Health and ergogenic effects of caffeine

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The indiscriminate use of caffeine by people of all ages may present health hazards. The public at large needs to be more informed of the presence of caffeine in commonly consumed foods and beverages, particularly by infants, children and pregnant women. It is the responsibility of all consumers to investigate the caffeine content of suspected products so that intake may be objectively monitored.

Although doubts still exist about the efficacy of caffeine as an ergogenic aid, particularly for exercise of high intensity and short duration, the IOC and the National Collegiate Athletic Association of the US have adopted bans on the use of caffeine to aid sport performance. Currently, both of these organizations prohibit the concentration of caffeine in urine to exceed 15 μg·mL⁻¹. That is to say, only very large amounts of caffeine are not permitted at present. Additional research is needed to confirm or deny the contraindications presented by the ingestion of caffeine on a chronic basis.

Introduction

The history of caffeine is almost as old as mankind, yet surprisingly little research in terms of long term effect exists. A recent upsurge of interest concerning the ergogenic properties of caffeine has resulted in investigations involving mainly endurance. However, strength, movement speed and vision studies are also reported.

Original isolation of caffeine from green coffee beans was first achieved in 1820 by a German scientist and the earliest study of the influence of caffeine in metabolism was carried out in 1850. Few investigations of caffeine occurred prior to the 1970s, but a growth in scientific interest in the drug resulted from a draft issued by a special committee on drugs generally recognized as safe by the Food and Drug Administration (FDA) of the US Public Health Service.

An ingredient in numerous beverages, foods and proprietary drugs, caffeine is currently the most widespread and indiscriminately used drug available to consumers of all ages. Although caffeine is readily accepted as an ingredient in coffee beverages at about 100 mg a cup, the xanthine derivative presents itself in a myriad of other sources such as tea, carbonated drinks, chocolates, soft candies, baked goods, frozen dairy products, gelatines, puddings and over-the-counter medications. Currently the FDA's National Center for Drugs and Biologics lists more than 1000 over-the-counter drugs as having caffeine as an ingredient.

Physiological action

Caffeine is only one of three xanthine derivatives that have similar physiological reactions. The other xanthine derivatives include theophylline and theobromine which are found in tea and cocoa respectively. Caffeine, theophylline and theobromine are alkaloids structurally identified as 1,3,7-trimethylxanthines. Due to structural similarities, it is thought to facilitate the use of uric acid and purine in the body. Caffeine, readily absorbed orally, rapidly empties from the stomach, and is absorbed from the gastrointestinal tract. Peak blood concentration occurs approximately between 30 and 60 minutes after ingestion.

Caffeine is a powerful CNS stimulant and affects the cardiac muscle, kidneys and possibly certain glands. The drug readily crosses the blood brain barrier and acts directly on the vagal, medullary, and vasomotor centres. Small amounts of caffeine may alter blood pressure, heart rate, respiratory rate and metabolic rate. Further physiological responses may include increased urine production and higher blood sugar levels.

The half-life of caffeine ranges from four to six hours to two days, depending on the individual's age, weight, sex, hormonal status and use of oral contraceptives. Tolerance to the effects of caffeine may develop after one to four days of regular consumption of 250 mg thrice daily. Infants and children do not eliminate caffeine as efficiently as adults and the effects of the drug may last as long as three to four days.

Health effects of caffeine

A 1978 official review committee to the FDA stated that it was not appropriate to include caffeine among the substances generally recognized as safe. Physically, caffeine may impair hand steadiness, induce trembling and tremors and can result in chronic muscle tension. Larger doses of caffeine may produce insomnia, nervousness, irritability, anxiety and wakefulness.
Unusually high doses of caffeine may cause nausea, diarrhoea and even death. Peptic ulcers, pancreatic cancer and endocrine tumours are possible conditions resulting from the use of caffeine.

Caffeine is also believed to be associated with certain breast disorders because the acceleration of the growth-promoting substance associated with fibrocystic breast disease may be increased by caffeine. One study revealed that 65% per cent of the women with benign lumps and thickening breast tissue experienced complete disappearance of all palpable breast nodules and other symptoms within one to six months after all food substances containing caffeine were eliminated from the diet.

