**CAFFEINE INCREASES ENDURANCE AND
ATTENUATES FORCE SENSATION DURING
SUBMAXIMAL ISOMETRIC CONTRACTIONS**

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Thesis submitted to the Faculty of Graduate Studies in partial fulfilment of
the requirements for the degree of

MASTER OF SCIENCE

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by **CARRIE JOANNA PLASKETT**

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ABSTRACT

Caffeine has known ergogenic effects, some of which have been observed during submaximal isometric contractions. We used 15 subjects in a randomized, double-blind, repeated measures experiment to determine caffeine's ergogenic effects on neuromuscular variables that would contribute to increased endurance capacity. Subjects performed repeated submaximal (50% MVC) isometric contractions of the right quadriceps to the limit of endurance (T_{LIM}) 1 hr after oral caffeine administration (6mg/kg). Contractile performance was assessed from maximal twitches and signal transmission by M waves evoked with electrical stimulation of the femoral nerve. Central activation was determined with twitch interpolation and surface electromyography. Time to reach T_{LIM} increased by 17% ($p < .02$) after caffeine administration compared to the placebo trial. Prolonged performance during the caffeine trial was associated with a greater decrement in twitch amplitude, maintenance of near maximal voluntary muscle activation and an increase in terminal EMG. These results could not account for the increase in T_{LIM} in the caffeine trial. In a separate randomized double-blind experiment using the same subjects, we used a constant sensation technique to determine if caffeine influenced force sensation during 100s of an isometric contraction of the quadriceps. The resultant force recordings were fit with a double exponential equation. The first rate constant was significantly slower in the caffeine trial ($p < .05$) but there was no difference in the second rate constant or end force. The change in rate constant indicates that caffeine alters force sensation during the first 10-20 s of the contraction. The rapidity with which this occurs may mean that caffeine exerts its effects neurally. Based on these data, the caffeine-induced increase in T_{LIM} may stem from alterations in muscle sensory processes.

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CHAPTER 1

OVERVIEW & PURPOSES

Overview

Limitations in muscular endurance may arise from a disturbance in any of the sequence of events within the neuromuscular system that must occur to produce and sustain a contraction. Generally, these events can be grouped as central or peripheral events. Central fatigue may occur as a result of a decrease in the excitability of the alpha motor neuron pool via mechanisms such as a decrease in cortical excitation (68), increased inhibitory input (29), decreases in motivation (5) and changes in neurotransmitter and neuromodulator release (28). Peripheral fatigue is a result of alterations in the neuromuscular mechanisms located distal to the alpha motor neuron pool. For example, during a sustained isometric contraction peripheral fatigue may arise from failure of any of the following: to transmit the electrical signal across the neuromuscular junction and along the sarcolemma (7), a decrease in blood flow to the active muscle (94), an impairment of excitation -contraction coupling (32) and altered calcium flux (1). Neuromuscular junction failure may occur from a depletion of neurotransmitter substance and as a result of a decrease in end plate excitability (57).

The widespread belief that caffeine has ergogenic properties has caused considerable growth of interest, especially in athletes over the past decade. The extensive supportive evidence on the performance benefits of caffeine in various types of physical activities has prompted sport organizations to classify caffeine as a restricted substance (17). Due to the ability of caffeine to diffuse through all tissues in the body, the cellular mechanisms of action are unclear and likely vary with the dosage and the physiological demands of different

activities. The ergogenic basis of action of caffeine is primarily focused on three areas: 1) changes to metabolism, 2) a direct action on muscle and 3) a direct influence on the central nervous system.

Caffeine has the potential to influence human neuromuscular performance through action on central and peripheral processes. Animal and human models have shown caffeine increases neurotransmitter release by blocking the inhibitory effects of adenosine (9) and it is well established that caffeine potentiates twitch and tetanic tension (40, 56, 64). Despite the potential benefits that caffeine may have on neuromuscular performance, there are only a few studies available that have investigated the effects of caffeine on endurance during isometric contractions (15, 53, 61, 92). For example, Lopes (61) found that 3 out of 5 subjects increased the endurance time of a sustained contraction of the adductor pollicis after caffeine ingestion. Using a larger subject sample, Kalmar and Cafarelli (53) found that caffeine significantly delayed fatigue during a sustained submaximal contraction of the quadriceps. Conflicting results in other investigations that found no ergogenic effect of caffeine (15, 92), may have been due to variability in methodologies, subject selection, caffeine dosage and individual sensitivities to an acute dose of caffeine.

Purposes

The studies by Kalmar and Cafarelli (53) and Lopes and colleagues (61) indicate that caffeine has performance enhancing effects on the neuromuscular system, however, the mechanisms responsible for these effects are not clear. The purposes of this investigation are:

1. To determine if the following selected physiological processes account for the increase in endurance capacity of isometric contractions following caffeine ingestion.
 - i*) maintaining central activation of motor units
 - ii*) protecting junctional and sarcolemmal transmission
 - iii*) preserving function of the contractile apparatus.
2. To determine if caffeine alters force sensation during a sustained submaximal isometric contraction.

CHAPTER 2

REVIEW OF LITERATURE

Events Involved in a Muscular Contraction

A complex sequence of events within the neuromuscular system must occur in order to produce and sustain a muscular contraction. Upon an initiation signal, input from subcortical and cortical structures is delivered to the motor cortex (80). This information traverses down the spinal cord and terminates on the alpha motor neuron pool which consists of cell bodies of alpha motor nerves that innervate skeletal muscle fibers. The excitatory and inhibitory synaptic inputs to the alpha motor neuron pool from descending drive (87), segmental connections and feedback from peripheral receptors (62) summate to determine the extent of recruitment of motor units and their firing rates. The transmission of the electrical signal to the muscle occurs via the action of the neurotransmitter acetylcholine (ACh). ACh is released from motor axon terminals at the neuromuscular junction and binds to receptors on the motor end plate of the sarcolemma. The binding of ACh to these receptors opens ion channels causing Na^+ inflow and K^+ outflow resulting in depolarization of the sarcolemma and the production of the end-plate potential. The action potential is propagated along the sarcolemma and into the transverse tubular system (t-system) triggering the voltage sensitive dihydropyridine (DHP) receptors which control the transmission of electrical conductance to the sarcoplasmic reticulum (79). DHP receptors are coupled with ryanodine receptors found in the terminal cisternae of the sarcoplasmic reticulum (36). The activation of the DHP receptors results in the opening of the ryanodine receptor channel proteins and the release of Ca^{2+} from the sarcoplasmic reticulum into the myoplasm (90). The binding of Ca^{2+} ions to the protein troponin, which is located on the

actin molecule, causes a position change in another protein tropomyosin, which then uncovers the binding site on the actin molecule for myosin. The crossbridge formation of myosin attaching to actin initiates the release of energy stored on the myosin molecule which results in a change in the protein conformation of myosin which causes sarcomeric shortening and muscle contraction (77). The binding of a molecule of ATP to myosin breaks the link between actin and myosin to allow for another contraction. Crossbridge activity continues as long as there is ATP available and Ca^{2+} is free to bind to troponin. The cessation of neural activity results in a decrease of cytosolic Ca^{2+} concentrations as Ca^{2+} is pumped back into the sarcoplasmic reticulum by the active-transport Ca^{2+} pump. The removal of Ca^{2+} binding to troponin causes tropomyosin to cover the activation site on actin which blocks the formation of crossbridges and the muscle fiber relaxes.

Limitations to Muscular Endurance

Limitations to muscular endurance may arise from a disturbance in any of the events that are required to produce a contraction. Generally, these can be grouped as either central or peripheral events. Central mechanisms of a muscular contraction reside in the motor cortex and associated cortical areas and also in the spinal cord down to the alpha motor neuron pool and peripheral mechanisms are found distal to the motor neuron pool. Electrical stimulation can be used to replace voluntary drive to assess function of the neuromuscular system and locate the site of failure along the motor pathway. When a supramaximal electrical shock is applied to a peripheral nerve innervating a skeletal muscle, the mechanical response of a twitch is produced which can be used to assess changes in the

function of the contractile apparatus. When the intensity of the shock remains constant, any decrement in the evoked twitch indicates failure distal to the site of stimulation. A reduction in force that can be restored by a supramaximal shock, indicates a limitation in force generation proximal to the site of stimulation. The electrical response to peripheral nerve stimulation is the production of a mass action potential (M wave) which reflects the transmission of the electrical signal from the point of stimulation to the point of the recording device on the muscle.

The administration of an electrical stimulus to a motor nerve during a maximal effort contraction can be used to assess if voluntary drive is truly maximal. Any additional force produced by the stimulation indicates that the neurons innervating the active muscle have not been all recruited or the discharging rate is sub-optimal. Voluntary activation can be quantified by comparing the superimposed twitch amplitude to the twitch amplitude evoked immediately following the contractions when the muscle is relaxed (2, 71). This technique is known as twitch interpolation and is more sensitive to small changes in voluntary activation than changes in EMG activity or maximal muscle force.

Peripheral limitations

During a sustained isometric contraction peripheral failure may result from a decrease in blood flow to the active muscle (94), an impairment of excitation-contraction coupling (32), altered calcium flux (1) and failure of transmission of the electrical signal across the neuromuscular junction and along the sarcolemma (7).

A reduction in perfusion pressure will result in a shorter time to fatigue during intermittent submaximal contractions, which may be the result of reduced blood flow to the muscle (94). A linear increase in intramuscular pressure occurs with increases in the amount of force produced during an isometric contraction. Thus, this may cause a reduction of force due to the depletion of energy substrates and the accumulation of metabolites from impaired blood flow. The rate of force loss, compared to a sustained maximum voluntary contraction, is substantially reduced when the contraction is performed intermittently. However, if the same intermittent contraction is performed with the blood supply occluded, the fatigue rate is the same as if the contraction was sustained (78). The duty cycle and force of the contraction have an influence on the rate at which fatigue develops and this reflects the degree to which blood flow meets the metabolic demands of the muscle.

During submaximal isometric contractions, a lack of metabolic substrates or an increase in the build up of metabolites are not the only limiting factors in muscular endurance (10, 32). During fatiguing, intermittent, submaximal isometric contractions of the quadriceps Vøllestad and colleagues (89), found a reduction in the maximum force generating capacity of the muscle without significant changes in ATP or phosphocreatine. Along with a diminished maximum force generating capacity from fatiguing muscle performing repeated, submaximal isometric contractions there is a slowing of the muscle conduction velocity and contractile speed (11). This indicates an impairment of excitation-contraction (E-C) coupling, which is a common contributing factor in the limitation of intermittent, submaximal isometric contractions (10, 13). Impairment of E-C coupling can

involve an alteration to any of the sequence of events between the initiation and propagation of an action potential along the sarcolemma to the activation of the contractile apparatus. Changes in Ca^{2+} flux are an important component in the control of a muscular contraction. Allen (1) found that the changes in Ca^{2+} concentration during fatigue could account for a decline in twitch amplitude. Less of a reduction in cytosol Ca^{2+} concentrations could be achieved with the application of K^+ which caused depolarization of the t-tubules, and with the addition of caffeine which increased Ca^{2+} release from the sarcoplasmic reticulum (1). Allen suggested the reduced Ca^{2+} release with fatigue lies in the coupling between t-tubule depolarization and the release of Ca^{2+} from sarcoplasmic reticulum Ca^{2+} release channels (1).

Increases in Mg^{2+} , H^+ , P_i and decreases in Ca^{2+} and ATP influence the release of Ca^{2+} from the sarcoplasmic reticulum and can reduce the activation of the contractile apparatus (59, 60, 69, 81). A reduction in the binding of Ca^{2+} to troponin would result in less force being produced from myofilaments. This could result from a decrease in the sensitivity of troponin to Ca^{2+} (1) caused by acidosis and P_i which increase as fatigue develops. An increase in the relaxation rate of a muscle is observed when a muscle begins to fatigue. If there is a decrease in the re-uptake of Ca^{2+} into the sarcoplasmic reticulum, a greater concentration of Ca^{2+} would remain in the myoplasm and reduce the concentration gradient across the sarcoplasmic reticulum. An inhibition of the sarcoplasmic reticulum Ca^{2+} pump occurs with an increase in acidosis which slows relaxation (58). An increase in

myoplasmic Ca^{2+} concentrations also reduces the flux of Ca^{2+} across the sarcoplasmic reticulum in response to depolarization of the t-tubules.

Neuromuscular transmission failure could occur at pre-synaptic sites that control ACh release or with post-synaptic mechanisms which include the function of cholinergic receptors and the excitation of the sarcolemma. For example, inadequate transmission of an electrical signal from the motor nerve to the muscle can result from a decrease in end plate excitability as a result of the post-synaptic membrane becoming less sensitive to ACh (57). This is only evident with high rates of stimulation which may influence maximal contractions when the excitation rates are high. Failure in the transmission of an action potential across the neuromuscular junction and along the sarcolemma can be detected by changes in M-wave characteristics. There are conflicts in the literature as to the contributions of failure of junctional and sarcolemmal transmission to the endurance of voluntary contractions. In humans, no change in M wave size with fatigue from maximal and submaximal voluntary contractions have been observed by Bellemare and Bigland-Ritchie (6), Thomas et al (88) and Bigland-Ritchie and colleagues (12), however, others have reported decreases in M waves in the same type of contractions (7, 41).

Central limitations

A central limitation to muscular endurance is suggested when the central nervous system no longer fully activates a muscle. Gandevia et al (42) observed a progressive decline in the ability to voluntarily activate the elbow flexor muscles during 3 minute maximum voluntary contractions (MVC). They concluded that neural drive was less than maximal

because magnetic stimulation of the motor cortex during the contractions produced additional force despite the attempt of the subjects to voluntarily produce a maximal contraction.

The reduction in the maximal activation by the central nervous system frequently persists following a fatiguing isometric contraction. McKay (68) combined transcranial magnetic and electrical stimulation to assess changes in motor cortex excitability following a sustained isometric MVC. Reductions in the motor evoked potential (MEP) amplitudes from both methods of cortical stimulation were observed following a fatiguing contraction of the tibialis anterior, even after MVC force had recovered. Peripheral nerve stimulation indicated that M wave amplitudes and twitch forces remained unchanged which eliminated possible peripheral mechanisms as a cause of the reduction in MEP amplitudes. In addition, there was also no reduction in MEP amplitudes following a fatiguing contraction that was induced by tetanic motor point stimulation of the tibialis anterior. McKay and colleagues (68) suggest that a reduction in cortical excitability following a fatiguing contraction could be caused by intracortical and/or subcortical inhibitory mechanisms.

An unwillingness to tolerate the discomfort and pain associated with a sustained contraction can reduce voluntary activation. Rutherford and colleagues (82) used percutaneous twitch superimposition and observed a decrease in the ability to voluntarily activate the quadriceps and biceps when muscle or joint pain was present. In highly motivated subjects, full muscle activation can be difficult even in fresh muscle. Belanger and McComas (5) concluded that complete activation of ankle dorsiflexors could be

achieved, but in contrast, maximal activation of the plantar flexors was always slightly submaximal. They suggested that there was a difference in the strength of synaptic input to the motor neurons innervating the dorsiflexor and plantar flexor muscles. Input from Ia afferents to the motor neuron pool supplying the plantar flexors may be stronger than the input to the motor neuron pool of the dorsiflexors. The dorsiflexor motor units may receive a stronger input from descending motor pathways which results in the ability to maximally activate the muscle with less effort than the plantar flexors.

Brain serotonin [5-hydroxytryptamine(5-HT)] effects arousal through a sedative influence that increases feelings of sleepiness (48). Increases in 5-HT occur during prolonged exercise (23) which may contribute to central fatigue by decreasing motivation. Bailey and colleagues (4) observed an earlier onset of fatigue in rats with pharmacologically increased levels of brain 5-HT, and in humans an acute administration of a 5-HT agonist reduced the exercise time to fatigue working at 70% $\text{VO}_{2\text{MAX}}$ (93).

Brain dopamine is related to the behavioral characteristics of arousal and motivation (55) and is involved in the control of movement (39). A decrease in dopamine levels occur as fatigue develops during prolonged exercise and an increase in dopaminergic activity, through the administration of amphetamines, increases endurance performance (24). The ability of dopaminergic activity to inhibit 5-HT synthesis and metabolism may delay the development of central fatigue and maintain levels of motivation (55, 4).

Force Sensation

The sensation of force that accompanies a contraction is an important component in the quality of the motor performance. When producing a muscular contraction at a constant force there is a continual increase in force sensation (85, 20) that may be a contributor to limiting endurance performance. Clarification of the definitions of sensation of force and perception of effort is necessary to distinguish the difference between the two. Force sensation refers to the feelings of force being produced by the muscle during a contraction and the accompanying intramuscular tension. This differs from the sensation of effort which is thought to be a measure of the magnitude of voluntary motor command required to generate a force (66).

The mechanisms involved in force sensation are likely a combination of both central feedforward and peripheral feedback components. The centrally mediated feedforward mechanism is based on the conception that an efferent relay of information from the motor cortex is sent to the sensory cortex as it is simultaneously being sent to the motor neuron pool. Feedback is generated from peripheral afferent receptors found in the muscles, tendons, ligaments, joints and skin which provide information about the active state of the contracting muscle. For example, Golgi tendon organs provide feedback on the tension developed by the muscle to the alpha motor neuron pool via Ib afferents (50) and muscle spindles provide sensory feedback via Ia and IIa afferents concerning muscle length (52). Group III and IV afferents are sensitive to both mechanical stimuli, such as pressure, and metabolic stimuli, such as lactic acid (54, 70, 83).

Vibration is an experimental technique that has been used to separate feedforward and feedback mechanisms (67, 20). The application of vibration to a muscle tendon activates muscle spindles and provides Ia input to the motor neuron pool (16). Vibration increases force sensation (19) indicating that muscle spindles are capable of signaling intramuscular tension, however, the increase in force sensation of a vibrated muscle does not occur during a fatiguing contraction (20). This suggests that muscle receptors other than spindles are more likely contributors to the increase in force sensation that develops with fatigue or that there is a greater contribution from feedforward mechanisms.

Measuring force sensation

Various methodologies have been used to measure changes in force sensation in humans under conditions such as fatigue, training and disease. These methods use the subject as the instrument of measurement as they are required to judge the degree of force or effort (18).

A common method used to measure force sensation under various experimental conditions is the category scale. This usually involves a sequence of numbers associated with descriptive words or phrases that subjects use to characterize their sensory intensity. This method is useful in measuring absolute levels of sensation. A similar technique referred to as direct scaling, requires the assignment of numbers by the subject that are proportional to the stimulus intensity.

Cain & Stevens (22) used what they called a “constant effort contraction” to measure how the feeling of effort developed during a fatiguing contraction. This technique

requires the subject to keep either force or effort during an isometric contraction constant without visual feedback. They charted the time course of the load reduction necessary to maintain a constant effort during hand grip contractions. Cain and Stevens found the reduction in force over time was similar from subject to subject and highly reproducible within trials of an individual. The rate of force loss could also be well described by a double exponential equation (22). Cain (21) followed this investigation with one that used the same technique to assess the roles of strength, blood flow and fatigue on effort when performing handgrip muscle contractions. These experiments indicated that the method of “constant effort contractions” was sensitive to experimental manipulation. Although there is no way of identifying the associated physiological sensory controls, Cain and Stevens (22) hypothesized that the initial rapidly decaying component of the constant effort contraction may be influenced by the activity of mechanoreceptors in tendons, skin and joints. Whereas the slow component of the contractions may reflect chemoreceptor activity responding to the build-up of metabolites.

Ergogenic Action of Caffeine

Caffeine (1,3,7 trimethylxanthine) is an alkaloid that is a constituent in widely consumed foods and beverages such as coffee and cola. Due to the solubility of caffeine in lipids, it can cross the blood brain barrier and is distributed to all tissues in the body (65). Approximately one hour after consumption of an acute dose of caffeine, peak plasma concentrations are obtained with a half life of 2.5 to 4.5 hours (3). Peak plasma levels reach approximately 2-15 $\mu\text{mol/l}$ with a dose of 100mg of caffeine, the equivalent of one cup

of coffee . The ergogenic benefits of caffeine have been observed with doses between 3-9 mg/kg (45). The standard dose of 6 mg/kg results in a peak plasma level of 35-45 $\mu\text{mol}/\text{l}$ (31). Toxic levels ($>200 \mu\text{mol}/\text{l}$) occur when consumption exceeds 15 mg/kg caffeine (3).

Considerable research has been conducted on the potential of caffeine to increase performance and on the underlying mechanisms responsible for the increase. However, because caffeine diffuses through all tissues in the body, its cellular mechanisms of action are difficult to sort out and likely vary with dose and type of activity. Nevertheless, investigations on the ergogenic action of caffeine have focused on three areas: 1) changes to metabolism, 2) a direct action on muscle and 3) a direct influence on the central nervous system.

The performance enhancing influence of caffeine began primarily with the experiment by Costill on aerobic endurance activities (26). Since these findings were reported, research has focused on the influence of caffeine on aerobic performance and recently has expanded to investigate the properties of caffeine to influence performance in other types of physical activities. For example, graded exercise reaches higher intensities after an acute dose of caffeine (35). The time to exhaustion in which subjects are performing at 90-100% of $\text{VO}_{2\text{MAX}}$ also increases after caffeine consumption (49, 91). Contrary to these results, no influence on the performance of short term high intensity activities after caffeine consumption has been reported (34, 47).

Only a few studies have investigated the effects of caffeine on the endurance of isometric contractions and there is considerable disagreement among them. This is probably

due to variability in methodologies, subject selection, caffeine doses and modes of caffeine administration. For example, Bugyi (15) and Williams (92) found no effect of caffeine on the endurance of hand grip contractions. Although Lopes (61) found no significant effect of caffeine on the endurance time of a sustained contraction of the adductor pollicis, there was an average 12% increase in endurance time during the caffeine trial for all 5 of the subjects. There was also no potentiation of force when subjects performed an MVC or when the muscle was stimulated at 100 Hz. Recently, Kalmar & Cafarelli (53) found that caffeine produced an increase in both maximum force generating capacity and endurance during a sustained submaximal contraction of the quadriceps.

Changes to metabolism

An acute administration of 300-600 mg of caffeine in humans has been shown to increase circulating plasma epinephrine and free fatty acids (FFA) (26, 44). The metabolic hypothesis of caffeine's ergogenic action is based on the observation that prolonged performance of aerobic activities with an acute dose is associated with an increase in plasma catecholamines, which increases fat oxidation resulting in a down regulation of carbohydrate metabolism (26, 33, 84). However, contradictions have arisen as to whether the ergogenic effect in endurance activities with caffeine are actually mediated by catecholamines (45). Increases in resting FFA levels and increases in plasma FFA with no change in epinephrine levels with exercise have been observed after caffeine ingestion (45, 73). This suggests that the increase in plasma FFA are the direct result of caffeine ingestion and not a response to increased catecholamines.

An alternative explanation for the increase in FFA release triggered by caffeine could be linked to the antagonism of adenosine receptors on adipose tissue. *In vivo* evidence has shown the ability of caffeine to increase FFA by inhibiting the A₁ receptors which normally suppress lipolysis through inhibition of adenylate cyclase activity (95).

An improvement in aerobic performance following caffeine consumption has been observed without increases in epinephrine, FFA or glycogen utilization. This makes it difficult to explain increases in performance solely with the metabolic theory (49). Moreover, this theory cannot explain an ergogenic influence of caffeine in activities that are not dependent on aerobic metabolism.

