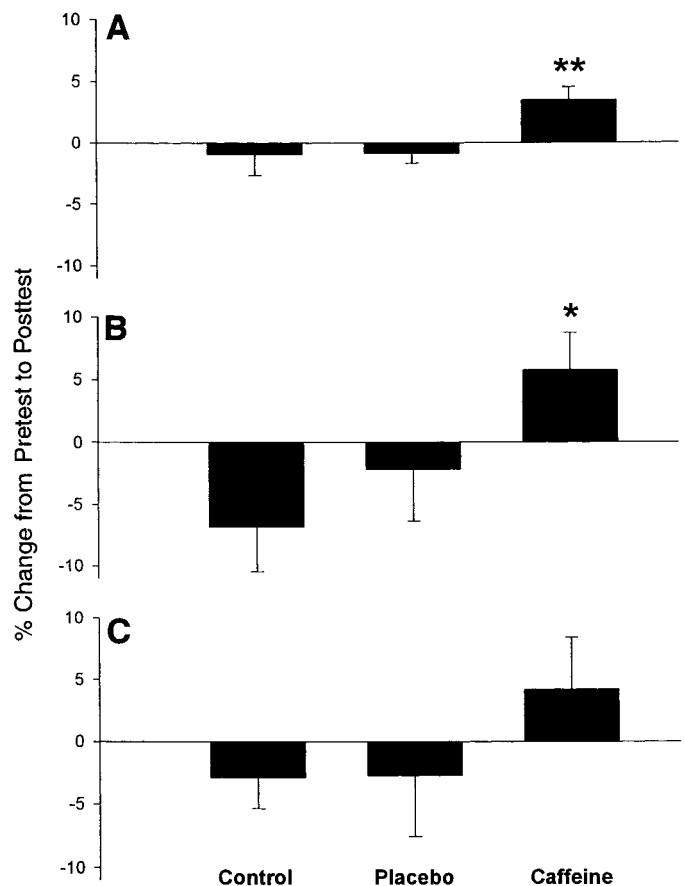


Fig. 3. Voluntary activation, peak force, and maximal EMG ( $EMG_{\max}$ ). Data were collected from *part B* of protocol. Percent change from pretest to posttest is shown for voluntary activation (A), MVC (B), and vastus lateralis  $EMG_{\max}$  (C). \*  $P < 0.05$ . \*\*  $P < 0.01$ .

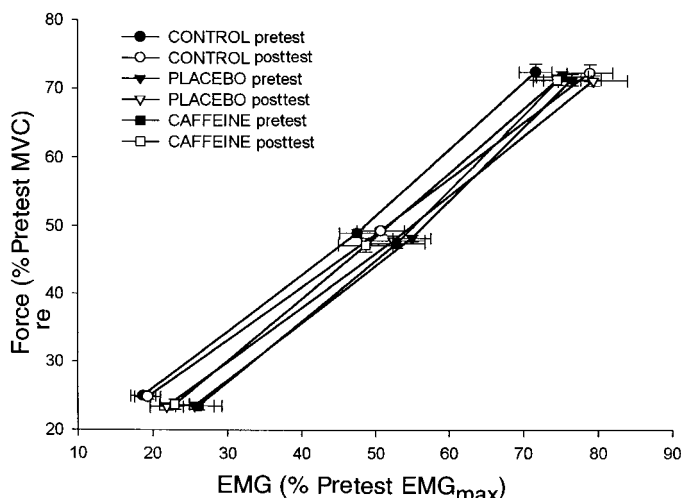


Fig. 4. Surface EMG of 25, 50, and 75% MVC contractions from *part C* of protocol. Data demonstrate that relationship between force and EMG did not change from pretest to posttest in any trial and was not altered by caffeine.

tions were not significantly changed from pretest to posttest in any condition (Fig. 5).