Recent investigations have found a possible link between caffeine and coronary artery disease, arrhythmias and elevated levels of cholesterol. Additionally, Jacobson has suggested a connection between caffeine and birth defects. Jacobson reported that 23.2 per cent of mothers who gave birth to abnormal babies drank eight or more cups of coffee per day.

Since caffeine is available to people of all ages, children are also susceptible to the effects of caffeine. A small child, after consuming only one can of caffeine-contained carbonated drink, may receive the equivalent of two to three cups of coffee for an adult. One investigator found evidence of tachycardia and insomnia in healthy pre-adolescent children after consuming twelve ounces of cola drink. Furthermore, Silver added 'children are more susceptible than adults, [and that] we should . . . withdraw these beverages from our children's diet.'

Caffeine in athletics

Early literature identifies caffeine as a doping agent capable of magnifying physical performance. A movement to prohibit the use of caffeine in combination with athletic events began in the 1930s. Although caffeine was considered an ergogenic aid, the Medical Commission of the British Commonwealth Games of 1971 concluded that caffeine, as consumed in coffee, could not be considered a doping agent. The following year, the International Olympic Committee (IOC) removed caffeine from the lists of doping agents. However, the continued speculation that caffeine could enhance performance as a doping agent and was readily available without regulatory restraint, prompted the IOC to reconsider its previous ruling. Prior to the 1984 Olympic Games caffeine was again added to the list of doping agents by the IOC. The current illegal dose of caffeine is 15 μg ml⁻¹ urine. This dose is equivalent to between 500 and 600 mg caffeine or five to six cups of coffee in a one to two hour period.

Studies regarding any ergogenic effects of caffeine in all areas have found confusing and confounding results. Many investigations similar in nature have further confused the issue by employing differences in protocols. Most studies involving human subjects have administered caffeine to only small groups of subjects. Additionally, many of the investigations did not distinguish between subjects who may have been tolerant to the drug prior to testing and others. The following summary of the ergogenic effects of caffeine is divided into these segments: endurance, strength, reaction and movement time, coordination, vision and alertness.

Endurance

The possible efficacy of caffeine as an endurance-enhancing aid was initially recognized in the late 1800s. Laboratory experimentation attempting to elucidate this relationship can be traced to the early 1900s when Schiritz found caffeine to increase work output during cycle ergometry. During the mid 1900s, Asmusen and Boje found caffeine capable of overcoming fatigue effects during exhaustive cycle ergometry with a task of 'longer' duration. More recently, Ivy and others demonstrated that caffeine (250 mg) increases total work output during prolonged (2 h) bicycle ergometry. Similarly, Costill and others found caffeine (330 mg) capable of increasing time to exhaustion during submaximal (80 per cent VO₂ max) cycle ergometry, while McNaughton demonstrated larger caffeine doses (10 mg kg⁻¹ and 15 mg kg⁻¹) capable of increasing exercise time during a much shorter, incrementally progressive, cycle ergometry test.

This array of findings demonstrating a positive influence of caffeine on endurance are opposed by an equally convincing body of research which fails to show caffeine enhancement in endurance activities. Perkins and Williams found three different caffeine doses (4, 7, and 10 mg kg⁻¹) had no influence on time to exhaustion during short, incrementally progressive, cycle ergometry. In similar cycle protocols, Toner and others using 305 mg caffeine, Powers and others and Gaesser and Rich both using 5 mg kg⁻¹, failed to demonstrate that caffeine increases exercise time to exhaustion. Finally, Butts and Crowell found no change in time to exhaustion during submaximal (75 per cent VO₂ max) cycle ergometry as a result of ingesting 300 mg caffeine.

In an attempt to resolve these dichotomous findings, a close examination of exercise protocols may be helpful. This is of importance since exercise intensity and duration are inversely related. Thus, exercise eliciting maximal oxygen uptake may be tolerated for less than one minute while submaximal exercise (60–85 per cent VO₂ max) may be endured for several hours by subjects who are habitually active.