Direct action on muscle

The direct action of caffeine on skeletal muscle has the potential to influence most types of physical activities. It is well established in *in vitro* studies that caffeine increases the force of contractions in fresh and fatigued skeletal muscle (40, 56, 64). This is caused by the stimulatory effect of caffeine on calcium release from the sarcoplasmic reticulum (40), as well as an increase in the sensitivity of troponin to calcium. These alterations to calcium kinetics occur at very high concentrations of caffeine of between 500 and 750 $\mu\text{mol/l}$ which is well above levels that are toxic to humans.

Antagonism of peripheral and central adenosine receptors occurs at concentrations that are much lower than those necessary to influence calcium kinetics and is more likely the mechanism that contributes to the ergogenic action of caffeine (37). There are two receptors of adenosine that alter cyclic AMP levels. Inhibition of adenyl cyclase occurs

through high affinity A1 receptors and a stimulatory effect occurs through low affinity A2 receptors. Some functions of peripheral adenosine include inhibition of lipolysis, relaxation of smooth muscle and suppression of cardiac contractility (95). A build up of adenosine has been suggested to be partially responsible for the early onset of fatigue in mammalian skeletal muscle by inhibiting depolarization-induced calcium release. (14).

Influence on the Central Nervous System

Caffeine is a widely known stimulant of the central nervous system. Low doses of caffeine can alleviate feelings of drowsiness and fatigue and consumption of higher doses can increase the stimulation to feelings of anxiety, restlessness, insomnia and to a greater extent, can evoke seizures (27). In concentrations which are safe for human consumption, caffeine can act as an adenosine receptor antagonist (9). The primary role of adenosine in the central nervous system appears to be an inhibitory one (30, 38). Adenosine inhibits the spontaneous firing of central neurons and also depresses locomotor activity (75). Consequently, the antagonism of adenosine receptors with caffeine shows the reversal of the action of endogenous adenosine by accelerating neuronal discharges which may increase CNS activation (76).

By blocking the inhibitory action of adenosine there is an increase in dopamine levels (72) which mediates the excitatory behavioral effects of caffeine (51). Bailey et al (4) demonstrated the association between a reduction in dopamine synthesis and metabolism, and the onset of fatigue during exercise. Furthermore, when concentrations of dopamine remain elevated, fatigue is delayed (4). The increase in dopamine concentration after

caffeine consumption may prolong muscle performance by attenuating the depletion of dopamine that occurs as fatigue develops.

Caffeine & Force Sensation

The mechanism to which caffeine may alter force sensation is unclear. Based on the theory that adenosine may be a metabolite contributing to ischemic muscle pain, Myers et al (74) used caffeine to inhibit experimental ischemic muscle pain of the forearm. Using a pain rating scale subjects reported lower ratings after the caffeine trial suggesting a hypoalgesic effect of caffeine. The increase in sensation accompanying long term aerobic activity is reduced following caffeine consumption (25, 26, 33, 43). However, after caffeine administration increases in performance can occur without an influence on effort (8) and furthermore, effort can be lower after caffeine consumption without an increase in performance (34).

Caffeine & Neuromuscular Function

Animal and human models have been used to show that caffeine can potentiate twitch and tetanic tension (86,63, 64). In humans, Tarnopolsky and colleagues (86) found consumption of 6mg/kg of caffeine potentiated force in the tibialis anterior during 2 min of 20 Hz stimulation of the peroneal nerve, but there was no influence on the force of a MVC. In another investigation, Green (46) observed that caffeine attenuated the force of the maximal twitch and the response of the vastus lateralis to low frequency stimulation at the end of a fatigue protocol. Similarly, Lopes (61) observed an increase in the tension development in the adductor pollicis from low frequency stimulation before and after

fatigue following a dose of 500 mg of caffeine. These experiments suggest that caffeine has an effect on skeletal muscle contractile properties at doses suitable for human consumption that is independent of neural activation.

Investigations by Kalmar & Cafarelli (53) and Williams (92) were conducted on the influence of caffeine on neuromuscular parameters during isometric contraction of human skeletal muscle. Kalmar and Cafarelli (53) observed an increase in the ability of subjects to more completely activate the motor unit pool during MVC of the quadriceps as assessed using the twitch interpolation technique. In the same study there were no alterations associated with caffeine in the force-EMG relationship nor in the average motor unit firing rates during submaximal isometric contraction in non-fatigued quadriceps muscle. Williams (92) investigated the effects of caffeine on maximal muscle activation during a hand grip contraction. The results of the experiment indicated caffeine did not alter maximal or submaximal muscle activation. However, activation in the study by Williams was only measured with integrated EMG which is not as sensitive to change as the twitch interpolation technique.

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CHAPTER 3
MANUSCRIPT

Caffeine Increases Endurance and Attenuates Force Sensation During Submaximal Isometric Contractions

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Abstract

Caffeine has known ergogenic effects, some of which have been observed during submaximal isometric contractions. We used 15 subjects in a randomized, double-blind, repeated measures experiment to determine caffeine's ergogenic effects on neuromuscular variables that would contribute to increased endurance capacity. Subjects performed repeated submaximal (50% MVC) isometric contractions of the right quadriceps to the limit of endurance (T_{LIM}) 1 hr after oral caffeine administration (6mg/kg). Contractile performance was assessed from maximal twitches and signal transmission by M waves evoked with electrical stimulation of the femoral nerve. Central activation was determined with twitch interpolation and surface electromyography. Time to reach T_{LIM} increased by 17% ($p<.02$) after caffeine administration compared to the placebo trial. Prolonged performance during the caffeine trial was associated with a greater decrement in twitch amplitude, maintenance of near maximal voluntary muscle activation and an increase in terminal EMG. These results could not account for the increase in T_{LIM} in the caffeine trial. In a separate randomized double-blind experiment using the same subjects, we used a constant sensation technique to determine if caffeine influenced force sensation during 100s of an isometric contraction of the quadriceps. The resultant force recordings were fit with a double exponential equation. The first rate constant was significantly slower in the caffeine trial ($p<.05$) but there was no difference in the second rate constant or end force. The change in rate constant indicates that caffeine alters force sensation during the first 10-20 s of the contraction. The rapidity with which this occurs may mean that caffeine exerts its effects

neurally. Based on these data, the caffeine-induced increase in T_{LIM} may stem from alterations in muscle sensory processes.

Introduction

The belief that caffeine has ergogenic properties has caused considerable growth of interest, especially in athletes, over the past decade. The exceedingly supportive evidence on the beneficial use of caffeine to increase performance has prompted sport organizations to classify caffeine as a restricted substance. Because caffeine readily diffuses into all fluid components and across the blood-brain barrier (3, 38), the ergogenic mechanisms are unclear and are likely multifaceted, varying with doses and the physiological demands of different activities.

Caffeine has the potential to influence human neuromuscular performance through action on many central and peripheral events along the motor pathway. The drug has central stimulatory effects by blocking the inhibitory effects of adenosine (6) and it is well established that caffeine potentiates contractile force in skeletal muscle (25, 36). Despite the evidence that caffeine may affect performance there are only a few studies available that have investigated the effects of caffeine on the muscular endurance during isometric contractions (10, 31, 34, 61). For example, Lopes (34) found that 3 of his 5 subjects increased endurance time of a sustained contraction of the adductor pollicis after ingestion of 500 mg of caffeine. There was a mean increase in endurance time of 12% in the caffeine trial, however, this was not significantly different from the placebo trial. Kalmar and Cafarelli (31) found that fatigue was significantly delayed during a sustained submaximal contraction of the quadriceps. Conflicting results from other investigations (10, 61) are

likely due to variability in methodologies, subject selection, caffeine doses and individual sensitivities to an acute dose of caffeine.

The sensation of force that accompanies a contraction is an important component in the quality of the motor performance. When producing a muscular contraction at a constant force there is a continual build-up of force sensation (11, 55). The ergogenic properties of caffeine during aerobic activities have frequently been associated with an attenuation in exercise sensory processes (14, 15) and a hypoalgesic effect with caffeine has also been observed during ischemic muscle contractions (42). These reports have mainly used category rating scales following the activity to determine single time point assessment of the influence of caffeine on these measurements. It is therefore possible that the attenuation of force sensation may contribute to the increased endurance capacity of a sustained, submaximal, isometric contraction. This has not previously been investigated.

The studies by Kalmar and Cafarelli (31) and Lopes and colleagues (34) indicate that caffeine has performance enhancing effects on the neuromuscular system, however, the mechanisms responsible for these effects are not clear. The purposes of this investigation are: 1) to determine how the following selected physiological processes may account for the increase in the endurance capacity of isometric contractions following caffeine ingestion: *i*) maintaining central activation of motor units, *ii*) protecting junctional and sarcolemmal transmission, and *iii*) preserving function of the contractile apparatus and 2) to determine if caffeine alters force sensation during a submaximal isometric contraction.

Methods

Subjects

Fifteen males ($\bar{x}$ age 22.6 ± 0.6 years, 77.1 ± 2.3 kg and 178.3 ± 1.9 cm) who were all non-smokers and non-caffeine users were paid volunteer subjects for the present investigation. Non-caffeine users were classified as those who consumed less than 200 mg of caffeine per week based on a survey of daily intake of foods and beverages. All subjects were provided with a list of caffeinated foods, drugs and beverages to avoid for a minimum of 5 days prior to their first experimental session and throughout their participation in the study. In response to an acute dose of caffeine, habituated caffeine users show a dampened rise in plasma epinephrine and smaller increases in blood pressure and heart rate (4, 50). However, these responses can be potentiated after 4 days of withdrawal. Van Soeren and Graham (58) observed an ergogenic effect after an acute dose of caffeine in habituated caffeine users regardless of the duration of a withdrawal period. This indicates that an ergogenic influence is obtainable in habituated caffeine users and a withdrawal period is not necessary.

Experimental Protocols

All techniques were approved by the York University Human Participants Review Committee. Two different protocols were used in the study: *i*) an endurance protocol to identify the central or peripheral neuromuscular alterations that enable caffeine to increase the endurance of an isometric contraction and *ii*) a sensory protocol to determine if caffeine alters force sensation during an isometric contraction. A double-blind repeated measures

design, with randomized experimental and placebo trials, was used over four separate test days. A “no-capsule control” group was not used because a previous study found no significant difference between placebo and no-capsule groups in a similar experimental protocol (31).

All experiments were conducted at least three days apart to control for fatigue, muscle soreness, and habituation to caffeine and were performed at approximately the same time in the morning to control for circadian rhythms, and to minimize sleeplessness. Subjects were instructed to refrain from physical activity and caffeine, and to eat the same meal before each experimental session. Compliance was monitored with verbal self report prior to each experiment. A preliminary session was conducted to familiarize the subjects with the experimental procedures. Following each experiment subjects were asked if they could identify if they had received caffeine or the placebo and to describe the basis of that decision.

Prior to starting the experiment, the subjects rested quietly in the apparatus for 10 min. We then recorded control measurements of resting heart rate and blood pressure, maximum potentiated evoked twitch (Tw_{max}), maximal voluntary contraction force (MVC) of the right quadriceps, maximal surface EMG and percent voluntary activation. MVCs were repeated until 3 contractions that were within 10% of each other were obtained. Subjects were then given a capsule containing either caffeine or flour. Control measures were repeated one hour after ingesting caffeine or the placebo (26, 58). This was followed by either the endurance or sensory protocol.

Endurance protocol

Five minutes following the second set of control measurements, subjects performed one MVC and then immediately commenced the endurance protocol. Isometric contractions at 50% MVC for 15 seconds were repeated with the target force displayed on a computer monitor. Every 15 s the right quadriceps was relaxed for the time needed to evoke a $T_{w_{max}}$ (approximately 1.5 s). Electrical stimulation was also administered in the middle of every isometric contraction to determine the degree of activation required to achieve the target force. The protocol was terminated when force declined to below 45% of MVC for longer than 2 s.

Sensory protocol

The sensory protocol commenced five minutes after the second set of control measurements. Visual feedback of a horizontal cursor was displayed on a computer monitor to obtain a target of 50% MVC of the knee extensors. When the target force was achieved, visual feedback was removed and the instructions were to maintain force sensation constant by increasing or decreasing the force. No further verbal commands or encouragement were provided once visual feedback was removed. Each trial lasted 100 s since this is the approximate time it takes to reach T_{LIM} under these conditions (31). Four trials were performed with 3 minutes between each (Figure 1A).

An advantage of using this constant sensation technique is that the measurements do not require the interpretation of numbers or categories. The technique also provides continuous data during these contractions that would not have been possible with a self

report rating scale. Finally, the technique has proven to be sensitive to experimental manipulation (12, 52).

Procedures

Dosage

One hour prior to the experimental trials 6 mg/kg of U.S.P. grade caffeine (A&C American chemicals Ltd., Montreal, PQ) or all-purpose flour in gelatin capsules was administered. Dosage was based on similar experimental protocols that have elicited an ergogenic effect (28, 31, 58).

Maximum Twitch & Electrical Stimulation

Two stimulating electrodes (12.5 cm x 7 cm) were used to depolarize the right femoral nerve and activate the right knee extensors. The anode was placed in the inguinal crease and the cathode midway between the superior aspect of the greater trochanter and inferior border of the iliac crest. Shocks were applied in 200 μ sec square wave pulses from a Digitimer (model DS7A, Hertfordshire, England) constant voltage (270V), high intensity stimulator triggered from Spike 2 software (version 3.0 CED Limited, Cambridge, UK). Maximal twitch was achieved when an increase in current produced no further increase in twitch force. The current was then increased by 15 mA to ensure maximality.

Maximum Voluntary Contraction

Brief voluntary submaximal isometric contractions were performed as a warm-up prior to the first attempt at an MVC for the control measures. With verbal encouragement, subjects were instructed to produce an isometric MVC of their right quadriceps as fast and

as forcefully as possible. A single supramaximal shock was administered to the femoral nerve at the peak of the MVC and another immediately following it to determine the degree of voluntary activation with the method of Allen et al (2).

Force

The isometric force produced by the quadriceps was measured in a dynamometer which was adjustable to accommodate each subject. The seat of the dynamometer was equipped with full back and head support and an adjustable lap belt was used to stabilize the hips in 90° of flexion. The entire unit was tilted back 45° to reduce gravitational pull on the leg and the arms were folded over the chest during all leg contractions. The right knee joint was positioned in 90° of flexion and a cast aluminum cuff attached to a force transducer was clamped 2 cm above the lateral malleolus.

Electromyography

A bipolar silver-silver chloride surface electrode (EQ. Inc, Chalfont, PA) with an inter-electrode distance of 2 cm was used to record electrical activity from the right vastus lateralis. The electrode was positioned approximately 10 cm proximal to the patella in the center of the vastus lateralis muscle belly. The skin surface was shaved and cleaned with 70% alcohol. The EMG signal was preamplified at the surface electrode and passed through a variable gain second stage amplifier, before being stored on magnetic tape. A strap electrode soaked in water and covered with plastic wrap to prevent evaporation was wrapped around the right upper thigh to serve as a ground.

Signal Processing

Force and EMG signals recorded on tape (Vetter, Rebersberg, Pennsylvania, VCR model 500D, PCM model 4000A) were analyzed off-line using Spike2. Force signals for maximum twitch, MVC and the muscle endurance protocol were sampled at a rate of 1000 Hz and smoothed using a Spike2 script that averaged every 25 points to eliminate high frequency noise. Surface EMG was sampled at 5000 Hz, and rectified prior to the determination of the RMS amplitude.

Endurance protocol

The limit of endurance (T_{LIM}) was defined as the point when force fell below 45% MVC for 2 s or longer. If force fell below 45% MVC and recovered back to the target force in less than 2 s, the target force needed to be maintained for 2 s or longer to continue with the protocol. T_{LIM} was calculated from the beginning of the first 50% isometric contraction until the target force could no longer be maintained. The changes in muscle contractile properties during the endurance protocol were analyzed from maximal twitches evoked every 15 seconds. The measurements consisted of peak twitch amplitude (Tw_{AMP}) and the maximum instantaneous ascending and descending slopes ($\pm dF/dt$). Voluntary activation of the vastus lateralis was assessed from the root mean square (RMS) amplitude of the surface EMG and from the superimposed twitch technique. The EMG was measured in 2 s epochs from each isometric contraction excluding the superimposed shock. Voluntary activation of the motor unit pool was determined from the superimposed shock administered in the middle of each isometric contraction. The force increase caused by the electrical

stimulation during the 50% MVC was compared to the force elicited by the electrical stimulation in the immediately following inactive period. Percent activation was determined by using the following equation (2):

$$\text{percent voluntary activation} = \left[1 - \frac{\text{superimposed } Tw_{AMP}}{\text{potentiated } Tw_{AMP}} \right] \times 100$$

The peak-to-peak amplitude of the M wave produced from electrical stimulation was used to assess the efficacy of transmission of the electrical signal across the neuromuscular junction and along the sarcolemma.

Sensory Protocol

In this technique, the reciprocal of the force recording is the analog of force sensation. To maintain force sensation constant from its initial level, force is typically reduced in a non-linear manner (13). A sharp reduction in force occurs within the first few seconds and then declines less rapidly over the duration of the contraction. The time course of the force recording is highly reproducible and can be best fit to the following double exponential function:

$$Y = C + Ae^{-K1t} + Be^{-K2t}$$

where Y is force, t is time, A and B are the values of the exponential processes, and K1 and K2 are rate constants (12, 13, 45).

An average of the four sensory trials was calculated using a Spike 2 script that averaged each trial over 100 s from the point at which visual feedback was withdrawn (Figure 1A). The averaged force tracing was transposed as numerical pixel points into Excel 97 (Microsoft Corp., Chicago, IL) and an arithmetic formula was used to obtain an average

of every 50 points (Figure 1B). This procedure was chosen to smooth the curve and still maintain enough data points so the image of the force tracing was not altered. The averaged pixel points from Excel were transposed into SigmaPlot 2000 for Windows, (SPSS Inc., Chicago, IL) and fit with the double exponential decay equation using an iteration process to produce the non-linear regression (Figure 1B).

Maximum Voluntary Contractions & Maximal Electromyography

MVCs performed for the control measures were averaged between the three highest trials that were within 10% force of each other. The RMS of the EMG signal during each contraction was measured for 1 s at the peak of the contraction prior to the stimulus artifact and also averaged. Voluntary activation, M wave and twitch were measured as described in the endurance protocol.

Statistical Analysis

Statistics were performed on Statistica (release 5.1, Statsoft Inc., Tulsa, OK). Control measurements were expressed as the ratio between post to pre capsule and compared between placebo and caffeine conditions using a one-way repeated measures ANOVA.

The dependent variables for the sensory protocol (final force, rate constant K1 and rate constant K2) were analyzed using a one-way repeated measures ANOVA between conditions. All of the dependent variables measured during the endurance protocol ($T_{W_{MAX}}$, $+dF/dt$, $-dF/dt$, EMG, percent voluntary activation and M wave amplitude) for each subject were individually fit to a linear regression using SigmaPlot. The slopes were compared between placebo and caffeine conditions for each variable with a one-way repeated measures

ANOVA. For all endurance protocol statistical analyses the dependent variables were expressed as a percent of the first measurement obtained during the endurance protocol (% initial) and the time for both conditions was normalized to placebo T_{LIM} .

Each dependent variable in the endurance protocol was compared between the caffeine and placebo trial at three different time points: 1) at placebo T_{LIM} , 2) at the time point in the caffeine trial corresponding to placebo T_{LIM} , and 3) at caffeine T_{LIM} , using a one-way repeated measures ANOVA with a Tukey post hoc when needed. This is illustrated in Figure 2. As with other fatigue protocols, difficulty in the statistical analysis arises because of individual differences in endurance time. In the present experiment, there was considerable variability in the time to T_{LIM} among subjects as well as between conditions for individual subjects. As shown in Figure 2, if subjects decreased T_{LIM} with caffeine there was no time point that corresponded with placebo T_{LIM} . To perform a matched repeated measures one-way ANOVA for each dependent variable at the three time points, three separate statistical analyses were conducted. The first included only subjects who had a positive change in T_{LIM} with caffeine. The second substituted any missing values from subjects who had a negative change in T_{LIM} with caffeine with their values measured at placebo T_{LIM} . The third variation substituted missing values with those assessed at caffeine T_{LIM} . The results of these analyses were all the same.

Results

Contractile properties of the knee extensor muscles and electrical activity of vastus lateralis during voluntary and evoked contractions along with systemic cardiovascular responses to the two treatments are shown in Table 1. These data were obtained immediately prior to and one hour post capsule ingestion in all experiments and were intended to assess the effects of caffeine in the rested state.

Systolic ($p<0.01$) and diastolic ($p<0.01$) blood pressure increased significantly one hour after caffeine ingestion, but there was no change in heart rate, which is consistent with previous findings (17, 50). MVC increased significantly ($p<0.01$) by $5 \pm 2\%$ in the caffeine condition and voluntary activation also increased ($p<0.01$) by $2 \pm 0.3\%$.

A total of 60 experimental sessions were conducted on 15 subjects. After each experimental session, subjects correctly identified which treatment they had received 77% of the time. They most often described feelings of alertness and restlessness associated with caffeine.

Endurance Protocol

Figure 3 is an example of the recordings obtained from one subject made during a complete endurance protocol. These are consistent with the pattern of fatigue associated with repeated submaximal isometric contractions (8). As T_{LIM} approached, there was a reduction in force generating capacity and slowing of the muscle as seen by the decrease in MVC (Figure 3A), twitch amplitude and positive and negative dF/dt (Figure 3B). Central drive increased throughout the endurance protocol which is seen in the increase of surface

EMG (Figure 3C). Neuromuscular transmission was preserved throughout the protocol as indicated by the constancy of the M wave shape and amplitude (Figure 3D).

The Limit of Endurance

Figure 4 shows the range of individual subject changes in T_{LIM} with caffeine compared to the placebo trial. In the caffeine trial, 9 of the 15 subjects increased T_{LIM} , 4 had no change ($\pm < 5\%$) and 2 subjects decreased their T_{LIM} . The mean T_{LIM} was 85.9 ± 4.5 for placebo and 98.4 ± 5.3 seconds for the caffeine trial ($p < 0.02$).

Contractile Properties

Figure 5 shows the average data points and linear regression line fit to the twitch amplitudes for the placebo ($r = .99$, $Y = 114.8 - .94x$) and caffeine ($r = .99$, $Y = 113.7 - .95x$) trials through the progression of the endurance protocol to T_{LIM} . The data points represent the averages from all subjects at the closest times corresponding to 20, 50, 80 and 100% placebo T_{LIM} , and at caffeine T_{LIM} . There was no difference in the slopes of the regression lines fit to every subject between conditions. Note that the twitch amplitude continued to decline during the prolonged caffeine trials (open triangles).

There were no differences in the results between the three statistical analyses comparing the end points of the dependent variables. The results reported here are from the analysis that used caffeine T_{LIM} values as a substitute for the missing values of the 4 subjects who had a negative change in T_{LIM} with caffeine. This analysis was selected because it is the most conservative and actually underestimates the ergogenic effects that were observed with caffeine. Figure 6 illustrates the comparison of the contractile

properties end point values in both conditions. During the caffeine trial at the time corresponding to placebo T_{LIM} (see, B in Figure 2) there was no difference in the twitch amplitude, $+dF/dt$ or $-dF/dt$ between the caffeine and placebo condition. Twitch amplitude decreased to $29.8 \pm 3.9\%$ of the initial twitch amplitude in the placebo trial and at the corresponding time in the caffeine trial to $26.3 \pm 3.4\%$ of the initial value. In the caffeine condition the increased T_{LIM} caused a further decrease in twitch amplitude to $17.0 \pm 2.5\%$ of the initial twitch amplitude value and slowing of the $+dF/dt$ to $20.4 \pm 2.8\%$ of the initial value. Both these variables were significantly ($p < 0.01$) different from placebo T_{LIM} and the corresponding time during the caffeine trial. There was no significant difference in $-dF/dt$ between conditions at these three time points.