*Part D: Muscular Endurance*

The average  $T_{lim}$  of the sustained submaximal contractions was consistent from day to day within subjects but varied considerably among subjects. The mean  $T_{lim}$  of the three pretest trials was  $66.4 \pm 3.5$  s (range = 19.6–137 s). The mean  $T_{lim}$  of the caffeine posttest increased by 25.8% ( $P < 0.05$ ); however, this value was elevated in one subject, who increased  $T_{lim}$  by 176%. If the data from this subject are removed, mean  $T_{lim}$  increased by  $10.8 \pm 6.3$  s ( $P < 0.05$ ).  $T_{lim}$  did not change in the control and placebo posttest trials. Thus there was a significant increase in the ability of subjects to sustain the 50% MVC in the caffeine posttest ( $P < 0.05$ ). Surface EMG and percent activation both in-

creased to peak values of  $<100\%$ ; however, it took longer to reach these values in the caffeine trial (Fig. 6). Maximal twitch amplitude was  $\sim 55\%$  smaller at the end of the sustained contraction in both the pretest and posttest of all three conditions. There were no significant differences in this decline between trials. MVC was  $\sim 30\%$  smaller at the end of the sustained contraction in all trials. There were no significant differences in this decline between trials.

**DISCUSSION**

The data from the present study demonstrate that caffeine has an ergogenic effect on peak force generation and muscular endurance and suggest mechanisms that may be responsible for these effects. Considerable research has been conducted on the cellular mechanisms responsible for the widespread effects of caffeine. Three mechanisms predominate. 1) Caffeine is a known inhibitor of phosphodiesterase; however, this only occurs when plasma caffeine concentrations reach pharmacological (mM) ranges that are toxic to humans (6, 16). 2) Dosages eliciting pharmacological plasma caffeine levels are also known to stimulate the release of  $Ca^{2+}$  from the sarcoplasmic reticulum, thereby increasing intracellular  $Ca^{2+}$  concentration and tetanic tension (3). However, it has been argued that because plasma concentrations must be very high for  $Ca^{2+}$  translocation to be observed in situ, it is unlikely that this mechanism is solely responsible for the physiological effects of caffeine. 3) A more attractive mechanism is the antagonistic effect of caffeine on adenosine receptors. Adenosine, an endogenous metabolite similar in structure to caffeine, inhibits neurotransmitter release and neuronal firing rates by binding to receptors of the central nervous system (31). Concentrations of caffeine much lower than those required to either inhibit phosphodiesterase or increase cytosolic  $Ca^{2+}$  concentration are antagonistic to the effects of adenosine (16).