Of the studies cited which failed to demonstrate that caffeine is an endurance-enhancing aid, all but one employed exercise protocol intensities or progressive intensities which limited or would limit exercise duration to several minutes at best. Likewise, of those studies cited which demonstrate a positive effect of caffeine, all but one utilized intensities which permitted or would permit exercise duration to be measured in hours. In the study of Butts and Crowell average exercise duration ranged between 60 and 70 min, yet caffeine failed to increase exercise time in both men and women. In the McNaughton study, average exercise duration was in the seven minute range, yet both a 10 and 15 mg kg⁻¹ dose increased cycling time to exhaustion. The 15 mg kg⁻¹ dose was approximately three times greater than the average dose cited in other studies. In contrast to the findings of McNaughton, Perkins and Williams, using a similar protocol, found 10 mg kg⁻¹ caffeine to be ineffective in increasing exercise time.
With these exceptions, it would appear that caffeine tends to be effective in prolonging exercise of durations exceeding one hour. In an attempt to explain this phenomenon, a brief review of human bioenergetics may be warranted. Exercise of high intensity (> 85 per cent VO₂ max) results in the accumulation of organic acid metabolites which impair mitochondrial enzyme activity, thereby severely limiting energy production and exercise duration. Exercise of lower intensity (60–85 per cent VO₂ max) does not result in increased accumulation of organic acids, since the slight increase is accordingly removed by the liver, kidneys, heart and active muscles. Exercise intensities of between 60 and 85 per cent VO₂ max would appear to be duration limited as a result of glycogen depletion, which may restrict energy production since carbohydrate substrates are essential to Krebs Cycle function. At exercise exceeding 85 per cent VO₂ max, the rate of muscle glycogen utilization is rapid but considerable quantities remain at exhaustion.

Costill and associates demonstrated that heparin-induced increases in plasma free fatty acid (FFA) resulted in decreased muscle glycogen depletion during 30 min of treadmill exercise at 70 per cent VO₂ max. Therefore, the suggestion that caffeine is an endurance-enhancing aid at predominantly aerobic intensities (60–85 per cent VO₂ max), may be due to the drug’s ability to spare glycogen by increasing fat metabolism and/or reducing carbohydrate metabolism.

Employing aerobic exercise intensities in combination with caffeine, a number of investigations have suggested one or more of the following glycogen-sparing mechanisms: increased plasma FFA levels; increased plasma glycerol levels; decreased respiratory exchange ratio (R) values; plasma free fatty acid (FFA) values; and increased plasma lactate levels. Equivocally, Butts and Cromwell did not find a difference in R with caffeine ingestion during approximately one hour of exercise at between 65 and 70 per cent VO₂ max, while Casal and Leon found an increase in FFA concentration following caffeine ingestion prior to exercise, but the increase did not remain during a 45 min treadmill run at 75 per cent VO₂ max. Essig and associates determined, through comparative muscle biopsies, that caffeine is capable of reducing glycogen depletion by 42 per cent.

In summary, there appears to be a strong case for the efficacy of caffeine as an endurance-enhancing aid during exercise eliciting between 60 and 85 per cent VO₂ max where the duration of exercise approaches or exceeds one hour. At higher intensities and shorter durations, results are equivocal but suggest that caffeine is ineffective in enhancing performance. The primary reason for the improved endurance during exercise of longer duration would appear to be increased fat utilization leading to a glycogen-sparing effect. However, two studies suggest enhanced neuromuscular facilitation in response to caffeine. These authors feel the following areas provide opportunities for additional study: the use of multiple, graduated caffeine dosages based on body weight; differentiation of subjects on the basis of VO₂ max and/or prior exercise history; differentiation of subject based upon habitual caffeine use; differentiation of exercise tasks with respect to intensity, duration and modality and the inclusion of actual competitive conditions in addition to controlled laboratory situations.

Finally, there are a number of risks to consider before using caffeine in an attempt to improve performance. Its diuretic effect and the propensity to provoke cardiac arrhythmias are well documented. Consequently, risks of caffeine use may outweigh potential benefits under hot, humid conditions or for those with a compromised cardiovascular electrophysiology.

Caffeine and muscular strength

Caffeine is absorbed according to the water content of the tissue, which consequently results in the highest concentrations of caffeine in muscle tissue. Reported effects of caffeine on muscle include enhanced contractile status, altered patterns of recruitment, potentiation of the rate of subrate utilization, facilitation of neuromuscular transmission and calcium manipulation.

A review of the effect of caffeine on neuromuscular properties indicates that a majority of investigations have utilized in vitro animal or insect skeletal muscle tissue. The following summary of research involves nonhuman muscle tissue which will be followed by studies of maximal voluntary contractions in humans under the influence of caffeine.