Muscle Activation

The data points displayed in Figure 7 are the averages for all subjects in both conditions. Data were measured at the closest times corresponding to each 10% interval up to 100% of placebo T_{LIM} and at caffeine T_{LIM} . There was an increase in EMG for both conditions through the progression of the endurance protocol to T_{LIM} . There was no significant difference between the slopes of the placebo ($r = .77$, $Y = 90.7 + .51x$) and caffeine ($r = .84$, $Y = 87.5 + .63x$) regression lines. EMG increased $41.3 \pm 13.2\%$ during the placebo trial and, at the same time point during the caffeine trial, it increased $47.5 \pm 12.3\%$ which was not significantly different. However, EMG at caffeine T_{LIM} was significantly ($p < 0.02$) elevated above the preceding time point by 28.6%.

The voluntary activation of the vastus lateralis increased at T_{LIM} from the initial contraction in both conditions. Figure 8 shows the data points that were averaged at the closest corresponding times to 10, 30, 60 and 100 % of placebo T_{LIM} and at caffeine T_{LIM} through the endurance protocol and the regression lines for the placebo ($r = .69$, $Y = 77.2 + .13x$) and caffeine ($r = .73$, $Y = 76.4 + .16x$) trials. There was no difference between conditions in the rate of increase in voluntary activation or at any of the end time points. Of the 9 subjects who increased T_{LIM} with caffeine, 8 achieved over 90% activation of the vastus lateralis at placebo T_{LIM} and all but one subject maintained or increased this level of activation during their extended endurance time during the caffeine trial.

The M wave amplitudes that were evoked in the rest period between isometric contractions were averaged between subjects for each condition at the closest corresponding times to 10, 30, 60 and 100 % of placebo T_{LIM} and at caffeine T_{LIM} . Because the M wave amplitudes did not change over time in each condition, the values were collapsed. Over the duration of the endurance protocol, the M wave amplitudes changed an average of $4.4 \pm 1.6\%$ in the placebo trial and $3.7 \pm 2.7\%$ in the caffeine trial, from the initial measurement obtained at the onset of the endurance protocol.

Maximum Force Generating Capacity

The mechanical and electrical measures obtained during the MVCs performed before and after the endurance protocol are shown in Table 2. There was a significant decrease in MVC force after the endurance protocol in both the placebo ($p < 0.01$) and caffeine ($p < 0.01$) conditions to values $66 \pm 5\%$ and $63 \pm 4\%$ of the pre endurance MVC force. There was no

significant difference observed between conditions. Subjects maintained the same level of voluntary activation following the endurance protocol with 13 of the 15 subjects in the placebo and 10 of the 15 in the caffeine condition achieving over 95% recruitment of the vastus lateralis motor unit pool which was not significantly different between conditions. EMG was maintained at the same levels before and after the endurance protocol and was not significantly different between caffeine and placebo. The potentiated twitches evoked following the MVCs maintained a significantly smaller amplitude ($p < 0.01$) and had a slower $+dF/dt$ ($p < 0.02$) and $-dF/dt$ ($p < 0.01$) in the caffeine trial compared to the placebo trial.

Sensory Protocol

In order to maintain a constant force sensation after withdrawal of visual feedback, there was an initial sharp reduction in force within the first few seconds and a less rapid decline over the remainder of the contraction. The decline in force was best fit with a double exponential function that was similar to previous findings (12, 13) and was reproducible within the subject's four trials (Figure 1A).

The correlation coefficients for individual subjects for both conditions ranged from $r = .976$ to $r = .999$ showing that the double exponential function fit the data extremely well. The first rate constant ($K1$) was significantly ($p < 0.01$) slower during the caffeine trial, but there was no difference in the second rate constant ($K2$) between conditions (Table 3). The average regression lines for the placebo ($Y = 4.83 + 19.62 e^{-.38t} + 26.85 e^{-.025t}$) and caffeine ($Y = 3.12 + 19.74 e^{-.22t} + 25.90 e^{-.019t}$) conditions are plotted in Figure 9. Because there was a smaller non-significant difference of 2.5% in the starting point of the caffeine trial

(determined by the addition of regression parameters $A + B + C$), the caffeine curve was adjusted upward by that amount to better illustrate the difference in rate constants. The smaller initial rate constant in the caffeine condition indicates that force sensation increased at a slower rate during that trial (Figure 9 inset). End point force reached an average of $11.5 \pm 2.2\%$ MVC in the placebo condition and $10.3 \pm 1.4\%$ with caffeine. These were not significantly different from each other.

Table 1.
Effects Of Caffeine & Placebo Ingestion On Control Measurements

VARIABLE	PLACEBO		CAFFEINE	
	PRE	POST	RATIO	RATIO
HR (bpm)	69.6±2.7	63.2±2.5	0.90±.02	0.93±.03
SBP (mmHg)	120.0±1.8	119.6±1.9	1.00±.01	1.06±.01*
DBP (mmHg)	78.3±0.9	78.2±0.5	1.00±.01	1.04±.01*
MVC (N)	514.9±37.0	501.8±35.6	0.98±.01	1.05±.02*
% Act	97.1±0.5	97.4±0.5	1.00±.003	1.02±.003*
EMG _{MAX} (V)	0.24±.03	0.25±.03	1.05±.02	1.09±.03
TW _{AMP} (N)	99.2±4.9	100.9±4.7	1.02±.01	1.05±.01
+dF/dt (Ns ⁻¹)	1631.9±109.6	1607.2±106.5	0.99±.02	1.01±.02
-dF/dt (Ns ⁻¹)	-905.3±59.4	-904.2±57.6	1.00±.02	1.03±.02
M _{AMP} (V)	3.8±0.4	3.8±0.4	0.99±.02	1.00±.02

Values are means ± sem. Ratio values are post/pre capsule ingestion.

* Significantly different from placebo (p<.01)

HR = heart rate, SBP = systolic blood pressure, DBP = diastolic blood pressure, MVC = maximum voluntary contraction

% Act = % voluntary activation, EMG_{MAX} = maximum EMG rms, TW_{AMP} = maximum potentiated twitch amplitude

+dF/dt = maximum instantaneous rate of tension development, -dF/dt = maximum instantaneous rate of tension relaxation

M_{AMP} = peak to peak M wave amplitude

Table 2.
Maximal Electrical & Contractile Characteristics Before & After Endurance Protocol

VARIABLE	PLACEBO			CAFFEINE		
	PRE	POST	RATIO	PRE	POST	RATIO
MVC (N)	501.8±35.6	330.7±35.6*	.66±.05	513.4±33.8	325.1±35.0*	.63±.04
% Act	97.4±0.5	97.7±1.0	1.00±.01	97.9±0.5	95.0±1.5	0.97±.01
EMG _{MAX} (V)	0.25±.03	.27±.03	1.12±.05	.26±.03	.30±.03	1.28±.09
TW _{AMP} (N)	100.9±4.7	35.4±5.7*	.34±.05	103.5±6.2	21.3±4.5*	.23±.07†
+dF/dt (N s ⁻¹)	1607.2±106.5	530.0±80.0*	.32±.04	1602.4±86.7	392.8±57.0*	.26±.05†
-dF/dt (N s ⁻¹)	-904.2±57.6	-327.1±26.8*	.37±.03	-905.1±51.8	-264.9±34.5*	.30±.04†
M _{AMP} (V)	3.8±0.4	4.1±.48	1.08±.06	3.7±0.3	4.2±.41	1.13±.07

Values are means ± sem. Ratio values are post/pre endurance protocol values

*Significantly different from pre endurance protocol values (p<.05) † Significantly different from placebo (p<.05)

MVC = maximum voluntary contraction, EMG_{MAX} = maximum EMG rms, % Act = % voluntary activation

M_{AMP} = peak to peak M wave amplitude, TW_{AMP} = maximum potentiated twitch amplitude

+dF/dt = maximum instantaneous rate of tension development, -dF/dt = maximum instantaneous rate of tension relaxation

Table 3.
Parameters of Double Exponential Equation Fit to Sensory Contractions

	PLACEBO						CAFFEINE					
	r	C	A	-K1	B	-K2	r	C	A	-K1	B	-K2
mean	0.99	4.83	19.62	0.38	26.86	0.025	0.99	3.12	19.74	0.22*	25.90	0.019
sem	0.002	1.18	1.50	0.08	2.00	0.004	0.002	1.70	3.10	0.04	2.71	0.004

$$Y = C + Ae^{-K_1t} + Be^{-K_2t}$$

Y = Force, t = time, A and B = values of exponential processes, C = asymptote, -K1 and -K2 = rate constants

* Significantly different from placebo (p<.05)

Figure 1

A. Four force tracings from the sensory protocol performed by one subject. **B.** The average of the 4 tracings shown in A were smoothed and then fit to a double exponential equation.

Figure 2. Each dependent variable for the endurance protocol was compared at 3 different time points, **A**) at placebo T_{LIM} ($PL T_{LIM}$), **B**) at the time point in the caffeine trial corresponding to placebo T_{LIM} and **C**) at caffeine T_{LIM} ($CF T_{LIM}$).

Figure 3. Example of the endurance protocol (EP) performed by 1 subject. **A.** Repeated isometric contractions at 50% MVC for 15 sec were performed until force dropped below 45% MVC for longer than 2 sec (T_{LIM}). A MVC was performed before and after the EP. Arrows indicate the application of electrical stimulation. **B.** Twitches extracted from inactive periods between contractions. Approaching T_{LIM} twitch amplitude and $\pm dF/dt$ decreased. **C.** EMG associated with isometric contractions. Electrical activity increased approaching T_{LIM} . **D.** M waves extracted from EMG recording. No changes were observed in M waves throughout the endurance protocol.

Figure 4. Limit of Endurance (T_{LIM}) for each subject. Positive values indicate a longer endurance time with caffeine. Nine subjects increased T_{LIM} , 4 had no change ($\pm < 5\%$) change and 2 subjects decreased T_{LIM} with caffeine. * $p < .02$

Figure 5. Twitch amplitudes for the placebo (closed circles) and caffeine (open triangles) conditions at corresponding time points during the endurance protocol. The regression lines were not significantly different between the placebo ($r=.99$, $Y=114.8-.94x$, solid line) and caffeine ($r=.99$, $Y=113.7-.95x$, dashed line) conditions. In the caffeine trial twitch amplitude declined to a greater extent than in the placebo trial.* Significantly different from placebo T_{LIM} value ($p<.01$). † Significantly different from time corresponding to placebo T_{LIM} in the caffeine trial ($p<.01$).

Figure 6. Contractile properties at T_{LIM} . There was no significant difference between conditions at values corresponding to placebo T_{LIM} for any of the contractile properties. At caffeine T_{LIM} twitch amplitude and +dF/dt were significantly smaller than the values corresponding to placebo T_{LIM} in the placebo and caffeine trial. * Significantly different from placebo T_{LIM} ($p < 0.05$) † Significantly different from time corresponding to placebo T_{LIM} in the caffeine trial ($p < .01$).

A, B and C are as defined in Figure 2.

Figure 7. EMG for the placebo (closed circles) and caffeine (open triangles) conditions at corresponding time points through the progression of the endurance protocol. The regression lines were not significantly different between the placebo (solid line, $r=.77$, $Y=90.7 + .51x$) and caffeine (dashed line, $r=.84$, $Y=87.5 + .63x$) trials. EMG was significantly higher at caffeine T_{LIM} compared to EMG at placebo T_{LIM} and the time of placebo T_{LIM} in the caffeine trial.

*Significantly different from placebo T_{LIM} $p<.02$. † Significantly different from caffeine value at placebo T_{LIM} $p<.05$.

Figure 8. Voluntary activation for the placebo (closed circles) and caffeine (open triangles) conditions at corresponding time points through the progression of the endurance protocol. The regression lines were not significantly different between the placebo (solid line, $r=.69$, $Y= 77.2 + .13x$) and caffeine (dashed line, $r=.73$, $Y= 76.4 + .16x$) conditions. Subjects achieved $91.2\pm3.4\%$ activation at placebo T_{LIM} which was not significantly different from the achieved $91.9\pm2.9\%$ activation at the corresponding time in the caffeine trial. At caffeine T_{LIM} voluntary activation increased to $93.6\pm2.5\%$ which was not significantly different than the voluntary activation at placebo T_{LIM} in both conditions.

Figure 9. Regression lines for placebo (solid) and caffeine (dashed) force tracings during the sensory protocol that were plotted from the average of the regression parameters fit to individual subjects. Force sensation was lower during the initial part of the contraction in the caffeine trial. The inset represents the regression lines from the first 10 s of the protocol.

Discussion

The present investigation was conducted to examine how caffeine may alter neuromuscular functions that contribute to an increase in muscular endurance. Our results replicate previous findings showing the property of caffeine to increase maximum force generating capacity and the endurance of submaximal isometric contractions of the quadriceps (31). However, the changes in contractile properties, motor unit activation and junctional and sarcolemmal transmission that occurred as the quadriceps reached T_{LIM} , could not account for the prolonged performance after caffeine ingestion. We also found that caffeine alters isometric force sensation very early in the contraction, an observation that has not been previously reported. This suggests that the increase in T_{LIM} during the caffeine trial may have been caused by a willingness to maintain near maximal activation because of a decrease in force sensation.

Effect of Caffeine on Muscle Endurance

Caffeine is a central nervous system stimulant (43) and is also known to increase the contractility of skeletal muscle (25, 36). Despite the evidence that caffeine may influence neuromuscular performance, only a few studies are available that have investigated this possibility (10, 31, 34, 61). The results of these studies conflict with reports of no ergogenic influence of caffeine (10, 34, 61). The interpretation of the data from all of these investigations is difficult because of the disparities in methodologies, subject selection and caffeine dosages.

There is often a marked variability in the magnitude of physiological responses (21) and ergogenic influences (26, 28, 36) among subjects after an acute dose of caffeine. To overcome these individual differences, we used a larger sample size in this study ($n=15$). We observed a mean increase of 17% in endurance time after caffeine ingestion, which agrees with previous observations (31) of a 26% increase in a sustained submaximal contraction of the quadriceps. Kalmar & Cafarelli (31) also used a larger sample size ($n=11$), controlled for caffeine habituation, and other factors such as smoking and obesity (32, 46). Moreover, only males were used as subjects because oral contraceptive use is known to alter caffeine pharmacokinetics (1). Lopes (34) found no significant increase in the endurance of a sustained contraction of the adductor pollicis, however, the subject sample was small ($n=5$) and there was an increase of 12% in endurance time during the caffeine trial. Three of the 5 subjects increased their endurance time after caffeine consumption. Of the remaining 2 subjects, 1 maintained and the other decreased endurance time with caffeine. Similarly, Williams et al (61) found no influence of caffeine on the endurance of hand grip contractions, however, they also used a small sample size ($n=6$). The wide range of caffeine-related changes in T_{LIM} emphasizes the necessity for adequate sample size when studying the ergogenic effects of caffeine.

The endurance of intermittent, submaximal, isometric contractions is not normally limited by substrate metabolism (7, 19). The length of performance is likely due to the failure of elements distal to the neuromuscular junction or the willingness to tolerate the discomfort associated with prolonged activity (5, 9). In highly motivated subjects,

impairment of excitation-contraction coupling reduces force generation and limits endurance. Although it is well established from *in vivo* studies that caffeine affects calcium kinetics in skeletal muscle (25, 36), this occurs at concentrations that are toxic to humans. Nevertheless, Tarnapolsky (57) found an increase in force generated by the tibialis anterior by 20 Hz stimulation of the peroneal nerve after consumption of 6mg/kg of caffeine. Similarly, Lopes (34) found an increase in tetanic force of the adductor pollicis produced by 20-50 Hz stimulation following a dose of 500 mg of caffeine. These data suggest an influence of caffeine on skeletal muscle that is independent of neural activation. However, it has yet to be shown that caffeine-induced alterations in calcium kinetics enhance human muscular endurance. In the studies by both Tarnapolsky and Lopes, there were no data on the influence of caffeine on a single twitch. In those studies, increases in calcium flux induced by caffeine may have been slight and that intracellular $[Ca^{2+}]$ was only changed sufficiently to alter performance after repetitive stimulation.

The possibility that the contractile apparatus was protected by caffeine was eliminated because the rate at which the evoked twitch amplitudes declined was not different between conditions. The smaller evoked twitch force at the end of the caffeine endurance protocol was undoubtedly caused by the prolonged performance and was not the reason that performance was prolonged. Alteration in junctional and sarcolemmal transmission was also eliminated because the M waves were not altered by either the protocol or caffeine. Transmission failure does not normally occur with this type of activity (8) and this may have masked any influence caffeine has in maintaining signal transmission.

Although voluntary activation increased by 2% from the time corresponding to placebo T_{LIM} to caffeine T_{LIM} , this was not sufficient to account for the 28.6% increase in EMG which is a reflection of both rate coding and recruitment. Thus, the increase we observed could be explained on the basis of a more rapid frequency of motor unit discharge, spontaneous bursts in the EMG signal or an increase in motor unit synchronization (53, 63).

Kalmar and Cafarelli (31) found no effect of caffeine on motor unit firing rates during various levels of brief non-fatigued submaximal contractions. Therefore, it is unlikely that an increase in firing rates caused the increase in EMG at the end of the caffeine trial. Another possibility is that the increase in EMG may have been caused by spontaneous bursts in the EMG recording. This type of EMG patterning has been observed during prolonged endurance contractions of the elbow flexors (53) and of the plantar flexors (56). However, these reports are from long duration contractions at force levels lower than 40% MVC (22, 53, 56). We are inclined to discard this explanation because visual analysis of the EMG recordings showed no evidence of bursts. Alternatively, an increase in the synchronization of motor unit firing may account for the large increase in EMG seen in the present study (63). Toward the end of an exhaustive isometric contraction, an increase in surface EMG and decrease in mean power frequency of the EMG signal have been associated with the occurrence of force tremors (59, 35). Force tremors are due to motor-unit synchronization that occurs at low frequencies (27, 37). Thus it is possible that the increase in EMG during the prolonged performance in the caffeine trial was the result of motor unit synchronization.

An acute dose of caffeine has a wide variety of effects on cardiovascular function which include an influence on heart rate, blood pressure (17, 50) and a reduction in blood flow to a number of vascular beds (44, 62, 54). These effects may be caused by central stimulation, increasing circulating catecholamines and inhibiting adenosine-induced vasodilation (3, 54). Few studies have investigated the effects of caffeine on cardiovascular dynamics during exercise and we are unaware of any studies that indicate how caffeine influences blood flow to an active muscle. Engles (20) observed an increase in resting blood pressure with no effect on heart rate, stroke volume or cardiac output following an acute dose of 5 mg/kg of caffeine. There was no difference in the effect of caffeine on these cardiovascular variables during a constant-load cycling activity compared to a resting state. Daniels (17) found that forearm blood flow was reduced during dynamic leg exercise, but no measurements were obtained of blood flow to the active muscles.

Fatigue develops more slowly during intermittent contractions compared to a single sustained contraction at the same relative intensity because of the blood flow that occurs between intermittent contractions (49). This is consistent with the present findings where the protocols lasted 18-22 sec longer than during a sustained contraction as in the previous experiment from our laboratory (31). The interval between contractions in our endurance protocol was brief (1.5 s) and the muscle was not completely relaxed because of the maximal twitch that was evoked. This was likely too little time to reverse the substrate depletion and metabolite build-up caused by the occluded blood flow during the contraction. Nevertheless, it is unlikely that blood flow played a significant ergogenic role because of

the short rest intervals and because they contained maximal evoked twitches. Also, there is no evidence to suggest the effect of caffeine on cardiovascular function will cause an ergogenic influence (17, 20).

In the central nervous system, adenosine inhibits the spontaneous firing of cortical neurons and suppresses neurotransmitter release (23, 47). The property of caffeine to excite central neurons by competitive inhibition of adenosine receptors may increase the ability to recruit motor units and/or increase the firing rate of active units (16, 23, 48). This may have caused the increase in voluntary activation during MVC by recruiting additional motor units, but there is no evidence that the property of caffeine to excite central neurons results in an increase in firing rates. Dopaminergic activity also increases in the presence of caffeine via the inhibition of adenosine receptors (41). Increases in dopamine are involved in arousal (30) and motor coordination (24) and decreases in dopamine concentrations occur during prolonged endurance activities (18). Davis and Bailey (18) suggest that increases in central dopamine levels may enhance endurance performance by reducing central fatigue. The ability to prolong muscular endurance may therefore be influenced by an increase in dopaminergic activity after caffeine administration. A lack of willingness to maintain a high level of muscle activation during an isometric contraction may result from an increase in force sensation that develops during a prolonged contraction (11, 55).

Caffeine and Force Sensation

The ergogenic properties of caffeine have been associated with an attenuation in sensation during aerobic activity (14, 15). Typically, category scales have been used to

assess the influence of caffeine following an exhaustive bout of physical activity (14, 15, 60). We chose to use the constant sensation technique because it does not require the interpretation of category scales (12, 13), it provides a continuous measurement of force sensation, is highly repeatable within individual trials (see Figure 1) and can be experimentally manipulated (12, 52). The instructions during this protocol were to maintain sensation constant by altering force from the point at which visual feedback was removed. There was likely some variability in the interpretation of these instructions. This variability in estimating force sensation arises from the ability to pay attention to both centrifugal motor command and muscular tension associated with a contraction (39, 51). Since the change in the first rate constant associated with caffeine ingestion occurred in the first few seconds of the sensory protocol, we assume that the mechanism involved is neural.

There are at least three possible explanations of how caffeine may alter muscle sensory processes. The first, is that it may cause changes in the chemical composition of the muscle's environment. Since the initial force was 50% MVC and falling, any feedback contributing to force sensation in the first 10 s of contraction would not likely be associated with significant changes in metabolite concentrations or increases in temperature. It is more likely that feedback from mechanoreceptors, such as Golgi tendon organs (29) and class III or IV muscle afferents (33, 40) that are sensitive to increases in tension or pressure, were influenced by caffeine. A second possibility is that caffeine may alter feedforward information. This is the central outflow to the sensory cortex sent simultaneously with the signal to the motor neuron pool. A third possibility is that caffeine may alter how

information from either feedforward or feedback is processed centrally. Currently, there are no data available in the literature that would provide insight into this problem.

In summary, we found caffeine increases the endurance of repeated submaximal isometric contractions of the quadriceps. There was no indication that caffeine preserved the function of the contractile apparatus as the muscle progressed to T_{LIM} or that caffeine protected junctional and sarcolemmal transmission. Central activation of motor units was maintained at near maximal levels for longer with caffeine which is likely the result of the willingness to prolong endurance. The caffeine-induced increase in T_{LIM} may stem from alterations in muscle sensory processes.

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CHAPTER 4

SUMMARY, CONCLUSION & RECOMMENDATIONS

Summary

1. Caffeine increases the maximum force generating capacity and endurance of repeated submaximal isometric contractions of the quadriceps.
2. Neuromuscular variables were investigated as possible contributors to the caffeine enhancement of muscular endurance. Recordings made during the endurance protocol were the same in both the caffeine and placebo conditions and followed the typical pattern of fatigue associated with repeated submaximal isometric contractions.
3. During the caffeine trial there was a greater decrement in twitch amplitude, a larger increase in EMG and near maximal muscle activation was maintained for longer. These observations are likely the result of prolonged muscular activity and not the cause of an increased time to T_{LIM} .
4. The results of the sensory protocol indicate that the effect of caffeine occurs very early in the contraction (<10 s) which suggests that the drug exerts its influence neurally.
5. The ergogenic influence of caffeine during muscular endurance may be the result of an alteration by caffeine to some aspect of force sensation.