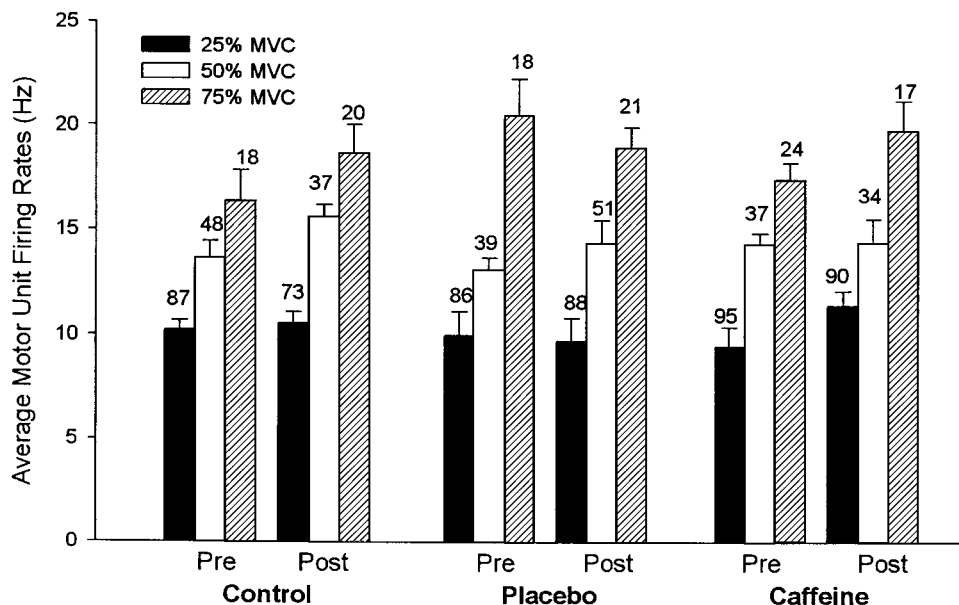
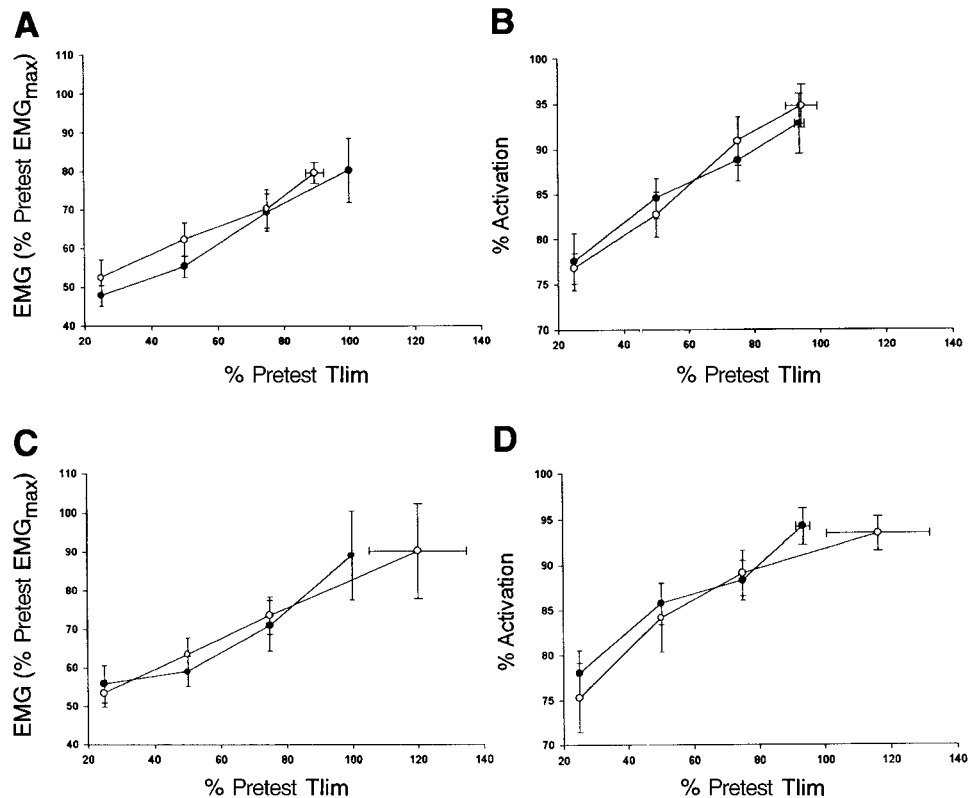


Fig. 5. Average motor unit firing rates during submaximal contractions from *part C* of protocol. Average firing rates of vastus lateralis motor units recorded during 25, 50, and 75% MVC are shown for pretest (Pre) and posttest (Post) trial of each condition. No. of recorded units for each contraction level is shown at top of each bar. There were no significant differences in firing rate at any contractile intensity among 3 conditions.

Fig. 6. Percent activation and surface EMG of sustained submaximal contractions from *part C* of protocol. Increase in surface EMG (expressed as %pretest  $EMG_{max}$ ) and percent activation over duration of 50% MVC are shown for placebo (*A* and *B*, respectively) and caffeine trials (*C* and *D*, respectively). ●, Pretest data; ○, posttest data. Bidirectional error bars for posttest values reflect variability in posttest time to fatigue ( $T_{lim}$ ). Bidirectional error bars for pretest %activation reflect timing of last superimposed stimulus relative to  $T_{lim}$ .