Conclusion

Caffeine increases the endurance of repeated submaximal isometric contractions of the quadriceps. There is no indication that caffeine preserves either contractile function or neural transmission as the muscle progressed to T_{LIM} . The caffeine-induced increase in T_{LIM} may stem from alterations in muscle sensory processes.

Recommendations

The following recommendations would facilitate better understanding of the neuromuscular mechanisms that cause an enhancement in muscular endurance observed with caffeine.

1. In the caffeine trial, during the prolonged performance, an increase in EMG was observed while muscle activation, assessed by twitch interpolation, remained at a near maximal level. This suggests that during prolonged endurance there was an alteration in firing rate and/or firing sequence of motor units. There is an increase in the excitability of cortical neurons with caffeine, however, it is not known if this has an effect on the modulation of rate coding during a sustained submaximal contraction. Changes in the firing rate of single motor units during a sustained contraction can be assessed with intraneural and intramuscular recordings.
2. The ability of caffeine to increase dopaminergic activity and excite cortical neurons suggests a possible reduction in the onset of central fatigue. In the present investigation, changes in central activation were indirectly assessed with peripheral stimulation. Transcranial magnetic stimulation should be utilized in a fatiguing

protocol to directly assess changes in cortical excitation that may influence performance.

3. The physiological processes underlying sensory perception are likely a combination of both central feedforward and peripheral feedback mechanisms. To investigate further the sensory mechanisms that may be affected by caffeine, central drive and peripheral feedback might be uncoupled experimentally. The initial rapid decline in force when performing a constant force sensation contraction is greater with a higher starting force. Caffeine may have a different influence at lower and higher levels of force sensation which can be assessed by performing a constant force sensation contraction with different starting force levels.
4. Junction and sarcolemma signal transmission were not affected by the endurance protocol which masked any influence that caffeine may have had. There are conflicts in the literature as to the contributions of failure of junctional and sarcolemmal transmission to the endurance of voluntary contraction, however, high rates of stimulation can cause changes to M wave characteristics. A protocol that incorporates voluntary contractions and high frequency stimulation should be used to investigate how caffeine may influence M wave characteristics in humans.
5. Caffeine increased systolic and diastolic blood pressure, however, we had no indication of how blood flow was altered locally or if this had an effect on performance. In the present investigation the interval between isometric contractions was likely too short for blood flow to fully reverse the energy depletion

and a metabolite build-up caused by the sustained contraction. Caffeine may have a different influence on a protocol that has a larger rest interval between contractions. Blood flow and perfusion pressure to the active muscle can also be manipulated with an occlusion cuff and limb position.

APPENDICES

SUBJECT PROFILE, EXPERIMENTAL SCHEDULE & PREDICTION ACCURACY

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SUBJECT #	AGE (years)	HEIGHT (cm)	WEIGHT (kg)	PROTOCOL SCHEDULE & CONDITION			
				SP-PL	SP-CF	EP-CF	EP-PL
1	22	167.6	61.8	SP-PL	SP-CF	EP-CF	EP-PL
2	24	182.9	81.8	SP-CF	EP-PL	SP-PL	EP-CF
3	22	180.3	76.4	EP-CF	SP-CF	EP-PL	SP-PL
4	25	188.0	75.5	EP-PL	SP-PL	SP-CF	EP-CF
5	27	172.7	61.8	SP-PL	EP-PL	EP-CF	SP-CF
6	23	182.9	93.9	SP-CF	EP-CF	SP-PL	EP-PL
7	24	185.4	78.2	EP-CF	EP-PL	SP-PL	SP-CF
8	24	185.4	90.0	EP-CF	SP-PL	EP-PL	SP-CF
9	24	172.7	77.5	EP-CF	SP-PL	EP-PL	SP-CF
10	22	180.3	80.0	SP-CF	EP-CF	EP-PL	SP-PL
11	19	185.4	81.8	SP-CF	SP-PL	EP-PL	EP-CF
12	20	175.3	76.4	SP-PL	EP-CF	SP-CF	EP-PL
13	20	165.1	75.5	EP-PL	SP-CF	EP-CF	SP-PL
14	19	180.3	81.8	EP-CF	SP-PL	SP-CF	EP-PL
15	24	170.2	64.5	EP-PL	EP-CF	SP-CF	SP-PL
Average	22.6	178.3	77.1				
SEM	0.6	1.9	2.3				
SD	2.3	7.2	9.1				

SUBJECT #	CORRECT PREDICTIONS		
	SP	EP	TOTAL
1	2	1	3
2	2	2	4
3	0	2	2
4	1	2	3
5	2	2	4
6	2	2	4
7	2	1	3
8	2	2	4
9	2	2	4
10	1	1	2
11	0	1	1
12	2	0	2
13	2	2	4
14	2	1	3
15	1	2	3
Average	1.5	1.5	3.1
SEM	0.2	0.2	0.2
SD	0.7	0.6	1.0

Correct predictions are number of accurate predictions made by each subject on what treatment they received on each experimental day.

EP= Endurance protocol, SP= Sensory protocol

CF= Caffeine, PL= Placebo

**PRE-POST CAPSULE INGESTION HEART RATE AND BLOOD PRESSURE
PLACEBO**

ENDURANCE PROTOCOL									
SUBJECT	PRE HR	POST HR	RATIO	PRE SBP	POST SBP	RATIO	PRE DBP	POST DBP	RATIO
1	72	56	0.78	115	115	1.00	75	78	1.04
2	64	60	0.94	114	110	0.96	72	72	1.00
3	64	68	1.06	130	134	1.03	83	80	0.96
4	64	68	1.06	122	117	0.96	78	79	1.01
5	80	72	0.90	120	122	1.02	80	79	0.99
6	56	56	1.00	115	118	1.03	78	80	1.03
7	80	72	0.90	140	142	1.01	78	78	1.00
8	76	64	0.84	120	120	1.00	77	79	1.03
9	72	68	0.94	114	116	1.02	77	78	1.01
10	76	68	0.89	118	118	1.00	79	76	0.96
11	68	60	0.88	132	122	0.92	82	80	0.98
12	48	44	0.92	118	118	1.00	81	77	0.95
13	56	48	0.86	115	118	1.03	76	80	1.05
14	76	68	0.89	117	117	1.00	74	78	1.05
15	72	64	0.89	114	114	1.00	79	77	0.97

SENSORY PROTOCOL									
SUBJECT	PRE HR	POST HR	RATIO	PRE SBP	POST SBP	RATIO	PRE DBP	POST DBP	RATIO
1	60	52	0.87	111	114	1.03	78	77	0.99
2	68	64	0.94	114	116	1.02	75	75	1.00
3	80	84	1.05	128	125	0.98	79	76	0.96
4	60	68	1.13	118	120	1.02	78	78	1.00
5	92	80	0.87	120	120	1.00	90	80	0.89
6	64	56	0.88	122	121	0.99	78	79	1.01
7	80	68	0.85	139	140	1.01	80	78	0.98
8	72	60	0.83	120	120	1.00	76	80	1.05
9	76	72	0.95	117	115	0.98	81	80	0.99
10	84	72	0.86	119	119	1.00	80	81	1.01
11	68	56	0.82	122	120	0.98	78	80	1.03
12	48	40	0.83	114	110	0.96	74	76	1.03
13	60	56	0.93	118	116	0.98	78	78	1.00
14	72	64	0.89	115	116	1.01	74	76	1.03
15	80	68	0.85	118	116	0.98	80	80	1.00
AVERAGE	69.6	63.2	0.9	120.0	119.6	1.0	78.3	78.2	1.0
SEM	1.9	1.8	0.0	1.3	1.3	0.0	0.6	0.4	0.0
SD	10.4	9.8	0.1	7.1	7.3	0.0	3.4	2.0	0.0

Ratio are post/pre capsule ingestion values
 HR = heart rate measured in beats per minutes
 SBP = systolic blood pressure measured in mmHg
 DBP = diastolic blood pressure measured in mmHg.

**PRE-POST CAPSULE INGESTION HEART RATE AND BLOOD PRESSURE
CAFFEINE**

ENDURANCE PROTOCOL									
SUBJECT	PRE HR	POST HR	RATIO	PRE SBP	POST SBP	RATIO	PRE DBP	POST DBP	RATIO
1	64	52	0.81	102	115	1.13	72	68	0.94
2	64	60	0.94	110	120	1.09	70	74	1.06
3	84	72	0.86	125	134	1.07	84	90	1.07
4	72	68	0.94	117	125	1.07	76	78	1.03
5	84	84	1.00	120	124	1.03	83	85	1.02
6	60	48	0.80	122	128	1.05	82	85	1.04
7	72	76	1.06	135	142	1.05	82	83	1.01
8	76	60	0.79	122	133	1.09	78	85	1.09
9	80	64	0.80	120	127	1.06	80	84	1.05
10	72	64	0.89	118	126	1.07	80	82	1.03
11	56	56	1.00	119	125	1.05	78	83	1.06
12	48	48	1.00	112	114	1.02	78	80	1.03
13	64	48	0.75	115	122	1.06	77	76	0.99
14	52	68	1.31	116	125	1.08	74	80	1.08
15	68	64	0.94	118	127	1.08	81	85	1.05

SENSORY PROTOCOL									
SUBJECT	PRE HR	POST HR	RATIO	PRE SBP	POST SBP	RATIO	PRE DBP	POST DBP	RATIO
1	60	48	0.80	112	120	1.07	78	75	0.96
2	68	60	0.88	110	118	1.07	71	75	1.06
3	76	76	1.00	125	139	1.11	83	90	1.08
4	72	60	0.83	115	120	1.04	78	78	1.00
5	76	76	1.00	121	125	1.03	82	83	1.01
6	56	52	0.93	122	126	1.03	79	83	1.05
7	80	72	0.90	138	145	1.05	80	80	1.00
8	76	72	0.95	122	130	1.07	76	84	1.11
9	80	68	0.85	122	129	1.06	79	84	1.06
10	68	68	1.00	118	128	1.08	80	84	1.05
11	64	64	1.00	122	128	1.05	80	82	1.03
12	44	48	1.09	115	120	1.04	72	76	1.06
13	64	56	0.88	116	124	1.07	76	83	1.09
14	60	64	1.07	118	124	1.05	74	82	1.11
15	68	64	0.94	118	130	1.10	79	84	1.06
AVERAGE	67.6	62.7	0.9	118.8	126.4	1.1	78.1	81.4	1.0
SEM	1.9	1.8	0.0	1.3	1.3	0.0	0.7	0.9	0.0
SD	10.3	9.8	0.1	6.9	7.1	0.0	3.7	4.7	0.0

Ratio are post/pre capsule ingestion values
 HR = heart rate measured in beats per minutes
 SBP = systolic blood pressure measured in mmHg
 DBP = diastolic blood pressure measured in mmHg.

CONTROL MEASURES PRE-POST CAPSULE INGESTION MVC FORCE

ENDURANCE PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	685.83	638.49	0.93	497.90	546.28	1.10
2	570.82	579.49	1.02	613.56	579.34	0.94
3	504.10	511.96	1.02	488.34	491.26	1.01
4	302.30	299.76	0.99	281.15	264.57	0.94
5	456.24	482.58	1.06	460.72	441.25	0.96
6	751.02	886.98	1.18	752.91	714.70	0.95
7	453.67	422.90	0.93	468.93	479.32	1.02
8	521.71	554.92	1.06	642.57	541.68	0.84
9	542.45	498.75	0.92	452.17	479.85	1.06
10	302.25	394.12	1.30	371.64	365.61	0.98
11	594.46	602.76	1.01	410.39	429.19	1.05
12	226.20	213.38	0.94	203.73	202.62	0.99
13	363.34	395.30	1.09	620.25	599.55	0.97
14	511.72	617.78	1.21	656.64	694.83	1.06
15	483.87	544.65	1.13	484.24	445.27	0.92

SENSORY PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	594.81	610.96	1.03	790.68	815.24	1.03
2	598.80	567.59	0.95	616.72	611.99	0.99
3	549.33	560.61	1.02	489.56	496.31	1.01
4	324.10	318.86	0.98	256.91	246.14	0.96
5	467.97	473.71	1.01	470.70	473.18	1.01
6	620.74	640.57	1.03	770.13	689.52	0.90
7	369.67	436.55	1.18	424.50	434.20	1.02
8	644.17	750.94	1.17	524.04	538.69	1.03
9	398.77	467.11	1.17	443.07	410.47	0.93
10	282.12	313.03	1.11	409.66	357.58	0.87
11	250.42	249.86	1.00	216.19	210.86	0.98
12	455.73	429.20	0.94	637.73	653.10	1.02
13	816.08	810.31	0.99	691.77	604.44	0.87
14	603.05	629.39	1.04	757.31	740.33	0.98
15	480.86	498.54	1.04	543.32	495.55	0.91
AVERAGE	490.89	513.37	1.05	514.91	501.76	0.98
SEM	26.82	28.52	0.02	29.32	28.39	0.01
SD	146.92	156.21	0.10	160.61	155.50	0.06

Ratio are post/pre capsule ingestion values

Pre and post capsule MVC force is expressed in newtons

CONTROL MEASURES PRE-POST CAPSULE INGESTION TWITCH AMPLITUDE

ENDURANCE PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	109.85	116.47	1.06	82.35	101.31	1.23
2	113.62	107.91	0.95	98.50	95.77	0.97
3	119.53	134.48	1.13	128.03	129.78	1.01
4	67.53	68.47	1.01	70.34	71.43	1.02
5	100.58	110.94	1.10	94.86	91.22	0.96
6	128.53	138.62	1.08	108.32	108.59	1.00
7	84.49	85.84	1.02	92.56	100.70	1.09
8	101.90	100.85	0.99	102.87	99.39	0.97
9	97.29	108.89	1.12	98.92	109.84	1.11
10	74.39	89.63	1.20	85.92	89.02	1.04
11	65.69	62.82	0.96	82.75	81.59	0.99
12	58.77	56.19	0.96	46.46	42.31	0.91
13	85.01	91.22	1.07	80.17	84.64	1.06
14	66.14	71.28	1.08	69.13	88.11	1.27
15	112.34	120.34	1.07	113.97	112.79	0.99

SENSORY PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	85.56	96.30	1.13	114.43	106.24	0.93
2	130.05	122.09	0.94	110.79	100.93	0.91
3	130.86	137.63	1.05	105.35	103.66	0.98
4	71.66	75.53	1.05	63.14	64.00	1.01
5	103.46	106.16	1.03	103.43	118.07	1.14
6	93.04	114.47	1.23	107.35	112.00	1.04
7	79.85	95.32	1.19	80.15	93.65	1.17
8	107.49	114.81	1.07	87.92	103.51	1.18
9	98.37	100.47	1.02	89.88	87.89	0.98
10	74.49	76.13	1.02	83.69	79.24	0.95
11	49.25	48.68	0.99	39.68	39.89	1.01
12	102.60	100.10	0.98	172.00	174.52	1.01
13	195.11	199.51	1.02	180.53	172.21	0.95
14	138.99	145.90	1.05	164.32	146.88	0.89
15	99.87	107.37	1.08	119.13	118.83	1.00
AVERAGE	98.85	104.03	1.05	99.78	100.97	1.02
SEM	5.41	5.63	0.01	5.92	5.59	0.02
SD	29.63	30.86	0.08	32.43	30.64	0.08

Ratio are post to pre capsule ingestion values

Pre and post capsule twitch amplitude is expressed in newtons

CONTROL MEASURES PRE-POST CAPSULE INGESTION **+dF/Dt**

ENDURANCE PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	2085.32	1728.92	0.83	1327.02	1660.67	1.25
2	1546.93	1562.09	1.01	1463.51	1334.61	0.91
3	1948.82	2100.48	1.08	2355.78	2267.31	0.96
4	1035.08	1076.78	1.04	1129.86	1251.19	1.11
5	1625.29	1736.50	1.07	1562.09	1455.93	0.93
6	1789.58	2001.91	1.12	1660.67	1478.68	0.89
7	1440.76	1395.27	0.97	1680.89	1804.75	1.07
8	1586.74	1440.77	0.91	1710.03	1545.54	0.90
9	1645.50	1800.96	1.09	1573.47	1618.96	1.03
10	1177.57	1429.39	1.21	1301.73	1402.81	1.08
11	1683.42	1486.25	0.88	1061.61	925.12	0.87
12	869.51	796.21	0.92	763.35	618.01	0.81
13	1440.77	1304.27	0.91	2604.75	2403.80	0.92
14	1923.55	2047.40	1.06	1741.55	2282.48	1.31
15	1694.80	1774.42	1.05	1635.39	1603.80	0.98

SENSORY PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	1579.79	1691.00	1.07	1943.77	1994.32	1.03
2	1741.56	1471.10	0.84	1453.40	1554.51	1.07
3	2352.62	2229.39	0.95	1943.77	1903.33	0.98
4	1088.16	1213.28	1.11	1086.89	917.54	0.84
5	1675.84	1691.00	1.01	1587.37	1812.33	1.14
6	1349.77	1490.05	1.10	1774.42	1471.10	0.83
7	1300.48	1493.85	1.15	1466.04	1448.35	0.99
8	1717.54	1903.33	1.11	1427.50	1637.92	1.15
9	1476.79	1637.92	1.11	1491.32	1440.77	0.97
10	1188.63	1311.85	1.10	1311.85	1254.98	0.96
11	655.93	568.57	0.87	503.00	500.48	0.99
12	1562.09	1410.44	0.90	2701.41	2540.30	0.94
13	3074.88	2828.45	0.92	2537.77	2396.21	0.94
14	1807.28	1766.83	0.98	2418.97	1971.58	0.82
15	1625.28	1683.42	1.04	1736.47	1717.54	0.99
AVERAGE	1574.00	1580.37	1.01	1627.81	1583.17	0.98
SEM	84.51	78.70	0.02	97.22	90.56	0.02
SD	462.90	431.07	0.10	532.50	496.04	0.11

Ratio are post/pre capsule ingestion values

Pre and post capsule +dF/dt is expressed in newtons sec⁻¹

CONTROL MEASURES PRE-POST CAPSULE INGESTION **-dF/Dt**

ENDURANCE PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	-935.23	-1069.20	1.14	-826.54	-1061.62	1.28
2	-909.96	-1023.70	1.13	-983.26	-940.29	0.96
3	-1006.64	-1008.54	1.00	-1117.23	-1008.54	0.90
4	-705.22	-561.14	0.80	-639.50	-568.72	0.89
5	-654.66	-750.71	1.15	-669.83	-652.14	0.97
6	-1080.58	-940.29	0.87	-803.79	-894.79	1.11
7	-932.71	-781.05	0.84	-1051.51	-1069.20	1.02
8	-997.16	-1046.45	1.05	-879.62	-844.83	0.96
9	-849.29	-765.88	0.90	-1099.53	-917.54	0.83
10	-844.23	-769.67	0.91	-889.70	-762.09	0.86
11	-1091.92	-1167.75	1.07	-793.68	-788.63	0.99
12	-457.50	-356.40	0.78	-361.45	-428.44	1.19
13	-633.18	-705.22	1.11	-1239.81	-1270.13	1.02
14	-1203.17	-1334.58	1.11	-1193.05	-1137.14	0.95
15	-1004.74	-1080.58	1.08	-955.45	-959.23	1.00

SENSORY PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	-894.79	-970.62	1.08	-1076.78	-925.12	0.86
2	-1056.56	-1091.95	1.03	-970.62	-777.25	0.80
3	-1076.78	-1198.11	1.11	-940.29	-917.54	0.98
4	-640.76	-614.22	0.96	-556.08	-686.26	1.23
5	-631.92	-727.96	1.15	-797.48	-849.29	1.06
6	-743.13	-993.37	1.34	-816.43	-803.79	0.98
7	-1000.95	-1061.62	1.06	-702.69	-1008.54	1.44
8	-913.75	-894.79	0.98	-837.92	-925.12	1.10
9	-822.75	-758.36	0.92	-816.43	-909.95	1.11
10	-657.18	-727.96	1.11	-877.10	-743.13	0.85
11	-420.85	-477.73	1.14	-366.51	-384.20	1.05
12	-705.21	-697.63	0.99	-904.26	-947.85	1.05
13	-1364.90	-1380.10	1.01	-1309.33	-1228.44	0.94
14	-1208.22	-1137.14	0.94	-1622.76	-1698.59	1.05
15	-912.48	-1061.62	1.16	-1059.09	-1016.12	0.96
AVERAGE	-862.45	-883.54	1.03	-893.19	-893.86	1.02
SEM	40.02	43.34	0.02	48.33	46.75	0.03
SD	219.22	237.36	0.13	264.73	256.08	0.14

Ratio are post/pre capsule ingestion values

Pre and post capsule -dF/dt is expressed in newtons sec⁻¹

CONTROL MEASURES PRE-POST CAPSULE INGESTION VOLUNTARY ACTIVATION

ENDURANCE PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	98.13	99.93	1.02	97.52	99.70	1.02
2	97.91	99.72	1.02	98.32	99.45	1.01
3	91.79	96.00	1.05	94.66	94.99	1.00
4	99.05	100.00	1.01	98.94	99.47	1.01
5	97.66	98.91	1.01	98.99	99.00	1.00
6	95.64	100.00	1.05	95.95	98.46	1.03
7	98.64	99.65	1.01	98.44	97.29	0.99
8	94.06	96.24	1.02	95.83	94.31	0.98
9	99.69	99.86	1.00	97.84	97.26	0.99
10	96.61	97.24	1.01	96.32	97.88	1.02
11	94.18	93.90	1.00	97.94	100.00	1.02
12	94.11	93.71	1.00	94.12	95.96	1.02
13	97.21	97.01	1.00	93.30	94.51	1.01
14	94.90	98.67	1.04	97.83	98.80	1.01
15	95.04	98.46	1.04	98.27	99.10	1.01

SENSORY PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	98.26	100.00	1.02	98.85	98.93	1.00
2	98.84	99.38	1.01	99.34	96.18	0.97
3	93.36	94.21	1.01	93.99	91.73	0.98
4	96.37	99.20	1.03	98.08	99.25	1.01
5	98.68	99.29	1.01	99.26	99.29	1.00
6	93.71	96.83	1.03	95.42	97.56	1.02
7	93.63	98.57	1.05	96.42	96.76	1.00
8	93.52	97.23	1.04	93.43	97.00	1.04
9	98.47	100.00	1.02	99.21	100.00	1.01
10	93.10	97.71	1.05	98.84	95.07	0.96
11	94.33	97.51	1.03	98.67	98.40	1.00
12	96.53	96.06	1.00	93.86	95.71	1.02
13	95.23	97.61	1.02	95.85	95.30	0.99
14	96.87	98.91	1.02	98.29	95.35	0.97
15	97.67	97.85	1.00	98.37	97.96	1.00
AVERAGE	96.19	97.95	1.02	97.00	97.24	1.00
SEM	0.41	0.35	0.003	0.37	0.38	0.003
SD	2.25	1.93	0.02	2.01	2.09	0.02

Ratio are post/pre capsule ingestion values

Pre and post capsule voluntary activation is expressed as a percent

CONTROL MEASURES PRE-POST CAPSULE INGESTION
EMG_{MAX}

ENDURANCE PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	0.57	0.57	1.00	0.65	0.68	1.04
2	0.45	0.44	0.98	0.44	0.45	1.04
3	0.09	0.10	1.12	0.19	0.19	0.99
4	0.22	0.25	1.10	0.21	0.22	1.06
5	0.25	0.29	1.16	0.26	0.26	1.01
6	0.18	0.28	1.57	0.13	0.13	1.03
7	0.10	0.12	1.28	0.19	0.19	0.99
8	0.18	0.14	0.81	0.09	0.09	1.07
9	0.21	0.21	1.00	0.25	0.24	0.97
10	0.19	0.19	0.98	0.18	0.19	1.05
11	0.21	0.22	1.02	0.30	0.38	1.28
12	0.15	0.17	1.11	0.15	0.14	0.95
13	0.41	0.48	1.18	0.13	0.14	1.05
14	0.20	0.25	1.28	0.21	0.28	1.36
15	0.26	0.31	1.19	0.26	0.23	0.91

SENSORY PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	0.76	0.75	0.99	0.21	0.29	1.35
2	0.35	0.31	0.87	0.45	0.47	1.04
3	0.16	0.22	1.36	0.21	0.21	1.00
4	0.23	0.23	0.99	0.23	0.22	0.96
5	0.23	0.19	0.82	0.24	0.25	1.07
6	0.14	0.15	1.06	0.17	0.17	0.96
7	0.14	0.17	1.25	0.14	0.17	1.28
8	0.08	0.12	1.45	0.08	0.11	1.37
9	0.21	0.22	1.05	0.24	0.23	0.95
10	0.16	0.17	1.07	0.18	0.18	0.98
11	0.27	0.25	0.92	0.25	0.24	0.96
12	0.17	0.16	0.93	0.19	0.19	1.00
13	0.15	0.16	1.07	0.15	0.14	0.93
14	0.25	0.28	1.16	0.50	0.57	1.13
15	0.28	0.28	0.98	0.25	0.24	0.98
AVERAGE	0.24	0.25	1.08	0.24	0.25	1.05
SEM	0.03	0.03	0.03	0.02	0.03	0.02
SD	0.15	0.15	0.18	0.13	0.14	0.12

Ratio are post/pre capsule ingestion values

Pre and post capsule EMG_{MAX} is expressed in volts

CONTROL MEASURES PRE-POST CAPSULE INGESTION M WAVE AMPLITUDE

ENDURANCE PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	7.22	7.30	1.01	8.08	8.56	1.06
2	6.51	5.94	0.91	6.53	6.38	0.98
3	1.93	2.02	1.05	3.72	3.61	0.97
4	3.60	3.44	0.95	3.53	3.48	0.99
5	5.09	4.97	0.98	4.60	4.36	0.95
6	3.31	3.49	1.05	2.42	2.53	1.04
7	1.93	2.57	1.33	2.71	2.63	0.97
8	3.98	3.94	0.99	1.74	1.75	1.01
9	3.31	3.24	0.98	3.87	3.68	0.95
10	2.72	2.72	1.00	2.71	2.77	1.02
11	3.10	2.65	0.85	5.89	5.37	0.91
12	3.04	3.35	1.10	2.59	2.51	0.97
13	5.73	5.77	1.01	2.67	2.62	0.98
14	2.77	2.21	0.80	2.77	4.06	1.47
15	3.18	4.04	1.27	3.12	3.05	0.98

SENSORY PROTOCOL						
Subject No.	CAFFEINE			PLACEBO		
	Precapsule	Postcapsule	Ratio	Precapsule	Postcapsule	Ratio
1	8.32	7.24	0.87	4.34	2.82	0.65
2	6.03	5.07	0.84	6.48	6.32	0.98
3	3.23	3.42	1.06	3.56	3.63	1.02
4	3.50	3.74	1.07	3.37	3.35	0.99
5	4.82	4.37	0.91	4.60	4.52	0.98
6	2.85	2.75	0.97	2.88	3.03	1.05
7	1.50	1.81	1.21	2.69	2.05	0.76
8	1.78	1.59	0.90	2.60	3.29	1.27
9	2.82	2.82	1.00	3.44	3.21	0.93
10	3.32	3.36	1.01	2.64	2.32	0.88
11	5.44	5.13	0.94	5.47	5.37	0.98
12	2.85	2.80	0.98	2.40	2.40	1.00
13	2.44	2.42	0.99	2.85	2.66	0.93
14	3.83	3.96	1.04	6.85	6.75	0.99
15	3.96	3.70	0.93	3.47	3.95	1.14
AVERAGE	3.86	3.77	1.00	3.88	3.78	0.98
SEM	0.31	0.27	0.02	0.29	0.30	0.02
SD	1.70	1.49	0.10	1.61	1.64	0.11

Ratio are post/pre capsule ingestion values

Pre and post capsule M wave amplitude is expressed in volts

ENDURANCE PROTOCOL **LIMIT OF ENDURANCE (T_{LIM})**

SUBJECT No.	PLACEBO		CAFFEINE		CAFFEINE T _{LIM} % change from placebo
	T _{LIM} (sec)	T _{LIM} (contractions)	T _{LIM} (sec)	T _{LIM} (contractions)	
1	91.10	5.18	99.10	5.50	8.78
2	80.14	4.40	101.20	5.80	26.28
3	67.45	3.70	99.47	5.00	47.47
4	81.80	4.76	76.99	4.47	-5.88
5	101.59	5.48	116.97	6.53	15.14
6	117.70	6.80	96.10	5.45	-18.35
7	64.44	3.78	92.03	5.19	42.82
8	72.90	4.16	74.22	4.13	1.81
9	77.30	4.44	74.97	4.28	-3.01
10	101.83	5.56	97.83	5.49	-3.93
11	64.92	3.75	78.35	4.27	20.69
12	71.88	4.23	124.10	7.15	72.65
13	78.02	4.50	78.70	4.27	0.87
14	96.73	5.32	128.57	7.48	32.92
15	120.46	7.00	137.80	8.00	14.40
AVERAGE	85.88	4.87	98.43*	5.53	16.84
SEM	4.54	0.26	5.30	0.32	6.26
SD	18.21	1.02	20.54	1.25	24.24

* Significantly different from placebo (p<.05)

ENDURANCE PROTOCOL **CONTRACTILE CHARACTERISTICS AT T_{LIM}**

Subject No.	TWITCH AMPLITUDE (N)			+dF/dt (N sec ⁻¹)			-dF/dt (N sec ⁻¹)		
	PL T_{LIM}	CF@PL T_{LIM}	CF T_{LIM}	PL T_{LIM}	CF@PL T_{LIM}	CF T_{LIM}	PL T_{LIM}	CF@PL T_{LIM}	CF T_{LIM}
6	43.3		33.4	37.7		38.5	32.5		29.4
4	28.5		12.9	42.2		14.1	17.9		28.2
10	20.2		16.5	31.9		26.8	24.6		16.6
9	12.9		17.2	12.6		15.1	28.5		25.0
13	40.1	18.4	18.4	46.0	22.6	22.6	24.6	26.5	26.5
8	35.4	19.1	19.1	30.5	15.4	15.4	55.8	33.1	33.1
1	0.3	8.4	8.4	10.6	11.1	11.1	24.3	37.2	37.2
15	22.6	27.3	15.3	30.4	17.1	19.9	21.1	31.7	14.3
5	15.8	19.1	6.7	16.4	26.8	6.9	58.0	48.8	56.3
11	54.9	55.9	39.9	50.7	66.7	47.3	58.1	41.4	37.9
2	21.1	26.3	14.8	30.8	30.4	21.3	27.0	24.3	18.9
14	24.9	18.9	3.3	26.2	23.0	9.1	30.3	32.4	29.0
7	50.9	42.1	11.3	55.4	33.7	19.2	30.9	38.4	18.4
3	42.9	40.6	26.4	34.8	40.3	24.2	45.5	31.7	33.8
12	33.6	37.8	11.1	40.8	38.5	14.5	30.5	66.0	46.0
Average	29.8	27.7	17.0	33.1	28.0	20.4	34.0	34.0	30.0
SEM	3.9	3.3	2.5	3.4	3.7	2.8	3.5	3.0	2.9
SD	15.1	14.0	9.8	13.1	15.4	10.8	13.6	11.7	11.4

Subjects are arranged from smallest to greatest change in T_{LIM} with caffeine

Values are expressed as a percent of the first measurement obtained at the beginning of the endurance protocol

PL = placebo CF = caffeine

PL T_{LIM} = value at time closest to the limit of endurance in the placebo trial

CF T_{LIM} = value at time closest to the limit of endurance in the caffeine trial

CF@PL T_{LIM} = value in the caffeine trial that occurs at the time corresponding to the limit of endurance in the placebo trial

ENDURANCE PROTOCOL **ELECTRICAL CHARACTERISTICS AT T_{LM}**

Subject No.	VOLUNTARY ACTIVATION (%)			EMG			M WAVE AMPLITUDE		
	PL T_{LM}	CF@PL T_{LM}	CF T_{LM}	PL T_{LM}	CF@PL T_{LM}	CF T_{LM}	PL T_{LM}	CF@PL T_{LM}	CF T_{LM}
6	84.1		99.2	102.3		153.8	90.8		91.7
4	99.6		98.1	102.3		105.7	107.0		108.8
10	99.6		100.0	129.6		142.4	114.8		126.0
9	100.0		99.6	115.6		115.2	94.1		61.7
13	50.0	70.0	70.0	89.9	114.2	114.2	104.0	110.3	110.3
8	100.0	99.3	98.3	165.6	182.1	190.3	107.6	94.6	94.6
1	93.8	100.0	100.0	168.9	103.9	109.4	107.2	107.5	107.5
15	96.9	100.0	96.4	121.7	132.0	135.1	105.8	95.2	93.1
5	96.8	92.4	97.8	301.8	275.7	370.0	115.5	111.7	118.2
11	77.6	68.2	75.1	105.6	106.6	103.6	98.2	89.4	88.5
2	98.0	89.6	97.4	143.6	140.0	150.0	96.9	94.1	91.2
14	90.9	97.8	90.5	130.2	112.9	123.2	115.9	124.6	142.0
7	92.7	99.6	100.7	157.7	180.0	275.5	144.2	112.5	124.4
3	93.6	81.7	83.7	161.3	211.3	268.0	109.9	131.9	138.1
12	93.7	83.6	96.3	124.1	137.4	285.7	105.2	104.3	104.3
Average	91.2	89.3	93.6	141.3	154.2	176.1	107.8	106.9	106.8
SEM	3.4	3.1	2.5	13.2	13.8	21.5	3.2	3.4	5.4
SD	13.0	11.9	9.7	51.0	53.4	83.3	12.6	13.3	21.1

Subjects are arranged from smallest to greatest change in T_{LM} with caffeine

Values are expressed as a percent of the first measurement obtained at the beginning of the endurance protocol

PL = placebo CF = caffeine

PL T_{LM} = value at time closest to the limit of endurance in the placebo trial

CF T_{LM} = value at time closest to the limit of endurance in the caffeine trial

CF@PL T_{LM} = value in the caffeine trial that occurs at the time corresponding to the limit of endurance in the placebo trial

ENDURANCE PROTOCOL TWITCH AMPLITUDE

PLACEBO (newtons)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
95.62	107.45	130.43	63.09	89.78	123.53	88.04	112.15	104.72	99.41	80.08	46.48	89.06	81.48	109.57
69.23	79.32	103.13	55.28	74.54	112.91	82.81	98.35	81.29	78.79	62.94	38.52	77.42	67.87	98.28
45.73	52.40	73.55	39.28	53.31	98.58	61.65	78.79	49.82	62.41	52.78	30.86	59.41	53.38	83.11
31.24	38.52	55.96	26.62	38.75	80.08	44.82	60.36	25.93	43.83	43.98	21.91	46.03	37.95	69.92
15.92	22.67		17.97	26.62	66.65		39.73	13.50	33.14		15.62	35.72	28.21	60.36
0.30				14.18	53.46				20.09				20.32	45.04
					42.01									32.99
														24.72

PLACEBO (% initial)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
72.40	73.82	79.07	87.62	83.02	91.41	94.06	87.89	77.62	79.25	78.60	82.87	86.93	83.29	89.69
47.82	48.76	56.40	62.26	59.38	79.80	70.03	70.25	47.57	62.78	65.91	66.39	66.71	65.52	75.85
32.67	35.85	42.91	42.19	43.16	64.82	50.90	53.82	24.76	44.09	54.92	47.15	51.68	46.58	63.81
16.65	21.10		28.49	29.65	53.96		35.43	12.89	33.33		33.61	40.10	34.62	55.09
0.32				15.79	43.28				20.21				24.94	41.11
					34.01									30.10
														22.56

CAFFEINE (newtons)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
112.53	118.75	128.23	61.65	105.02	135.36	91.60	117.38	100.85	96.53	63.85	56.19	97.59	71.89	124.44
94.26	98.50	102.37	48.83	85.61	130.12	72.27	93.04	75.30	77.50	58.05	47.62	78.48	61.27	109.35
68.02	67.11	67.11	31.55	64.76	98.73	53.84	65.06	38.45	60.28	46.14	37.91	52.17	46.86	92.13
46.03	45.12	52.10	21.31	45.57	77.57	38.52	43.83	15.17	49.29	35.68	27.98	32.15	34.65	72.19
27.83	31.24	33.90	7.96	27.00	58.84	20.70	22.37	17.37	33.14	25.48	21.23	17.97	22.03	55.81
9.48	17.52			20.02	45.19	10.31			15.92		16.53		13.61	42.62
				7.05							12.51		7.85	33.97
											6.22		2.39	24.87
														19.03

CAFFEINE (% initial)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
83.76	82.95	79.83	79.21	81.52	96.13	78.89	79.26	74.66	80.28	90.91	84.75	80.42	85.23	87.87
60.44	56.51	52.34	51.17	61.66	72.94	58.77	55.43	38.12	62.45	72.27	67.48	53.46	65.19	74.04
40.90	37.99	40.63	34.56	43.39	57.31	42.05	37.34	15.04	51.06	55.88	49.80	32.94	48.21	58.01
24.73	26.31	26.43	12.92	25.70	43.47	22.60	19.06	17.22	34.33	39.90	37.79	18.41	30.64	44.85
8.42	14.75			19.06	33.39	11.26			16.50		29.42		18.93	34.25
				6.71							22.27		10.92	27.30
											11.07		3.32	19.99
														15.30

Twitch amplitudes for every subjects evoked between isometric contractions during the endurance protocol.

Values are expressed in newtons and as a % of the initial measurement as indicated.

ENDURANCE PROTOCOL

+dF/dt

PLACEBO (newtons)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1637.92	1478.68	2280.06	1023.70	1433.18	1812.33	1478.68	1789.58	1683.42	1448.35	588.72	743.13	1327.02	1084.36	1645.51
1114.70	1023.70	1713.75	1000.95	1251.19	1562.09	1258.77	1600.01	1296.89	1114.70	417.06	599.05	1156.40	921.33	1509.01
858.67	773.47	1213.28	818.96	872.04	1425.80	902.38	1145.03	882.47	796.21	348.82	492.89	951.66	882.47	1205.69
599.05	470.14	796.21	588.72	781.05	1213.28	818.96	1046.45	500.48	538.39	288.15	409.48	743.13	519.43	1220.86
386.73	454.98		432.23	508.06	894.79		545.97	212.32	462.56		303.32	610.43	405.89	947.87
174.41				235.07	697.63				462.56				284.36	841.71
					682.47									581.14
														500.48

PLACEBO (% Initial)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
68.06	69.23	74.83	97.78	87.30	86.19	85.13	89.41	77.03	76.96	73.33	80.61	87.14	84.97	91.71
52.31	52.31	52.98	80.00	60.85	78.66	61.03	83.98	40.54	54.97	61.33	66.33	71.71	62.94	73.27
36.57	31.79	34.77	55.56	54.50	66.95	55.38	58.47	29.73	37.17	50.67	55.10	56.00	47.90	74.19
23.61	30.77		42.22	35.45	49.37		30.51	12.61	31.94		40.82	48.00	37.41	57.60
10.65				16.40	38.49				31.94				26.22	51.15
					37.66									34.10
														30.41

CAFFEINE (newtons)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1918.49	1744.08	2070.15	970.62	1865.41	1971.58	1483.52	1728.92	1708.17	1387.69	784.84	887.21	1410.43	1171.57	1903.33
1584.84	1463.52	1736.50	811.38	1577.26	1645.51	1069.20	1387.69	1311.85	1251.19	792.42	735.55	1152.81	951.66	1675.84
955.46	1023.70	1137.45	470.14	1243.61	1539.34	773.47	1129.86	674.88	1000.95	553.56	644.55	818.96	796.21	1433.18
629.39	705.22	834.13	303.32	841.71	1054.03	492.89	530.81	310.90	561.14	523.22	492.89	454.98	584.93	1081.95
553.56	530.81	500.48	136.49	705.22	796.21	272.99	265.40	257.82	485.31	371.57	341.23	318.48	329.86	818.96
212.32	371.57			500.48	758.30	280.57			371.57		288.15		268.19	530.81
				128.91							128.91		163.03	326.07
											128.91		106.16	219.91
														379.15

CAFFEINE (% Initial)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
82.61	83.91	83.88	83.59	84.55	83.46	73.06	80.26	76.89	90.16	100.97	82.91	81.72	81.23	88.05
49.80	58.70	54.95	48.44	66.67	78.08	52.85	65.35	39.56	72.13	70.53	72.85	58.06	67.96	75.30
32.81	40.43	40.29	31.25	45.12	53.46	33.68	30.70	18.22	40.44	66.67	55.56	32.26	48.22	57.37
28.85	30.43	24.16	14.06	37.80	40.38	18.65	15.35	15.11	34.97	47.34	38.46	22.58	28.16	43.03
11.07	21.30			26.83	38.46	19.17			26.78		32.48		22.98	27.89
				6.91							14.53		13.92	17.13
											14.53		9.06	11.55
														19.92

+ dF/dt values for every subject from twitches evoked between isometric contractions during the endurance protocol.

Values are expressed in newtons and as a % of the initial measurement as indicated.

ENDURANCE PROTOCOL -dF/dt

PLACEBO (newtons)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
-1061.62	-825.12	-1000.95	-636.97	-614.22	-887.21	-832.71	-788.63	-832.71	-864.46	-326.07	-447.40	-724.17	-683.51	-1008.54
-758.30	-652.14	-743.13	-394.31	-482.89	-743.13	-773.47	-674.88	-688.72	-743.13	-326.07	-386.73	-549.78	-454.98	-765.88
-401.90	-348.82	-581.47	-288.15	-385.73	-591.47	-583.56	-599.05	-462.56	-553.56	-257.82	-250.24	-341.23	-352.61	-674.88
-280.57	-310.90	-454.98	-280.57	-204.74	-470.14	-288.15	-385.73	-204.74	-355.40	-189.57	-197.16	-326.07	-238.86	-600.48
-371.57	-250.24		-113.74	-219.81	-600.48		-439.61	-265.40	-242.66		-136.49	-178.20	-197.18	-379.15
-257.82				-356.40	-477.73				-212.32				-200.95	-288.15
					-288.15									-379.15
														-212.32

PLACEBO (% Initial)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
71.43	70.49	74.24	61.90	80.25	83.76	82.93	85.58	80.98	85.96	100.00	86.44	75.92	68.57	75.94
37.86	37.70	59.09	45.24	62.96	66.67	59.35	75.96	49.59	64.04	79.07	55.93	47.12	53.14	66.92
26.43	33.61	45.45	44.05	33.33	52.99	30.69	49.04	21.95	41.23	58.14	44.07	45.03	36.00	49.62
35.00	27.05		17.96	35.80	56.41		56.77	28.46	28.07		30.51	24.61	29.71	37.59
24.29				58.02	53.85				24.56				30.29	28.57
					32.48									37.59
														21.05

CAFFEINE (newtons)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
-1099.53	-841.71	-1064.03	-691.47	-606.84	-1160.19	-647.87	-917.54	-909.95	-1099.53	-659.72	-379.15	-773.47	-667.30	-1220.86
-735.55	-765.88	-661.14	-326.07	-482.56	-1046.45	-765.88	-743.13	-688.72	-661.14	-443.60	-363.98	-545.97	-587.68	-894.79
-667.30	-356.40	-600.48	-303.32	-447.40	-644.55	-447.40	-326.07	-333.65	-379.15	-388.11	-280.57	-333.65	-405.69	-720.38
-417.06	-265.40	-333.65	-212.32	-409.46	-667.30	-363.98	-379.15	-379.15	-477.73	-272.99	-242.66	-265.40	-333.65	-615.64
-250.24	-204.74	-356.40	-168.63	-212.32	-578.31	-326.07	-303.32	-227.49	-318.48	-250.24	-250.24	-204.74	-261.61	-371.57
-409.46	-159.24			-265.74	-341.23	-174.41			-181.99		-174.41		-216.11	-409.46
				-341.23							-212.32		-185.78	-386.73
											-174.41		-193.37	-424.65
														-174.41

CAFFEINE (% Initial)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
66.90	90.99	53.24	55.13	76.25	90.20	80.90	80.99	62.50	51.03	67.24	96.00	70.59	68.07	73.29
60.69	42.34	47.48	51.28	73.75	55.56	47.20	35.54	36.67	34.48	60.34	74.00	43.14	60.80	59.01
37.93	31.53	31.65	35.90	67.50	57.92	38.40	41.32	41.67	43.45	41.38	64.00	34.31	50.00	42.24
22.76	24.32	33.81	28.20	35.00	49.67	34.40	33.06	25.00	28.97	37.93	66.00	26.47	39.20	30.43
37.24	16.92			48.75	29.41	18.40			16.55		46.00		32.39	33.54
				56.25							56.00		27.64	31.66
											46.00		26.98	34.78
														14.29

- dF/dt values for every subject from twitches evoked between isometric contractions during the endurance protocol.

Values are expressed in newtons and as a % of the initial measurement as indicated.