Quantifying muscle activation during a putative MVC reveals that subjects are frequently unable to produce maximal voluntary output with maximal effort (2). In the present experiment, subjects were able to activate the motor unit pool more efficiently after caffeine administration. For example, the two subjects who averaged 100% activation in three attempts to produce MVC did so in the posttest of the caffeine trial. There are at least two possible explanations for this finding. Adenosine exerts an effect on the cerebral cortex by depressing spontaneous and evoked potentials, suppressing neurotransmitter release, and diminishing firing rates (10, 17, 33). The antagonistic effect of caffeine on these actions (34) suggests that the increase in maximal voluntary activation seen in some of our subjects may occur because of a release of inhibition in the motor cortex. Alternatively, the diminished inhibition may increase the excitability of the motoneuron pool at the level of the spinal cord.

Our H-reflex data do not support the latter explanation, suggesting that caffeine exerts its effects on activation supraspinally. Although no other data are available that quantify maximal voluntary activation after caffeine administration, one previous study documented the effects of caffeine on alpha motoneuron excitability by eliciting H reflexes (13). That paper reported a potentiation of maximal H reflex after the consumption of 1.3 g of instant coffee by five subjects. However, the H reflexes were not normalized to the M wave even though a potentiation of the M wave was also reported. This change in the recorded M response may have been caused by an increase in electrical

conductance, or a change in electrode position rather than an effect of caffeine.

The effects of caffeine on muscle activation have only been investigated in one prior study (38). The authors reported no increase in maximal integrated EMG during MVC and concluded that the ability to maximally activate muscle is not affected by an acute administration of caffeine. However, MVCs were performed on a handgrip dynamometer, which measures the force of finger flexion, whereas EMG was recorded from the flexor carpi radialis and palmaris longus muscles, both wrist flexors. The maximal EMG recorded during MVCs in the present study was not significantly altered by caffeine; however, the twitch-interpolation data suggest that surface EMG is not sufficiently sensitive to measure small changes in activation.

Animal and human models have demonstrated a caffeine-induced potentiation of directly and indirectly evoked muscle tension (3, 9, 28, 37). Previous studies have examined the force-EMG relationship to determine whether enhanced muscle contractile properties require the recruitment of fewer motor units per unit of force. Williams et al. (38) reported no effect of caffeine on electrical activation during submaximal handgrip force production. However, because it represents a summation of both motor unit recruitment as well as discharge rate, surface EMG may not be the correct procedure to measure the effects of caffeine on excitation-contraction efficiency during submaximal contractions. Caffeine, via its adenosine-receptor antagonism, may increase the firing rates of central neurons (10). If this is the case, the increase in firing rates could offset

the decrease in motor unit recruitment so that the force-EMG relationship would appear unaltered. No shift was observed in the force-EMG relationship constructed from the surface EMG of 25, 50, and 75% knee-extension MVCs in the present study. Firing rates of motor units recorded during these contractions were also unaffected by caffeine administration. It therefore appears that 6 mg/kg of caffeine do not alter the neural control of brief, submaximal contractions.

The ergogenic effects of caffeine on aerobic performance have been well established (21). However, considerably less is known about these effects on the neuromuscular system. An improved ability of the contractile apparatus to generate force would manifest itself as a potentiation of evoked maximal twitch amplitude, whereas an increase in voluntary performance would be apparent in such tasks as maximal voluntary force production and the ability to sustain a submaximal contraction. Improvement in voluntary tasks may be secondary to an enhancement of muscle contractile properties or neural activation.

The effects of caffeine on fatigue during sustained isometric contractions have been investigated by Williams et al. (38) by using handgrip dynamometry and Lopes et al. (28) by using thumb adduction. Neither study reported an improvement in the ability to sustain 50% MVC. However, in both cases small samples ( $n = 5-6$ ) were used. This, in combination with a small effect size, would result in low statistical power. Three of the five subjects recruited by Lopes et al. (28) sustained the contraction longer, and one subject maintained the same duration, in the caffeine trial. The mean endurance time of the sustained contraction in the present study increased by 24% from pretest to posttest in the caffeine trial. Thus our results do deviate from previously published data; however, this discrepancy may be due to differences in the muscle group selected for the study or the larger sample size. Moreover, many physiological, lifestyle, and dietary factors can alter caffeine absorption, distribution, elimination, and habituation (4). Even when care is taken to select a sample population that is free from factors that alter caffeine pharmacokinetics, such as cigarette smoking, oral contraceptives, and obesity, individual variations in the response to caffeine are frequently reported (25, 28, 36). Therefore, a recommendation for future studies may be to use a sample size sufficiently large enough to overcome individual caffeine sensitivities.