ENDURANCE PROTOCOL VOLUNTARY ACTIVATION

PLACEBO (%)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
89.06	84.47	81.10	64.90	71.45	84.84	83.38	73.90	74.58	83.45	87.50	71.29	70.75	85.11	77.02
87.51	85.37	87.43	78.74	76.40	75.82	89.74	85.50	79.94	83.93	82.41	78.35	64.84	84.58	77.70
89.05	98.26	79.28	77.61	81.22	77.69	87.95	84.60	92.85	97.08	63.22	69.53	62.35	93.25	78.47
97.57	94.88	93.63	87.75	83.95	71.40	92.72	100.00	97.95	92.91	77.59	83.39	28.85	97.20	82.10
93.81	97.99		99.58	91.74	80.09		100.00	100.00			93.69	50.00	98.39	95.35
				98.79	77.59				99.62				90.86	95.96
					84.12									99.77
														96.93

PLACEBO (% Initial)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
98.27	101.06	107.79	121.32	106.92	89.37	107.64	115.70	107.19	100.57	94.18	109.90	91.64	99.38	100.88
100.00	116.32	97.75	119.57	113.67	91.58	105.48	114.48	124.49	116.34	72.25	97.54	88.12	109.57	101.87
109.56	112.32	115.45	135.20	117.49	84.16	111.21	135.32	131.33	111.34	88.67	116.98	37.95	114.21	106.60
105.34	116.00		153.42	128.39	94.41		135.32	134.08	119.84		131.42	70.67	115.60	123.79
				135.46	91.46				119.38				106.75	124.58
					99.15									129.53

CAFFEINE (%)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
74.66	84.23	75.58	78.75	69.10	73.56	86.42	83.72	72.56	81.30	67.40	67.61	81.04	75.00	76.78
87.61	85.30	77.70	86.80	71.92	85.08	93.91	87.53	83.48	88.94	73.29	70.38	81.64	76.61	80.10
89.63	90.28	85.76	88.22	78.92	86.94	91.97	91.14	89.55	88.68	80.85	65.80	82.56	81.96	87.49
96.21	88.24	81.66	88.58	80.67	94.92	99.61	85.50	94.50	88.46	68.23	73.71	93.40	83.37	89.18
99.46	89.56	83.67	98.10	66.57	94.33	88.64	99.32	89.56	94.51	75.15	83.57	70.04	87.61	88.72
100.00	97.40			92.42	99.16	100.00			100.00		80.73		97.77	83.63
				97.85							95.76		88.89	96.43
											96.34		90.48	100.00
														96.41

CAFFEINE (% Initial)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
117.34	101.27	102.81	113.09	104.09	115.67	108.67	104.55	115.08	109.40	108.73	104.10	100.74	102.15	104.32
120.05	107.19	113.48	114.94	114.22	118.20	106.42	108.88	123.42	109.07	119.96	97.32	101.87	109.28	113.94
128.86	104.76	108.05	128.43	117.03	129.04	115.25	114.07	130.24	108.80	101.23	109.02	115.25	111.16	116.15
133.21	106.33	110.71	127.81	96.35	128.24	102.57	118.63	137.22	116.24	111.50	123.61	86.43	116.81	115.55
133.94	115.64			133.76	134.81	115.71			123.00		119.41		130.36	108.92
				141.61							141.63		118.52	125.59
											142.49		120.63	130.24
														125.57

Voluntary activation values for every subject, obtained during each submaximal contraction
Values are expressed as a percent of maximum activation and as a percent of the initial value obtained.

ENDURANCE PROTOCOL **M WAVE AMPLITUDE**

PLACEBO (volts)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
8.8	6.7	4.0	3.7	4.6	2.5	2.4	1.8	3.9	2.7	5.6	2.6	2.6	3.6	2.8
9.3	6.9	4.1	3.7	4.6	2.5	2.9	1.9	3.9	2.8	5.6	2.6	2.6	3.7	3.0
9.4	6.9	4.3	3.7	4.8	2.5	2.9	2.1	3.8	2.8	5.6	2.7	2.5	3.8	3.1
9.7	6.7	4.3	3.8	5.0	2.5	3.4	2.0	3.8	2.9	5.5	2.7	2.6	4.0	3.1
9.9	6.5		3.9	5.2	2.4		2.0	3.7	3.0		2.7	2.7	4.0	3.1
9.4				5.3	2.3				3.1				4.2	3.0
					2.3									3.1
														2.9

PLACEBO (%Initial)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
105.6	103.4	104.1	100.8	101.6	96.8	121.0	103.7	100.1	101.4	100.1	101.3	98.4	102.8	107.0
106.4	103.3	107.5	101.5	105.3	97.4	123.9	113.2	97.1	104.5	101.0	102.4	96.6	103.4	111.3
110.0	100.5	109.9	102.9	109.2	97.4	144.2	106.7	96.0	107.6	98.2	103.7	99.5	109.6	111.2
112.4	96.9		107.0	114.2	95.6		107.6	94.1	111.3		105.2	104.0	110.8	112.3
107.2				115.5	91.6				114.8				115.9	109.6
					90.8									110.4
														105.8

CAFFEINE (volts)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
6.7	6.4	2.3	3.7	5.2	3.4	2.3	4.1	3.3	2.8	2.7	3.4	5.5	2.2	4.2
6.8	6.4	2.6	3.8	5.2	3.3	2.5	4.2	3.2	2.8	2.4	3.4	6.0	2.2	4.0
7.0	6.3	2.8	3.8	5.4	3.3	2.6	4.1	3.0	2.9	2.5	3.4	6.8	2.3	4.1
7.1	6.3	3.0	4.0	5.4	3.3	2.6	4.1	3.0	3.1	2.4	3.5	7.2	2.4	4.3
7.2	6.0	3.2	4.1	5.6	3.1	2.8	3.9	2.0	3.3	2.4	3.5	6.0	2.4	4.1
7.2	5.8			5.8	3.1	2.9			3.5		3.6		2.7	4.1
				6.1							3.8		3.0	4.0
											3.5		3.1	4.0
														3.9

CAFFEINE (% Initial)														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
101.6	100.6	111.2	102.7	100.6	99.4	107.0	101.2	96.9	102.4	91.7	101.2	109.5	102.8	95.8
103.7	99.7	121.9	102.8	103.0	98.9	114.1	99.9	93.0	105.6	93.7	102.0	124.4	104.1	97.7
105.2	98.5	131.9	107.4	103.7	96.9	112.5	98.3	91.2	114.1	89.4	102.5	130.5	108.6	104.1
106.7	94.1	138.1	109.8	106.9	93.4	123.3	94.6	61.7	121.2	88.5	104.3	110.3	110.9	98.7
107.5	91.2			111.7	91.7	124.4			126.0		107.2		124.6	98.4
				118.2							112.9		137.4	95.2
											104.3		142.0	95.6
														93.1

M wave amplitude values for every subject, obtained during each submaximal contraction performed. Values are expressed in volts and as a percent of the initial value obtained.

ENDURANCE PROTOCOL EMG FOR PLACEBO TRIAL

97

1		2		3		4	
TIME	EMG	TIME	EMG	TIME	EMG	TIME	EMG
10.6	100.0	7.7	100.0	14.1	100.0	13.2	100.0
21.0	85.1	20.3	105.8	22.5	132.2	21.3	91.8
29.3	89.4	30.9	101.8	31.4	120.8	33.1	93.1
41.7	86.1	39.9	114.5	41.2	126.1	40.1	92.2
50.3	93.0	50.8	139.8	51.5	130.1	51.6	93.6
60.5	106.1	60.9	112.0	60.0	137.3	61.0	94.6
70.3	127.6	71.6	137.1	69.7	132.7	72.1	96.3
81.1	143.4	81.8	141.2	79.6	151.8	81.1	104.7
86.8	143.7	92.5	160.1	93.4	190.2	90.3	103.5
93.5	168.9	100.9	143.6	99.1	161.3	100.4	102.3

5		6		7		8	
TIME	EMG	TIME	EMG	TIME	EMG	TIME	EMG
10.2	100.0	8.7	100.0	10.1	100.0	17.4	100.0
20.9	112.9	18.9	106.8	19.3	107.6	22.7	104.0
30.0	119.3	31.0	98.5	33.7	147.7	31.4	113.6
39.1	131.0	41.1	99.2	42.0	100.0	41.0	118.1
50.7	159.6	50.8	98.9	49.8	123.3	49.2	118.8
58.4	170.2	62.7	102.8	60.7	131.9	64.2	118.6
70.6	203.1	70.8	104.0	69.8	133.5	72.2	125.4
80.5	222.3	81.2	119.0	81.2	142.4	80.1	138.6
89.3	251.9	91.4	118.4	90.3	176.1	92.0	165.3
100.9	301.8	96.3	102.3	95.8	157.7	100.0	165.6

9		10		11		12	
TIME	EMG	TIME	EMG	TIME	EMG	TIME	EMG
12.9	100.0	12.5	100.0	8.8	100.0	9.0	100.0
21.7	99.6	19.4	98.2	21.1	107.6	19.3	111.5
32.2	104.1	30.4	97.8	34.8	105.8	30.3	105.7
40.4	107.7	40.3	99.5	40.6	113.5	40.4	114.6
53.8	113.0	51.4	102.5	50.4	105.0	50.8	103.9
62.0	110.0	61.9	110.3	61.1	117.7	60.9	123.4
69.3	114.9	70.9	108.3	70.5	81.3	70.5	125.8
80.2	104.4	80.9	112.1	79.3	105.1	79.1	149.7
91.0	120.7	90.7	121.1	89.7	135.3	83.9	154.1
100.3	115.6	100.1	129.6	100.6	105.6	92.7	124.1

13		14		15	
TIME	EMG	TIME	EMG	TIME	EMG
13.5	100.0	8.6	100.0	4.1	100.0
21.1	96.7	20.6	107.7	20.1	102.2
32.8	96.5	31.4	106.5	31.1	108.7
40.2	91.6	38.7	111.3	40.4	113.6
52.8	94.4	50.8	112.4	50.5	113.4
61.1	92.5	62.7	112.1	60.1	113.0
73.1	92.2	70.9	117.2	71.4	114.2
80.5	97.8	80.9	119.5	79.3	126.6
93.1	97.0	89.3	125.4	89.2	122.9
97.7	89.9	98.6	130.2	92.2	121.7

TIME is expressed as a percent of placebo T_{LIM} and EMG is expressed as a percent of the initial measurement obtained at the beginning of the endurance protocol.

ENDURANCE PROTOCOL EMG FOR CAFFEINE TRIAL

98

1		2		3		4	
TIME	EMG	TIME	EMG	TIME	EMG	TIME	EMG
19.1	100.0	9.7	100.0	12.7	100.0	13.63	100.00
29.6	100.4	19.0	111.4	21.1	128.0	22.77	95.87
41.0	83.9	31.3	114.2	30.2	123.7	33.14	96.79
51.7	82.8	41.4	132.6	40.2	115.9	44.16	93.93
60.4	74.6	51.8	122.9	53.0	125.8	56.27	102.07
71.1	99.9	60.2	115.3	61.6	145.7	65.32	106.43
81.0	86.8	70.9	144.8	70.2	146.0	70.70	107.86
89.9	101.8	80.9	136.1	78.7	163.5	77.96	111.67
98.1	103.9	91.5	160.1	91.7	180.2	84.54	113.87
103.67	119.57	101.0	140.0	102.2	211.3	92.37	109.57
107.6	109.4	124.3	150.0	145.1	268.0	99.40	105.69

5		6		7		8	
TIME	EMG	TIME	EMG	TIME	EMG	TIME	EMG
9.0	100.0	11.5	100.0	12.2	100.0	14.7	100.0
19.9	121.3	20.1	91.4	22.6	121.9	20.1	109.4
30.4	120.1	28.3	106.7	31.0	132.3	30.4	115.6
40.3	146.7	34.6	101.4	42.7	131.1	40.8	139.1
50.7	165.4	41.8	102.2	52.5	148.3	50.6	143.8
60.2	173.6	52.1	106.1	62.3	124.1	61.6	166.0
70.5	209.3	60.1	110.2	71.1	154.2	70.4	151.3
80.7	198.9	69.2	118.3	79.4	187.6	78.4	147.4
93.4	241.1	74.5	121.3	91.8	180.1	90.1	151.1
100.3	275.7	83.4	124.0	100.3	180.0	99.0	182.1
114.4	370.0	90.0	153.8	138.0	275.5	101.7	190.3

9		10		11		12	
TIME	EMG	TIME	EMG	TIME	EMG	TIME	EMG
10.0	100.0	10.5	100.0	10.5	100.0	15.5	100.0
18.1	101.8	17.6	109.8	19.4	95.4	24.3	116.0
25.6	101.7	26.0	106.5	28.7	109.3	29.2	110.0
36.2	103.3	34.3	105.0	42.9	99.6	41.2	115.9
44.9	101.5	44.6	105.4	51.9	111.4	49.6	111.0
58.3	106.9	52.7	108.8	57.6	123.3	61.9	111.5
67.2	106.6	62.7	110.8	70.5	117.2	71.4	117.3
78.1	117.4	71.0	116.6	79.5	98.3	80.9	123.3
86.0	112.2	81.9	120.6	90.0	130.1	90.9	144.5
90.9	112.3	94.5	140.7	99.2	106.6	99.4	137.4
99.7	115.2	99.4	142.4	119.5	103.6	162.7	285.7

13		14		15	
TIME	EMG	TIME	EMG	TIME	EMG
16.0	100.0	8.0	100.0	11.4	100.0
20.6	95.0	20.3	103.7	20.2	96.8
29.5	95.8	31.0	104.4	29.5	104.2
40.0	107.8	41.6	103.8	40.5	102.0
50.5	102.0	51.7	110.3	51.0	105.5
61.0	104.5	60.1	105.6	60.5	115.6
70.6	114.0	70.1	109.5	70.9	117.2
81.6	120.7	81.0	112.4	80.9	117.2
90.0	117.2	91.6	116.3	91.5	120.9
92.38	117.6	100.1	112.9	100.1	132.0
100.8	114.2	131.3	123.2	113.2	135.1

TIME is expressed as a percent of placebo T_{LM} and EMG is expressed as a percent of the initial measurement obtained at the beginning of the endurance protocol.

ENDURANCE PROTOCOL **Regression Parameters: Twitch Amplitude**

Subject no.	PLACEBO			CAFFEINE		
	r	Yo	a	r	Yo	a
1	0.99	112.81	-1.11	1.00	116.72	-1.02
2	0.98	113.54	-1.06	0.99	112.53	-0.98
3	0.99	117.95	-1.06	0.99	115.19	-0.93
4	0.99	120.11	-1.08	1.00	120.89	-1.26
5	0.99	117.94	-0.95	0.99	112.54	-0.89
6	1.00	111.86	-0.65	0.99	116.41	-0.81
7	0.96	120.21	-0.98	0.99	114.35	-1.01
8	1.00	117.22	-0.93	1.00	117.25	-1.13
9	0.99	116.89	-1.26	0.94	114.69	-1.27
10	0.99	109.41	-0.84	1.00	113.23	-0.90
11	0.95	113.60	-0.88	0.99	115.62	-0.81
12	1.00	115.37	-0.99	0.98	105.68	-0.72
13	0.99	113.40	-0.87	0.99	116.07	-1.11
14	0.99	112.44	-0.85	0.98	108.38	-0.82
15	1.00	109.63	-0.64	0.98	105.37	-0.63
AVERAGE	0.99	114.83	-0.94	0.99	113.66	-0.95
SEM	0.003	0.89	0.04	0.003	1.11	0.05
SD	0.01	3.45	0.17	0.01	4.30	0.19

$$Y = Y_o + ax$$

ENDURANCE PROTOCOL
Regression Parameters: Voluntary Activation

Subject no.	PLACEBO			CAFFEINE		
	r	Y _o	a	r	Y _o	a
1	0.62	86.57	0.10	0.92	77.39	0.24
2	0.80	83.32	0.16	0.84	82.88	0.10
3	0.14	79.41	0.11	0.67	75.85	0.07
4	0.95	62.55	0.37	0.92	77.13	0.25
5	0.99	68.05	0.28	0.69	64.98	0.24
6	0.00	78.32	0.01	0.93	75.52	0.31
7	0.80	83.33	0.10	0.44	88.18	0.07
8	0.92	72.72	0.28	1.00	81.92	0.16
9	0.96	72.98	0.29	0.98	72.29	0.28
10	0.86	82.70	0.19	0.91	81.13	0.18
11	0.46	88.04	-0.19	0.00	70.41	0.04
12	0.73	67.22	0.21	0.92	61.23	0.19
13	0.59	73.64	-0.35	0.00	84.04	-0.05
14	0.56	85.10	0.11	0.83	74.99	0.15
15	0.91	73.52	0.25	0.85	77.73	0.17
AVERAGE	0.69	77.16	0.13	0.73	76.38	0.16
SEM	0.077	2.00	0.05	0.085	1.84	0.03
SD	0.30	7.75	0.19	0.33	7.13	0.10

$$Y = Y_o + ax$$

ENDURANCE PROTOCOL **Regression Parameters: EMG**

Subject no.	PLACEBO			CAFFEINE		
	r	Yo	a	r	Yo	a
1	0.88	65.15	0.90	0.49	82.21	0.21
2	0.88	92.50	0.59	0.86	102.22	0.44
3	0.87	97.35	0.73	0.96	78.38	1.20
4	0.65	91.06	0.11	0.80	92.77	0.19
5	0.98	59.01	2.15	0.95	59.64	2.19
6	0.54	97.36	0.14	0.86	83.91	0.55
7	0.80	94.17	0.68	0.93	81.36	1.19
8	0.93	84.89	0.73	0.92	94.49	0.85
9	0.81	98.11	0.19	0.91	97.08	0.18
10	0.92	89.82	0.32	0.88	93.05	0.41
11	0.21	102.32	0.10	0.31	102.51	0.10
12	0.78	94.12	0.51	0.87	63.41	1.07
13	0.44	97.60	-0.05	0.89	91.94	0.27
14	0.96	98.34	0.29	0.95	98.50	0.17
15	0.93	99.23	0.27	0.96	91.02	0.37
AVERAGE	0.77	90.73	0.51	0.84	87.50	0.63
SEM	0.057	3.22	0.14	0.048	3.32	0.15
SD	0.22	12.47	0.53	0.19	12.85	0.58

$$Y = Y_o + ax$$

MAXIMAL CONTRACTILE CHARACTERISTICS PRE & POST ENDURANCE PROTOCOL

SUBJECT No.	FORCE						TWITCH AMPLITUDE					
	PLACEBO			CAFFEINE			PLACEBO			CAFFEINE		
	PRE	POST	RATIO	PRE	POST	RATIO	PRE	POST	RATIO	PRE	POST	RATIO
1	680.76	185.10	0.27	624.72	308.10	0.49	103.77	0.53	0.01	106.39	18.35	0.17
2	595.66	339.79	0.57	573.54	363.91	0.63	98.35	23.28	0.24	115.00	19.72	0.17
3	493.78	308.40	0.62	536.29	299.60	0.56	116.72	57.10	0.49	136.06	29.27	0.22
4	255.36	180.40	0.71	309.31	176.99	0.57	67.72	21.91	0.32	72.00	9.33	0.13
5	457.22	260.40	0.57	478.14	299.07	0.63	104.64	18.05	0.17	108.55	9.18	0.08
6	702.11	629.99	0.90	763.78	714.62	0.94	110.29	62.48	0.57	126.54	57.40	0.45
7	456.76	292.48	0.64	429.73	266.92	0.62	97.18	46.71	0.48	90.58	15.70	0.17
8	540.19	453.08	0.84	652.93	355.26	0.54	101.45	48.61	0.48	107.83	19.64	0.18
9	445.16	315.45	0.71	482.93	345.78	0.72	98.86	16.76	0.17	104.68	8.95	0.09
10	361.59	203.53	0.56	353.57	243.67	0.69	84.13	18.43	0.22	82.86	12.66	0.15
11	320.03	311.36	0.97	426.31	421.77	0.99	60.74	24.19	0.40	55.75	66.12	1.19
12	427.86	156.06	0.36	321.29	123.45	0.38	108.42	18.96	0.17	78.14	10.09	0.13
13	601.99	563.26	0.94	602.81	225.59	0.37	128.43	79.01	0.62	145.37	15.01	0.10
14	717.58	425.25	0.59	623.59	418.66	0.67	117.50	58.92	0.50	108.59	7.51	0.07
15	470.41	336.23	0.71	521.59	312.95	0.60	115.81	36.63	0.32	113.85	20.25	0.18
AVG	501.76	330.72	0.66	513.37	325.10	0.63	100.93	35.44	0.34	103.48	21.28	0.23
SEM	35.60	35.57	0.05	33.79	34.98	0.04	4.73	5.71	0.05	6.24	4.52	0.07
SD	137.89	137.75	0.20	130.86	135.47	0.17	18.31	22.11	0.18	24.16	17.52	0.28

Force and twitch amplitude pre and post endurance protocol values are expressed in newtons.

Ratio is the post/pre endurance protocol value.

MAXIMAL CONTRACTILE CHARACTERISTICS PRE & POST ENDURANCE PROTOCOL

SUBJECT No.	+dF/dt						-dF/dt					
	PLACEBO			CAFFEINE			PLACEBO			CAFFEINE		
	PRE	POST	RATIO	PRE	POST	RATIO	PRE	POST	RATIO	PRE	POST	RATIO
1	1827.50	144.08	0.08	1709.98	417.06	0.24	-993.37	-447.40	0.45	-1019.91	-181.99	0.18
2	1444.56	409.48	0.28	1516.60	424.65	0.28	-858.77	-310.90	0.36	-1057.83	-83.41	0.08
3	2085.32	909.95	0.44	2164.94	470.14	0.22	-963.04	-288.15	0.30	-1103.32	-272.99	0.25
4	1084.37	477.73	0.44	1145.03	219.91	0.19	-627.49	-151.66	0.24	-587.68	-144.08	0.25
5	1634.13	310.90	0.19	1713.75	379.15	0.22	-750.71	-288.15	0.38	-739.34	-197.16	0.27
6	1474.89	758.30	0.51	1745.98	841.71	0.48	-849.29	-477.73	0.56	-966.83	-500.48	0.52
7	1626.55	849.29	0.52	1444.56	197.16	0.14	-1038.87	-333.65	0.32	-921.33	-295.74	0.32
8	1591.73	690.05	0.43	1672.05	227.49	0.14	-884.98	-485.31	0.55	-970.62	-341.23	0.35
9	1529.87	219.91	0.14	1719.44	136.49	0.08	-913.75	-288.15	0.32	-762.12	-348.82	0.46
10	1328.90	272.99	0.21	1370.62	333.65	0.24	-752.61	-288.15	0.38	-748.82	-242.66	0.32
11	712.80	219.91	0.31	1027.41	894.79	0.87	-586.42	-265.40	0.45	-822.74	-439.81	0.53
12	1579.15	265.40	0.17	1103.33	189.57	0.17	-688.14	-189.57	0.28	-527.01	-128.91	0.24
13	2400.01	1205.69	0.50	2066.36	371.57	0.18	-1249.28	-341.23	0.27	-1042.66	-88.25	0.07
14	2127.03	667.30	0.31	1907.12	485.31	0.25	-1417.86	-485.31	0.34	-1235.86	-447.40	0.36
15	1660.67	553.56	0.33	1728.92	303.32	0.18	-987.67	-265.40	0.27	-1071.10	-280.57	0.26
AVG	1607.16	530.30	0.32	1602.40	392.80	0.26	-904.15	-327.08	0.37	-905.14	-264.90	0.30
SEM	106.49	79.96	0.04	86.70	57.08	0.05	57.56	26.82	0.03	51.77	34.52	0.04
SD	412.45	309.68	0.15	335.79	221.08	0.19	222.93	103.89	0.10	200.51	133.68	0.14

+ dF/dt and - dF/dt pre and post endurance protocol values are expressed in Nsec⁻¹

Ratio is the post/pre endurance protocol value.

MAXIMAL ELECTRICAL CHARACTERISTICS PRE & POST ENDURANCE PROTOCOL

SUBJECT No.	M WAVE AMPLITUDE						EMG					
	PLACEBO			CAFFEINE			PLACEBO			CAFFEINE		
	PRE	POST	RATIO	PRE	POST	RATIO	PRE	POST	RATIO	PRE	POST	RATIO
1	5.69	9.06	1.59	7.27	7.01	0.96	0.48	0.61	1.26	0.66	0.42	0.63
2	6.35	6.54	1.03	5.50	5.74	1.04	0.46	0.45	0.97	0.37	0.50	1.35
3	3.62	4.35	1.20	2.72	3.26	1.20	0.20	0.22	1.08	0.16	0.22	1.38
4	3.41	3.86	1.13	3.59	3.82	1.06	0.22	0.24	1.08	0.24	0.23	0.98
5	4.44	5.13	1.16	4.67	5.85	1.25	0.25	0.38	1.51	0.24	0.45	1.85
6	2.78	2.38	0.86	3.12	3.27	1.05	0.15	0.16	1.07	0.22	0.28	1.31
7	2.34	3.53	1.51	2.19	2.57	1.17	0.18	0.25	1.40	0.15	0.20	1.34
8	2.52	1.95	0.77	2.77	4.08	1.47	0.10	0.11	1.06	0.13	0.21	1.84
9	3.44	3.68	1.07	3.03	2.90	0.96	0.23	0.27	1.16	0.21	0.29	1.34
10	2.54	3.25	1.28	3.04	3.45	1.14	0.18	0.21	1.15	0.18	0.26	1.47
11	5.37	5.46	1.02	3.89	2.30	0.59	0.31	0.33	1.05	0.24	0.17	0.74
12	2.45	2.67	1.09	3.07	3.58	1.16	0.17	0.19	1.10	0.16	0.27	1.66
13	2.64	2.58	0.98	4.09	7.46	1.82	0.14	0.15	1.05	0.32	0.39	1.24
14	5.41	4.05	0.75	3.09	3.06	0.99	0.43	0.27	0.84	0.27	0.27	1.02
15	3.50	2.93	0.84	3.87	4.23	1.09	0.24	0.28	1.18	0.29	0.34	1.18
AVG	3.77	4.09	1.08	3.73	4.17	1.13	0.25	0.27	1.12	0.26	0.30	1.28
SEM	0.35	0.48	0.06	0.33	0.41	0.07	0.03	0.03	0.05	0.03	0.03	0.09
SD	1.35	1.85	0.24	1.29	1.60	0.27	0.12	0.13	0.19	0.13	0.10	0.33

M wave peak to peak amplitude and EMG pre and post endurance protocol values are expressed in volts.
Ratio is the post/pre endurance protocol value.

MAXIMAL ELECTRICAL CHARACTERISTICS PRE & POST ENDURANCE PROTOCOL

SUBJECT No.	VOLUNTARY ACTIVATION (%)					
	PLACEBO			CAFFEINE		
	PRE	POST	RATIO	PRE	POST	RATIO
1	99.31	100.00	1.01	99.97	85.54	0.86
2	97.81	100.00	1.02	99.55	98.08	0.99
3	93.36	84.73	0.91	95.11	90.16	0.95
4	99.36	99.31	1.00	99.60	93.50	0.94
5	99.15	96.22	0.97	99.10	100.00	1.01
6	98.01	99.88	1.02	98.41	98.81	1.00
7	97.03	100.00	1.03	99.11	96.62	0.97
8	95.65	98.91	1.03	96.73	99.23	1.03
9	98.76	99.10	1.00	100.01	100.00	1.00
10	96.47	100.00	1.04	97.47	97.01	1.00
11	99.20	94.04	0.95	95.71	84.06	0.88
12	95.83	96.00	1.00	94.89	100.00	1.05
13	94.91	98.37	1.04	97.31	86.87	0.89
14	97.07	100.00	1.03	98.79	100.00	1.01
15	98.53	98.14	1.00	98.15	95.51	0.97
AVG	97.36	97.65	1.00	97.99	95.02	0.97
SEM	0.47	1.03	0.01	0.45	1.46	0.01
SD	1.82	4.00	0.04	1.73	5.67	0.06

Voluntary activation pre and post endurance protocol values are expressed as a percent of maximum.
Ratio is the post/pre endurance protocol value.

SENSORY CONTRACTION AVERAGE FOR EACH SUBJECT

Subjects performed 4 sensory contractions which were averaged to produce one curve. The average curve was then smoothed to obtain an average of every 50 pixel point. The average values are displayed in the following table expressed as % MVC.

PLACEBO																
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Avg	SEM
35.6	50.9	45.8	48.6	39.9	48.4	46.1	43.9	47.5	44.7	50.4	46.1	49.2	24.1	51.6	44.8	1.8
28.8	45.6	40.1	46.0	34.7	44.1	39.0	40.7	42.9	36.2	43.3	45.7	47.5	23.4	47.6	40.4	1.8
24.8	41.8	36.6	43.4	32.4	40.7	36.7	38.4	38.8	33.6	39.9	44.8	46.5	20.3	47.0	37.7	1.9
22.9	39.8	33.5	40.6	31.2	38.4	34.9	34.5	37.3	30.2	37.6	44.7	44.8	19.1	46.9	35.8	2.0
21.1	37.7	31.8	38.7	30.7	36.6	33.9	32.0	35.5	28.2	34.5	43.0	44.1	18.5	46.0	34.2	2.0
19.7	34.8	30.1	36.4	29.7	34.7	30.8	32.1	32.9	27.2	32.3	42.2	43.2	18.1	43.6	32.7	1.9
18.2	32.2	27.8	36.4	29.6	33.3	27.9	31.1	32.6	25.6	30.5	40.8	42.7	19.9	41.7	31.4	1.9
18.7	29.7	25.8	34.1	29.7	31.9	26.8	31.4	31.3	24.7	29.5	39.0	41.5	18.1	39.4	30.1	1.8
19.0	30.3	24.4	32.6	27.5	31.5	25.2	30.4	29.6	23.7	27.8	38.0	41.4	18.9	37.0	29.2	1.7
18.2	29.6	23.5	31.7	28.8	30.9	23.9	29.3	28.5	22.8	25.1	38.6	40.8	19.0	35.8	28.4	1.7
17.8	29.3	22.7	30.7	28.7	29.9	23.0	28.3	28.0	22.4	25.2	38.5	39.7	18.2	36.7	27.9	1.7
17.4	27.7	23.0	29.3	28.1	29.1	22.1	27.6	25.6	22.2	26.6	38.2	39.3	17.1	36.1	27.3	1.7
16.1	26.7	21.7	28.7	27.1	28.5	23.0	27.8	26.3	21.2	24.7	37.3	39.4	15.5	36.2	26.7	1.8
14.5	26.5	21.6	28.7	27.5	27.9	22.4	26.7	26.0	20.4	23.8	37.2	37.6	15.2	36.1	26.2	1.8
13.5	25.9	22.1	27.8	27.9	27.2	21.6	24.0	24.6	20.3	23.9	35.7	37.6	16.3	35.8	25.6	1.8
12.7	25.4	21.7	27.0	27.8	27.0	20.5	24.3	24.3	19.5	23.3	35.4	37.6	16.7	35.4	25.2	1.8
11.8	25.3	21.5	26.8	27.1	26.6	20.9	24.5	23.9	19.3	25.4	34.7	37.6	15.8	34.4	25.0	1.8
10.9	24.8	21.8	26.6	26.6	26.2	21.3	24.0	25.0	19.1	24.0	33.8	37.6	15.3	34.6	24.7	1.8
10.6	24.3	22.2	26.9	25.9	25.7	20.3	23.1	24.9	19.2	23.8	33.1	37.6	15.5	34.0	24.5	1.8
10.4	23.2	20.8	26.7	25.8	25.4	19.7	22.3	24.8	18.8	23.1	33.5	37.6	14.7	32.7	24.0	1.8
10.6	22.3	20.6	26.5	25.4	24.9	18.5	19.8	25.9	17.7	21.6	33.1	37.6	14.5	31.8	23.4	1.8
10.6	21.8	20.5	25.8	25.3	24.5	17.9	19.8	25.2	17.8	20.8	32.8	37.6	15.7	29.7	23.0	1.8
10.6	22.0	20.0	25.4	24.5	24.0	17.5	19.4	22.8	17.9	20.2	31.9	37.6	15.5	29.6	22.6	1.7
10.3	22.0	20.0	24.6	24.4	24.0	17.6	19.9	23.2	18.1	20.6	30.7	37.6	15.7	29.0	22.5	1.7
10.5	21.0	18.7	23.9	24.2	23.5	16.2	20.5	23.1	17.3	20.0	29.4	37.6	15.4	28.5	22.0	1.7
9.1	20.8	17.8	24.0	23.6	23.0	15.1	20.1	21.5	16.8	19.3	29.6	37.6	15.3	29.4	21.5	1.8
9.3	20.3	17.9	23.0	22.7	22.4	14.9	19.2	22.0	17.1	19.2	28.6	37.6	13.3	29.4	21.1	1.8
9.1	20.5	18.5	22.5	22.7	21.9	16.2	19.2	21.1	16.8	19.4	27.8	37.6	13.4	30.6	21.1	1.8
8.6	19.9	17.4	22.2	23.4	21.4	17.1	18.1	21.6	16.0	19.3	26.5	37.6	13.1	30.4	20.8	1.8
7.7	19.1	16.4	21.9	22.8	21.0	15.4	17.7	20.6	15.9	18.3	26.7	37.6	14.0	30.0	20.3	1.8
9.4	19.0	15.7	21.4	22.2	21.1	15.4	17.0	19.6	15.4	18.2	25.9	37.6	15.2	31.0	20.3	1.8
9.2	19.0	15.9	21.2	21.6	20.6	16.5	16.2	19.1	15.1	18.0	26.3	37.6	15.0	31.1	20.2	1.8
8.8	19.2	15.9	20.8	21.2	19.8	16.1	15.3	19.3	15.0	17.4	25.6	37.6	14.5	29.8	19.8	1.8
8.3	19.2	15.8	20.5	21.4	19.4	15.8	16.1	19.2	15.0	16.8	24.9	37.6	13.7	29.9	19.6	1.8
8.1	19.0	16.1	20.3	21.6	18.9	15.2	15.9	17.3	14.5	15.8	24.4	37.6	14.5	30.1	19.3	1.8
7.5	19.0	16.2	20.1	21.2	18.4	15.0	15.5	17.4	14.0	15.4	23.5	37.6	14.0	29.7	19.0	1.9
7.8	18.8	16.0	19.2	21.0	18.2	15.6	14.6	17.1	13.5	16.3	23.6	37.6	13.4	30.9	18.9	1.9
7.2	18.6	15.3	18.5	20.6	18.2	15.6	14.8	17.4	14.0	15.6	24.1	37.6	13.5	30.6	18.8	1.9
7.0	18.3	15.0	18.6	20.2	17.7	15.7	12.6	16.9	13.8	16.3	23.0	37.6	14.2	29.8	18.4	1.9
7.1	18.6	14.1	18.5	20.4	17.2	16.0	11.8	16.7	13.6	15.5	23.7	37.6	14.3	29.5	18.3	1.9
6.7	18.4	14.2	18.4	20.5	16.9	15.8	12.5	16.2	13.8	15.0	24.1	37.6	12.9	28.9	18.1	1.9
7.1	18.3	13.9	18.0	20.3	16.8	13.8	13.9	15.8	13.6	14.6	24.2	37.6	14.4	28.6	18.1	1.9
7.3	18.7	14.3	17.5	20.0	16.9	13.6	13.7	14.7	13.7	14.8	23.6	37.6	15.1	27.7	18.0	1.9
6.7	18.8	14.4	17.1	20.0	16.8	13.6	12.5	14.6	14.6	15.0	23.4	37.6	15.0	27.6	17.8	1.9
7.4	18.6	13.7	17.2	20.5	16.4	13.4	12.2	14.5	13.9	14.9	23.0	37.6	12.9	27.7	17.6	1.9
7.4	19.1	13.7	16.9	19.7	16.6	12.3	12.5	14.3	13.3	14.1	23.3	37.6	11.9	27.9	17.4	1.9
7.1	18.6	13.5	15.9	19.2	16.0	11.3	12.5	13.6	13.5	13.5	25.8	37.6	13.0	28.8	17.3	2.0
7.2	18.7	13.1	15.4	18.8	16.0	11.3	12.3	13.1	13.5	13.3	25.9	37.6	12.5	28.6	17.1	2.0
6.9	18.7	13.2	15.0	19.0	15.9	11.7	12.6	13.4	13.5	14.1	24.1	37.6	11.0	28.2	17.0	2.0
6.4	18.9	12.7	14.8	18.8	15.6	11.7	12.3	13.2	13.5	13.9	23.3	37.6	12.8	27.1	16.8	2.0
6.5	18.9	13.0	14.7	18.4	15.6	11.5	12.1	13.3	13.3	13.4	23.2	37.6	13.0	26.8	16.7	2.0
6.7	19.0	13.1	14.6	18.1	15.7	12.2	11.7	13.5	12.6	14.5	23.3	37.6	11.7	28.7	16.9	2.0
6.0	19.1	13.2	13.9	17.9	15.6	12.3	11.5	13.0	12.1	16.7	22.4	37.6	13.9	27.6	16.9	2.0
6.7	18.9	13.8	14.8	17.8	15.4	12.2	11.4	12.6	13.0	15.7	22.4	37.6	12.2	25.8	16.7	1.9
6.4	18.8	14.2	15.2	17.9	15.4	12.6	11.4	11.9	13.1	15.5	22.0	37.6	11.1	26.8	16.7	2.0
5.2	18.5	14.4	15.0	17.6	15.6	12.2	11.1	11.8	12.7	14.1	22.0	37.6	12.6	26.4	16.4	2.0
6.7	18.0	14.4	15.0	17.1	15.3	11.8	11.2	12.2	12.1	12.9	21.6	37.6	11.9	25.0	16.2	1.9
7.0	18.3	13.7	15.1	16.7	14.9	11.5	11.1	12.4	12.2	13.1	21.4	37.6	11.1	24.8	16.1	1.9
6.6	18.7	13.4	15.2	16.4	14.5	10.8	11.3	13.3	12.2	13.1	21.3	37.6	10.2	25.4	16.0	2.0

PLACEBO																
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Avg	SEM
6.0	18.7	13.1	15.0	16.1	14.6	9.2	11.3	13.1	12.6	12.5	21.2	37.6	9.9	24.6	15.7	2.0
5.6	18.5	12.1	14.8	15.9	14.4	9.3	11.4	13.0	12.7	12.3	20.8	37.6	9.6	25.5	15.6	2.0
5.6	18.4	11.4	14.4	15.8	14.4	9.4	11.3	13.3	12.7	12.7	21.5	37.6	10.5	26.2	15.7	2.0
5.6	18.6	11.4	13.7	15.7	14.0	9.4	10.8	12.2	12.0	12.6	20.9	37.6	9.1	25.9	15.3	2.1
5.2	18.8	12.0	13.4	15.4	13.7	9.8	10.8	11.8	12.2	12.9	20.7	37.6	11.5	25.3	15.4	2.0
4.8	19.0	11.5	13.1	15.3	13.7	9.5	9.9	11.7	12.2	13.6	19.7	37.6	11.5	26.5	15.3	2.1
4.8	19.0	10.5	12.2	16.2	13.7	9.4	10.0	12.2	12.5	13.4	19.4	37.6	10.4	25.1	15.1	2.0
5.2	18.8	10.5	11.9	16.0	13.4	9.3	10.5	12.6	12.1	12.5	19.4	37.6	6.0	23.5	14.6	2.1
4.9	18.7	10.3	11.9	15.4	13.4	9.4	10.8	12.3	12.4	11.9	18.1	37.6	7.7	23.2	14.5	2.0
5.9	18.3	10.2	11.5	15.2	13.2	9.6	10.9	11.3	12.8	12.7	18.1	37.6	6.0	23.2	14.4	2.0
6.6	18.0	9.8	11.2	15.2	13.0	9.5	10.7	10.7	12.8	13.1	18.4	37.6	6.0	23.0	14.4	2.0
7.0	17.9	9.5	11.0	14.9	12.8	9.4	10.7	10.5	12.5	12.5	18.8	37.6	5.6	22.3	14.2	2.0
7.0	17.9	9.5	11.0	14.9	12.8	9.4	10.7	10.5	12.5	12.5	18.8	37.6	5.6	22.3	14.2	2.0
6.4	18.2	9.7	10.8	14.8	12.3	9.3	10.5	10.7	12.7	12.4	18.2	37.6	4.4	21.9	14.0	2.1
6.2	17.0	9.8	10.6	14.5	12.0	9.6	9.3	10.6	12.7	12.4	18.2	37.6	4.7	22.9	13.9	2.1
6.1	17.2	9.6	10.5	14.1	12.4	9.8	9.4	10.4	12.4	11.6	18.4	37.6	3.8	23.1	13.8	2.1
6.0	16.6	9.6	10.3	14.7	12.3	10.5	9.2	9.6	12.2	11.4	18.4	37.6	4.2	22.7	13.7	2.1
6.0	16.4	9.4	10.1	15.0	12.2	10.5	8.5	9.2	12.0	11.2	17.8	37.6	2.8	22.4	13.4	2.1
6.1	15.8	8.9	10.0	14.9	12.4	10.8	8.1	9.3	12.0	11.6	18.7	37.6	3.5	21.9	13.4	2.1
5.3	15.5	8.9	9.7	15.0	12.5	10.3	8.5	8.7	12.3	10.6	17.9	37.6	2.7	21.1	13.1	2.1
5.3	15.0	8.5	9.9	14.9	12.7	10.1	9.6	9.0	12.6	13.3	17.0	37.6	5.3	19.7	13.4	2.0
5.2	14.9	8.5	10.0	14.7	12.4	10.1	10.0	8.9	12.6	12.8	16.2	37.6	6.5	19.5	13.3	2.0
5.1	15.0	9.2	9.9	14.8	12.2	9.8	10.0	9.2	12.4	12.4	17.4	37.6	6.9	20.8	13.5	2.0
5.3	15.0	8.7	9.7	14.7	12.2	9.4	10.3	9.7	12.2	11.9	17.3	37.6	7.8	21.7	13.6	2.0
5.5	15.1	8.6	9.4	14.2	11.9	9.4	10.4	9.6	11.6	11.3	16.5	37.6	5.7	22.5	13.3	2.1
5.2	14.4	8.7	9.1	14.1	11.6	9.3	10.8	9.3	11.6	12.4	17.2	37.6	5.4	23.1	13.3	2.1
5.0	13.5	8.8	9.0	13.8	11.6	8.1	11.3	8.9	11.5	12.2	18.0	37.6	6.1	21.5	13.1	2.1
5.1	13.0	8.6	8.6	13.7	11.7	7.9	11.4	8.7	11.1	12.1	17.8	37.6	5.6	20.3	12.9	2.1
5.5	13.0	8.9	8.5	13.7	11.9	9.5	11.0	8.8	11.7	11.6	18.6	37.6	5.4	19.5	13.0	2.0
5.1	12.9	9.1	8.2	13.7	11.7	9.7	10.9	8.6	11.3	11.0	18.0	37.6	5.3	20.5	12.9	2.1
5.4	12.4	8.9	8.3	13.4	11.2	10.0	11.0	9.3	10.7	11.7	17.3	37.6	5.5	22.1	13.0	2.1
5.0	12.1	8.3	8.1	13.7	11.2	10.1	11.0	8.9	10.8	12.1	16.2	37.6	4.5	20.9	12.7	2.1
4.7	12.2	8.3	8.1	13.6	11.4	9.7	10.9	8.9	11.2	12.5	14.9	37.6	3.8	22.3	12.7	2.1
5.0	12.0	8.7	8.0	13.4	11.4	10.2	10.5	8.8	11.0	12.1	17.2	37.6	4.0	23.4	12.9	2.1
5.1	11.7	8.5	8.1	13.2	11.0	9.9	10.1	8.3	11.2	11.6	17.5	37.6	5.6	22.5	12.8	2.1
5.3	11.3	8.3	7.7	12.9	10.9	10.0	9.9	8.3	11.3	12.4	15.8	37.6	5.8	21.9	12.6	2.1
5.8	10.7	7.9	7.8	12.6	10.6	10.0	9.6	8.9	11.3	12.4	14.6	37.6	5.0	21.7	12.4	2.1
5.4	10.2	7.5	7.8	12.8	10.2	9.8	9.3	9.2	11.2	11.7	14.3	37.6	5.8	21.8	12.3	2.1
5.1	10.0	7.8	7.7	12.7	10.2	10.3	9.1	9.0	11.0	10.6	14.0	37.6	3.3	21.8	12.0	2.1
4.6	10.1	7.6	7.2	12.6	9.9	10.0	8.6	9.4	11.3	11.2	13.6	37.6	0.9	20.9	11.7	2.2
4.6	10.0	7.6	6.9	12.5	9.5	9.9	8.6	9.3	11.4	12.0	12.1	37.6	0.1	20.0	11.5	2.2

SENSORY CONTRACTION AVERAGE FOR EACH SUBJECT

Subjects performed 4 sensory contractions which were averaged to produce one curve. The average curve was then smoothed to obtain an average of every 50 pixel point. The average values are displayed in the following table expressed as % MVC.