Increases in twitch tension after the administration of caffeine have been seen in animal models by using dosages eliciting plasma concentration in the millimolar range. This is purportedly due to slowing  $Ca^{2+}$  reuptake into the sarcoplasmic reticulum as well as increased sarcoplasmic reticular  $Ca^{2+}$  permeability, which would increase intracellular  $Ca^{2+}$  availability (3). However, the caffeine dosages required to observe these effects are well above levels that would be toxic to humans (16). Nonetheless, tetanic potentiation has been observed in studies utilizing animal (9) and human models (28, 37) with micromolar plasma concentrations of caffeine. Our data show that the amplitude

of the twitches after the sustained 50% MVC was always significantly less than the twitches evoked immediately before the contraction. This precontraction-to-postcontraction deficit in twitch amplitude is a measure of peripheral fatigue (12). It would therefore be reasonable to assume that contractions of longer duration, such as during the caffeine posttest, would be accompanied by a greater deficit in the postcontraction twitch amplitude. However, this was not the case. Although the contraction was held on average 25.8% longer in the caffeine posttest, the precontraction-to-postcontraction twitch deficit remained the same as in the control and placebo trials. This suggests that peripheral fatigue occurred more slowly in the posttest of the caffeine trial and that  $T_{lim}$  was reached when the twitch declined to the same submaximal value that occurred in the absence of caffeine. These data are consistent with a caffeine-induced increase in  $Ca^{2+}$  availability in fatigued muscle and lend support to a previous study that showed faster recovery of twitch and tetanic force after caffeine administration (22).

Central factors may also play a role in the observed increase in  $T_{lim}$ . The strong correlation between dopaminergic activity and endurance performance has been reviewed by Davis and Bailey (11). Caffeine is an antagonist to the  $A_1$  adenosine receptor; the release of central neurotransmitters, including dopamine, increases via this mechanism. The increase in  $T_{lim}$  may also be due to alterations in sensation. For example, caffeine ingestion may increase  $T_{lim}$  by inhibiting pain sensation associated with sustained isometric contraction. In fact, caffeine has been reported to decrease sensation of effort (8) as well as ischemic muscle pain (30) and in this way may act as an ergogenic aid. Although this idea awaits confirmation by further study, the increase in  $T_{lim}$  observed in the present study may have been attributable to the central effects of caffeine.

Another possible ergogenic effect of caffeine is manifest in the ability to generate greater force with maximal effort. Williams et al. (38) found that handgrip MVC did not increase after the administration of 7 mg/kg caffeine. Our data indicate that caffeine increases the ability to maximally activate skeletal muscle with attempts to produce maximal voluntary knee extension. This increase in activation was associated with a significant increase in force. Therefore, caffeine may improve the ability to produce MVC in subjects who are otherwise unable to maximally activate the vastus lateralis voluntarily.

The ergogenic effects of caffeine seen in the present study caused an increase in maximal activation. Because caffeine did not alter the amplitude of H reflexes, but did increase the ability to activate motor units voluntarily, it appears that the increase in excitability occurs supraspinally. In addition, we observed an increase in the ability to sustain a submaximal voluntary contraction. However, it is difficult to determine whether changes in the contractile properties of muscle or central mechanisms, such as motivation or sensation, are responsible for this effect. There was no difference



in the decline of twitch amplitude after the 50% sustained MVC in the caffeine trial despite an increase in  $T_{lim}$ . Although the effects of caffeine on skeletal muscle  $Ca^{2+}$  availability at the dosage used in the present study are not documented, it is possible that caffeine diminishes the decline of  $Ca^{2+}$  that may occur in fatigued muscle.

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