CAFFEINE																
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Avg	SEM
44.2	40.0	39.9	44.9	43.7	56.6	41.9	41.7	45.8	43.2	35.1	46.3	49.9	48.8	49.3	44.8	1.3
37.3	36.7	34.2	42.4	38.3	52.4	36.6	32.6	44.4	33.9	29.2	43.3	49.2	47.6	50.1	40.5	1.8
32.1	34.6	31.6	39.5	38.4	49.8	34.2	28.4	40.5	30.1	27.7	43.0	47.8	45.6	48.5	38.1	2.0
29.1	33.0	28.7	36.9	36.4	48.3	30.8	25.5	37.7	26.1	25.8	41.8	46.4	41.0	46.9	35.6	2.1
26.8	32.4	26.9	34.7	35.5	45.7	28.5	23.2	34.4	23.7	23.4	38.9	47.4	45.1	44.2	34.0	2.2
26.3	30.9	24.5	33.0	33.9	44.8	26.9	21.8	31.3	22.6	22.2	38.3	47.5	42.9	42.8	32.6	2.3
25.0	29.4	23.3	31.2	31.2	43.6	24.4	20.5	30.1	21.4	20.3	36.5	45.8	43.7	41.5	31.2	2.3
23.6	28.6	21.9	29.5	33.2	41.1	23.0	19.2	30.4	20.1	20.1	34.7	44.8	43.6	39.2	30.2	2.3
24.0	28.0	20.7	28.3	32.5	40.0	22.0	18.8	29.2	19.3	19.7	34.0	43.7	44.2	37.6	29.5	2.3
22.8	27.7	20.3	27.1	32.2	41.6	20.1	17.4	27.3	18.2	17.8	33.1	41.5	42.3	36.9	28.4	2.3
21.7	27.5	19.7	26.2	31.9	41.0	19.2	17.2	26.1	16.8	15.9	33.7	40.4	44.2	37.2	27.9	2.5
20.6	26.8	18.9	25.2	30.9	39.3	18.5	17.2	24.2	15.3	16.1	32.2	41.8	45.0	34.7	27.1	2.5
20.3	26.3	18.4	24.3	29.4	37.7	17.8	16.8	24.5	14.9	15.6	33.1	40.3	43.9	33.9	26.5	2.5
20.3	25.9	18.0	23.7	31.0	37.0	16.6	16.3	24.9	14.3	14.9	32.1	40.5	45.1	33.1	26.2	2.5
21.3	25.2	17.8	22.9	31.1	36.2	16.3	16.0	24.1	13.7	15.1	30.7	40.1	45.3	35.0	26.0	2.6
20.1	24.3	17.9	22.2	30.5	34.3	16.0	15.9	23.1	13.9	14.8	29.2	39.5	42.3	34.1	25.2	2.4
19.1	24.1	17.3	21.4	30.1	34.4	15.5	15.9	23.0	14.5	14.8	29.5	37.8	39.7	33.4	24.7	2.3
18.3	23.9	16.9	20.4	28.9	33.6	14.9	15.7	22.5	14.6	13.9	28.1	37.9	39.4	35.0	24.3	2.3
18.7	23.9	16.8	19.9	28.7	32.9	14.5	15.2	21.9	15.2	13.8	27.4	36.9	39.1	34.2	23.9	2.2
18.4	23.5	16.7	19.4	29.5	32.9	14.4	14.9	21.8	14.6	13.4	27.2	35.1	37.0	34.9	23.6	2.2
17.8	23.5	16.4	19.2	29.8	32.3	14.4	14.5	22.1	14.1	13.0	27.2	33.9	37.8	34.5	23.3	2.2
17.3	24.3	15.8	18.9	29.2	31.2	14.2	13.6	21.6	13.6	12.7	26.9	36.0	37.2	33.6	23.1	2.3
17.0	22.9	15.3	18.2	28.7	30.4	14.3	13.4	21.5	13.2	12.3	26.6	34.0	36.3	33.1	22.5	2.2
15.8	22.3	15.3	17.7	28.0	29.2	13.8	13.2	20.5	12.9	12.5	26.0	33.6	34.6	31.9	21.8	2.1
15.6	21.6	14.6	17.1	28.4	29.4	13.5	12.8	20.0	13.7	12.2	26.1	33.9	30.8	30.6	21.4	2.0
15.8	22.0	14.7	16.8	28.8	28.7	13.2	12.8	20.3	14.0	12.0	26.0	32.6	31.4	28.9	21.2	1.9
16.2	21.1	14.5	16.5	27.8	29.2	13.4	12.6	19.9	13.3	12.4	26.3	32.3	31.6	28.4	21.0	1.9
16.8	21.0	14.0	16.1	27.1	29.2	13.5	12.3	20.0	13.1	12.2	25.4	34.3	31.0	26.5	20.8	1.9
17.1	20.6	13.7	16.4	26.4	28.6	13.5	11.9	20.0	14.3	11.9	24.8	32.5	29.3	28.5	20.6	1.8
17.5	20.5	14.0	16.4	25.5	28.2	13.6	11.9	18.8	14.1	11.9	24.4	30.2	28.5	30.0	20.4	1.8
18.6	20.2	14.3	16.2	25.8	27.4	13.8	11.8	18.4	13.2	11.7	24.4	33.6	28.7	29.0	20.5	1.8
19.0	20.6	14.3	16.0	27.1	27.4	13.5	11.8	18.8	12.9	11.7	24.6	31.7	28.0	28.9	20.4	1.8
17.8	20.4	14.4	16.1	27.3	29.3	13.6	12.1	18.6	12.6	11.6	23.5	31.4	27.1	27.9	20.2	1.8
16.8	20.7	15.4	15.9	27.1	29.0	13.4	11.6	18.1	12.9	11.8	23.0	27.9	28.7	27.5	20.0	1.7
15.8	20.0	15.5	15.2	27.4	28.4	13.5	11.4	17.7	12.5	11.5	23.2	28.0	29.3	28.5	19.9	1.8
15.1	20.0	15.1	14.7	27.1	26.3	13.9	11.3	17.8	12.2	11.3	24.5	32.4	29.7	27.8	19.9	1.9
14.7	20.3	14.9	14.8	26.2	26.0	13.6	11.1	17.5	11.6	11.2	23.8	29.8	27.1	27.3	19.3	1.7
14.4	20.8	14.5	14.5	25.3	26.2	13.2	11.1	17.0	11.8	11.3	22.4	32.1	26.9	26.8	19.2	1.8
14.8	20.5	14.7	13.6	24.0	26.1	13.2	10.9	16.3	12.7	11.1	22.9	32.6	26.1	27.0	19.1	1.8
14.6	20.6	14.2	13.1	23.7	25.8	13.0	10.9	16.4	13.0	11.0	22.8	31.0	26.1	26.2	18.8	1.7
14.6	20.6	14.1	13.4	25.0	26.3	12.4	10.8	16.4	12.3	10.7	21.5	30.1	24.1	25.8	18.5	1.7
16.1	19.9	13.8	13.1	25.7	26.5	12.3	10.8	15.7	12.3	10.5	21.3	31.7	25.4	26.1	18.8	1.8
15.9	19.4	13.1	12.9	25.2	26.0	12.2	10.6	15.7	12.2	10.3	20.9	30.0	24.5	25.2	18.3	1.7
14.8	18.8	13.0	12.5	24.6	25.8	12.1	10.4	15.2	11.8	10.2	21.0	29.5	23.0	24.4	17.8	1.7
13.9	18.2	12.6	12.0	23.5	26.2	12.3	10.3	14.8	12.5	10.5	21.2	28.5	24.2	23.5	17.6	1.6
13.8	18.4	12.7	12.0	23.8	26.9	12.2	10.2	14.3	12.9	10.9	20.7	32.1	22.4	23.8	17.8	1.7
14.8	18.4	13.0	11.8	22.7	25.7	11.9	9.9	14.2	13.0	10.9	20.1	31.0	20.8	24.5	17.5	1.6
14.4	17.6	12.7	11.6	22.8	25.5	11.8	9.7	14.9	13.0	10.3	20.0	29.3	20.9	23.7	17.2	1.6
13.8	17.4	12.4	11.0	22.7	25.0	11.5	9.4	13.9	12.8	9.9	21.7	27.8	18.8	23.5	16.8	1.6
13.7	18.0	12.4	10.3	21.8	24.8	11.7	8.8	13.2	12.7	9.7	21.2	25.6	20.1	22.7	16.4	1.5
13.2	17.9	12.3	10.1	20.7	24.3	11.3	8.4	12.9	12.4	9.7	20.7	26.6	18.9	23.3	16.3	1.6
13.0	18.0	12.3	10.4	21.4	23.9	11.3	8.1	12.6	12.4	9.1	21.2	26.5	17.5	22.9	16.0	1.5
12.3	17.8	12.0	10.5	21.0	24.3	10.8	7.7	12.4	12.9	9.4	20.6	24.7	18.7	23.3	15.9	1.5
12.6	18.2	11.9	10.7	21.1	23.6	11.1	7.6	12.3	12.8	9.5	20.5	25.0	18.6	21.8	15.8	1.5
12.7	18.2	11.7	10.7	21.2	24.0	11.2	7.6	12.4	12.4	9.3	20.7	24.2	18.2	22.5	15.8	1.5

CAFFEINE

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1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Avg	SEM
12.1	17.7	11.7	10.7	19.9	24.3	11.2	7.7	13.2	12.0	9.3	20.6	26.6	18.1	23.6	15.9	1.6
12.1	17.6	12.0	10.7	19.8	23.2	11.1	7.4	13.0	11.8	9.4	20.2	24.8	18.4	23.5	15.7	1.5
11.8	17.2	11.5	10.5	20.0	22.8	11.0	7.2	12.9	11.8	10.2	20.0	24.9	17.1	23.9	15.5	1.5
12.0	16.6	11.1	10.5	19.6	22.4	11.1	7.2	12.3	11.7	10.4	20.3	23.9	18.0	23.5	15.4	1.4
11.6	16.7	11.2	10.1	18.8	23.4	11.5	7.3	11.5	11.8	9.4	19.9	23.2	21.1	22.2	15.3	1.5
10.9	16.3	11.0	9.8	19.9	22.6	11.0	7.6	10.6	11.7	8.9	19.3	23.1	16.5	21.7	14.7	1.4
10.4	15.7	10.7	9.5	20.8	22.9	10.7	7.7	10.9	12.0	8.5	19.0	24.7	16.3	21.5	14.7	1.5
11.4	15.6	10.3	9.1	19.9	22.4	10.5	7.6	10.8	12.2	8.3	19.0	25.6	15.3	23.8	14.8	1.5
10.7	15.1	10.2	9.1	19.1	22.1	10.3	7.5	10.5	11.9	8.9	18.9	22.8	14.4	22.8	14.3	1.4
10.3	14.8	10.2	8.9	18.2	21.5	10.1	7.5	10.1	11.2	8.5	19.2	22.0	14.2	21.9	13.9	1.4
9.4	14.8	10.0	8.6	18.5	21.8	9.8	7.5	9.8	11.4	8.4	18.3	21.1	12.0	21.7	13.5	1.4
10.9	14.7	9.5	8.6	18.2	22.1	9.3	7.2	9.8	12.1	8.5	17.8	23.3	12.0	24.0	13.9	1.5
11.5	14.3	9.3	8.5	18.1	22.1	9.4	7.1	9.3	12.4	8.1	17.6	22.0	12.3	26.6	13.9	1.6
12.4	13.7	8.9	8.2	17.4	21.5	9.7	7.1	8.9	11.9	8.7	17.5	21.3	12.9	28.4	13.9	1.6
12.8	13.2	8.8	8.1	16.8	21.5	9.6	7.1	8.9	10.8	9.1	17.1	21.4	11.1	27.8	13.6	1.6
11.7	13.1	8.8	8.0	17.5	20.8	9.3	6.9	8.7	10.4	9.1	17.8	21.2	11.0	27.5	13.5	1.6
11.7	13.1	8.8	8.0	17.5	20.8	9.3	6.9	8.7	10.4	9.1	17.8	21.2	11.0	27.5	13.5	1.6
12.8	13.1	8.7	7.8	17.8	21.0	9.4	7.0	8.4	10.9	8.5	18.7	21.6	10.4	27.2	13.6	1.6
11.6	12.8	8.5	7.9	17.0	20.6	9.1	6.8	8.3	11.2	8.7	18.7	20.7	11.0	27.5	13.4	1.6
11.3	12.7	8.1	7.9	16.5	19.7	8.9	6.9	7.9	11.2	8.4	18.4	20.2	10.1	27.7	13.0	1.6
11.0	12.4	8.0	7.8	15.9	19.8	8.7	6.8	7.7	10.9	7.7	18.1	19.7	10.1	26.8	12.9	1.6
10.2	12.0	8.2	7.7	16.8	19.6	8.8	6.7	7.6	10.2	6.8	17.7	18.5	11.8	26.6	12.7	1.6
8.6	12.0	8.0	7.2	16.3	19.5	8.5	6.2	8.0	10.2	7.5	17.0	19.6	11.8	27.9	12.5	1.6
10.0	11.9	8.0	6.9	16.3	20.2	8.0	6.1	7.8	10.4	8.8	17.7	19.7	10.6	29.0	12.8	1.7
11.6	11.8	7.7	7.0	17.0	19.5	8.0	6.1	7.6	9.7	8.4	17.9	18.4	14.0	27.7	12.8	1.6
12.6	11.4	7.5	6.9	17.4	19.5	8.0	6.0	7.0	9.6	8.8	17.8	17.7	11.4	24.7	12.4	1.5
12.3	11.3	7.5	6.5	16.8	18.3	8.1	5.8	6.9	9.4	9.5	17.6	17.6	10.3	25.7	12.3	1.5
10.8	11.6	7.5	6.6	16.5	18.1	8.0	5.4	6.9	10.3	10.2	18.1	20.1	9.3	26.2	12.4	1.6
10.4	11.2	7.4	6.6	16.3	17.9	7.8	5.0	6.9	9.7	9.9	17.6	18.6	8.4	24.9	11.9	1.5
9.2	11.0	7.5	6.4	15.2	18.1	7.9	4.7	6.8	9.7	8.5	16.5	17.2	8.6	24.9	11.5	1.5
8.7	11.6	7.5	6.0	15.0	17.6	8.1	4.7	6.6	9.9	9.0	17.0	16.6	9.4	25.2	11.5	1.5
9.9	10.7	7.5	5.8	15.6	17.4	8.0	4.6	7.1	10.6	9.3	16.1	16.3	9.0	25.9	11.6	1.5
9.2	10.2	7.5	5.8	15.7	17.8	8.1	4.8	6.7	10.3	8.7	15.5	17.7	9.0	25.0	11.5	1.5
9.6	10.2	7.5	5.9	14.9	18.2	8.3	4.8	6.9	10.0	8.6	16.0	19.4	8.6	24.8	11.6	1.5
9.5	10.0	7.4	5.5	14.3	17.3	7.9	5.0	7.0	9.9	8.2	15.5	18.1	7.7	26.8	11.3	1.5
8.8	9.5	7.3	5.4	13.7	16.6	7.7	5.0	7.1	9.9	8.5	16.3	16.6	7.8	26.0	11.1	1.5
8.1	9.3	7.4	5.4	13.9	17.4	7.5	5.0	7.3	10.2	8.7	15.3	16.7	7.4	24.9	11.0	1.4
9.5	9.4	7.4	5.0	14.0	17.6	7.3	5.0	6.9	10.1	8.7	15.0	17.6	7.3	22.9	10.9	1.4
9.6	9.4	7.6	5.0	13.6	16.8	7.5	5.0	6.7	10.0	7.4	14.9	15.3	8.1	22.4	10.6	1.3
9.1	9.2	7.8	4.9	13.2	16.6	7.7	4.7	7.1	10.4	6.7	14.2	14.3	8.1	24.1	10.5	1.3
8.6	9.4	7.7	4.8	13.8	16.1	7.7	4.5	6.8	10.0	6.9	14.1	14.9	9.0	23.5	10.5	1.3
7.9	9.7	7.6	4.8	14.0	15.1	7.8	4.7	6.9	9.6	7.2	13.9	14.0	8.0	23.5	10.3	1.3
7.9	9.4	7.4	4.9	14.0	15.2	7.6	4.7	6.9	9.7	7.5	13.6	13.3	7.4	22.7	10.2	1.2
7.7	9.2	7.2	4.9	13.8	15.0	7.4	4.5	6.8	9.7	6.9	14.7	13.5	6.7	23.7	10.1	1.3
6.5	8.9	6.9	5.1	14.0	15.9	7.8	4.4	6.6	9.6	7.6	14.8	13.4	6.4	25.5	10.3	1.4

REGRESSION PARAMETERS & END FORCE FOR SENSORY CONTRACTIONS

PLACEBO							
SUBJECT	r	C	A	-K1	B	-K2	END FORCE
1	0.996	5.37	24.87	0.91	21.67	0.062	4.61
2	0.990	0.00	29.56	0.18	25.72	0.007	10.04
3	0.998	3.21	25.82	0.28	23.44	0.017	7.61
4	0.999	0.00	18.11	0.21	35.03	0.016	6.86
5	0.999	8.63	21.36	1.03	24.06	0.018	12.50
6	0.999	9.08	17.37	0.36	28.12	0.028	9.53
7	0.996	8.48	21.43	0.27	21.25	0.035	9.89
8	0.997	9.11	11.90	0.83	31.33	0.046	8.61
9	0.997	6.05	18.78	0.39	29.65	0.026	9.27
10	0.998	11.38	24.75	0.49	18.52	0.048	11.43
11	0.997	11.15	23.98	0.39	23.83	0.041	11.98
12	0.995	0.00	17.07	0.06	31.39	0.007	12.07
13	0.992	0.00	9.28	0.19	42.17	0.009	37.63
14	0.966	0.00	10.98	0.01	10.93	0.015	0.11
15	0.992	0.00	19.04	0.15	35.77	0.006	20.01
AVERAGE	0.994	4.83	19.62	0.38	26.86	0.025	11.48
SEM	0.002	1.18	1.50	0.08	2.00	0.004	2.17
SD	0.008	4.562	5.810	0.310	7.755	0.017	8.42

CAFFEINE							
SUBJECT	r	C	A	-K1	B	-K2	END FORCE
1	0.993	5.23	28.22	0.34	18.58	0.016	8.53
2	0.996	0.00	13.61	0.30	30.24	0.011	8.91
3	0.976	8.25	-14.06	0.05	37.74	0.046	6.91
4	1.000	0.00	22.80	0.15	26.14	0.017	5.08
5	0.996	0.00	14.30	0.58	35.75	0.010	13.96
6	0.998	0.00	22.15	0.13	36.31	0.008	15.90
7	0.999	0.00	30.18	0.19	17.30	0.009	7.61
8	0.999	1.87	31.52	0.42	18.95	0.020	4.37
9	0.998	0.00	22.51	0.26	30.75	0.017	6.59
10	0.996	0.00	34.35	0.26	15.28	0.005	9.63
11	0.996	6.86	21.48	0.20	9.82	0.023	7.59
12	0.998	0.00	18.96	0.11	29.26	0.007	14.82
13	0.994	0.00	6.44	0.15	45.72	0.011	13.37
14	0.994	0.00	27.54	0.02	25.11	0.019	6.42
15	0.976	24.60	16.02	0.07	11.63	0.068	25.46
AVERAGE	0.994	3.12	19.74	.22*	25.90	0.019	10.343
SEM	0.002	1.70	3.10	0.04	2.71	0.004	1.426
SD	0.008	6.575	12.015	0.152	10.499	0.017	5.523

$$Y = C + Ae^{-K_1t} + Be^{-K_2t}$$

Y = Force, t = time, A and B = values of exponential processes,

-K1 and -K2 = rate constants

* Significant from placebo (p<.05)

STATISTICAL ANALYSIS CONTROL MEASURES

VARIABLE (post/pre ratio)	DF EFFECT	MS EFFECT	DF ERROR	MS ERROR	F	p
Heart rate	1	0.008	29	0.011	0.7	0.410
Systolic blood pressure	1	0.067	29	0.001	105.9	0.001*
Diastolic blood pressure	1	0.027	29	0.001	22.2	0.0001*
Maximum voluntary contraction	1	0.077	29	0.007	10.4	0.003*
Voluntary activation	1	0.004	29	0.000	13.4	0.001*
Twitch amplitude	1	0.013	29	0.005	2.6	0.115
+dF/dt	1	0.009	29	0.012	0.8	0.393
-dF/dt	1	0.004	29	0.018	0.2	0.632
EMG	1	0.016	29	0.019	0.9	0.358
M wave amplitude	1	0.001	29	0.021	0.0	0.865

SENSORY PROTOCOL

VARIABLE	DF EFFECT	MS EFFECT	DF ERROR	MS ERROR	F	p
K1	1	0.213	14	0.019	11.4	0.005*
K2	1	0.000	14	0.000	0.8	0.385
End force	1	9.627	14	27.224	0.4	0.562
Starting force	1	0.038	14	42.795	0.0	0.977

STATISTICAL ANALYSIS ENDURANCE PROTOCOL

VARIABLE	DF EFFECT	MS EFFECT	DF ERROR	MS ERROR	F	p
T _{LM}	1	1179.9	14	175.2	6.7	0.0212*
Twitch amplitude slope	1	0.001	14	0.01	0.1	0.7781
EMG slope	1	0.008	14	0.04	0.2	0.6522
Voluntary Activation slope	1	0.007	14	0.01	0.7	0.4105
Missing values for subjects 4,6,9 and 10 included in analysis						
Twitch amplitude	2	732.6	20	56.9	12.9	0.0003*
+dF/dt	2	624.0	20	61.3	10.2	0.0009*
-dF/dt	2	100.5	20	83.9	1.2	0.3227
Voluntary activation	2	16.7	20	30.7	0.5	0.5891
EMG	2	5928.4	20	1306.3	4.5	0.0237*
M wave amplitude	2	37.6	20	70.9	0.5	0.6239
Missing values for subjects 4,6,9 and 10 substituted with placebo T _{LM} values						
Twitch amplitude	2	720.9	28	50.4	14.3	0.0001*
+dF/dt	2	660.3	28	60.8	10.9	0.0003*
-dF/dt	2	85.1	28	65.6	1.3	0.2894
Voluntary activation	2	30.5	28	26.4	1.2	0.3299
EMG	2	5769.5	28	1011.7	5.7	0.0084*
M wave amplitude	2	19.7	28	85.1	0.2	0.7953
Missing values for subjects 4,6,9 and 10 substituted with caffeine T _{LM} values						
Twitch amplitude	2	659.7	28	54.7	12.1	0.0002*
+dF/dt	2	615.7	28	63.9	9.6	0.0007*
-dF/dt	2	78.8	28	66.1	1.2	0.3183
Voluntary activation	2	22.6	28	27.0	0.8	0.4434
EMG	2	5166.5	28	1054.8	4.9	0.0150*
M wave amplitude	2	47.0	28	83.1	0.6	0.5743
PRE-POST ENDURANCE PROTOCOL: Ratio Values						
MVC force	1	0.01	14	0.01	0.8	0.3810
Twitch amplitude	1	0.22	14	0.01	23.3	0.0027
+dF/dt	1	0.08	14	0.01	6.3	0.0253
-dF/dt	1	0.08	14	0.01	7.3	0.0170
Voluntary activation	1	0.005	14	0.002	2.2	0.1646
EMG	1	0.003	14	0.07	0.0	0.8357
M wave amplitude	1	0.01	14	0.02	0.7	0.4226
PRE-POST ENDURANCE PROTOCOL: Placebo						
MVC force	1	185683.8	14	2859.65	64.9	0.0000
Twitch amplitude	1	25428.1	14	292.5	86.9	0.0000
+dF/dt	1	6581269.0	14	61275.6	107.4	0.0000
-dF/dt	1	1874786.0	14	27701.2	67.7	0.0000
Voluntary activation	1	9.9	14	5.6	1.8	0.2054
EMG	1	0.0	14	0.0	2.8	0.1177
M wave amplitude	1	0.6	14	0.1	10.8	0.0054
PRE-POST ENDURANCE PROTOCOL: Caffeine						
MVC force	1	220193.300	14	1382.32	159.3	0.0000
Twitch amplitude	1	43824.7	14	204.3	214.5	0.0000
+dF/dt	1	9344510.0	14	50630.9	184.6	0.0000
-dF/dt	1	24344.8	14	15816.0	153.9	0.0000
Voluntary activation	1	14.6	14	18.2	0.8	0.3851
EMG	1	0.0	14	0.0	2.4	0.1414
M wave amplitude	1	1.1	14	0.2	6.5	0.0206

Experimental Set-up

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HOW DOES CAFFEINE PROLONG MUSCLE PERFORMANCE DURING REPEATED ISOMETRIC CONTRACTIONS

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INFORMED CONSENT

Department of Kinesiology and Health Science, Faculty of Graduate Studies York University
(416) 736-2100, x33859

Our research team is interested in studying the effects of caffeine on the human neuromuscular system during prolonged muscle performance. The research team is headed by Dr. E. Cafarelli, and the Human Participants Review Committee has approved the study. There are no risks inherent in these procedures, with the exception of those listed below:

- You may experience sleeplessness and/or mild malaise lasting six to ten hours following the consumption of caffeine in a dose comparable to 3 to 5 cups of coffee. All experiments will begin 8-9 am to offset these effects.
- Electrical shocks will be administered to a nerve in your leg to produce a contraction of your thigh muscles. The procedure will not damage tissue, however, some people find these shocks unpleasant and your muscle may be sore 24-48 hours afterward. No experiments will be done during this period.
- You may experience some muscle soreness due to the repetitive and prolonged contractions you will be performing throughout the protocol.

Each day, on four separate test days, 2-3 hours of participation will be required. Subject identity will be kept confidential in all future publications. Results of the study will be made available to the subjects upon request.

PARTICIPANTS NAME: _____ PHONE: _____
SUBJECT CODE: _____

I have been informed about the nature and procedures of the study, and understand them in full. I know that I may withdraw at any time if I feel uncomfortable with any of the procedures. I agree to serve as a participant in the study. I know that any concerns or comments regarding my participation in the study can be addressed to the ethics committee at York University extension 55055.

Signature of participant

Signature of witness

Date

Name of witness

4700 KEELE STREET • TORONTO • ONTARIO • CANADA • M3J 1P3

June 21, 1999

Professor Enzo Cafarelli
346 Bethune College

Re: Ethics Approval
How Does Caffeine Prolong Muscle Performance During Repeated Isometric Contractions?

I am writing to inform you that the Human Participants Review Sub-Committee has reviewed and approved the above project.

Yours sincerely,

Greg Jacobs
Secretary
Human Participants Review Sub-Committee