Varagic and Zugic suggested that caffeine may not only have an effect on neuromuscular transmission due to an increase in acetylcholine, but also that the drug enhances muscle twitch response by either direct or indirect stimulation. Correspondingly, Walden postulated that caffeine may reduce the threshold of neuronal excitability. However, Butcher and Sutherland found similar potentiating effects in denervated muscle after caffeine treatment. Bianchi found caffeine to reduce membrane binding of calcium in the myoplasm, which subsequently increased calcium permeability and ionic activity in skeletal muscle. Bianchi also found that low doses of caffeine promoted striated muscle shortening from resting length and high doses caused ‘contractures’. Several investigations have noted caffeine-induced muscle contractures which may be linked to a lower mechanical threshold of the muscle tissue.

The notion that caffeine primarily effects the calcium transport mechanisms within the muscle tissue is well documented. Muscle contractures usually caused as a result of caffeine treatment are absent in calcium-depleted muscle tissue and no effect has been found on myofilaments. Consequently, the tension generating action of caffeine on muscle tissue is thought to be calcium-dependent.

In examining the effect of caffeine on calcium transport, Fabiato and Fabiato suggested that caffeine generates a release of calcium from the reticular system, thereby provoking muscle contraction. Other investigations indicate caffeine as an agent that promotes a decrease in the rate of calcium uptake by the sarcoplasmic reticulum and/or an increase in permeability of the sarcoplasm. Butcher and Sutherland found caffeine to increase intracellular cyclic AMP levels which may promote reconversion of glycogen to glucose (glycogenolysis) in the liver. The process of glycogenolysis provides a rapid emergence of glucose available for muscular contraction. Additionally, Van Handle suggests a synergistic...
effect of caffeine and adrenaline that may increase glucose-6-phosphate which has been shown to increase muscle contractility\textsuperscript{46}.

The assumption that vertebrate and insect skeletal muscle tissue is similarly affected by caffeine has led to investigations involving the effect of caffeine on human muscle contraction\textsuperscript{46}.

One recent study found no improvements in maximal hand grip strength as a result of the ingestion of 170–500 mg caffeine\textsuperscript{56}. Lopes and associates investigated the effects of an oral administration of 500 mg caffeine on voluntary isometric and electrically-stimulated contractions\textsuperscript{56}. The subjects performed three maximal voluntary contractions followed by electrical stimulation of the ulnar nerve at 10, 20, 30, 50 and 100 Hz following at 15–30 s interval between each stimulation. No difference was found between control and experimental groups in the maximal voluntary contraction or with 100 Hz stimulation. A curve force with stimulation frequency table showed that caffeine produced an increase in tension for all stimulation frequencies lower than 100 Hz. Although a trend toward enhanced endurance was found, there was no significant difference between endurance time between caffeine and placebo group\textsuperscript{56}. The authors suggested that failure to generate force at high frequencies of stimulation may be due to a change in excitability of the cell membrane and/or neuromuscular block. They concluded that caffeine had a direct effect on electrically-induced skeletal muscle contraction before and after fatigue, and that no effect was found in muscular endurance\textsuperscript{56}.

Williams and associates investigated the influence of 7 mg.kg\textsuperscript{-1} caffeine on maximal motor unit activation, isometric force production (handgrip) and muscular endurance\textsuperscript{56}. The results indicated a slightly higher, but statistically insignificant, activation of motor units, and no difference in isometric force or muscle endurance. Furthermore, Williams and others found caffeine to produce 'little' effect in EMG tracings during submaximal and maximal contractions when compared with control\textsuperscript{56}. The authors concluded that the caffeine-related improvements in contractility and endurance evident in vitro due to calcium engineering by the reticular system were not evident in their investigation and the absence of EMG difference may be due to the specific muscle investigated.

Bond and associates were the first to investigate the effect of caffeine on voluntary dynamic contraction\textsuperscript{72}. Using caffeine in a dose 5 mg.kg\textsuperscript{-1} and a placebo, tests included isokinetic knee flexion and extension at selected velocities of 30, 150 and 300 degrees.s\textsuperscript{-1}. No significance was observed between the experimental and control groups. The authors concluded that caffeine at low doses has no influence on muscle function at low, moderate, and high velocities of contraction.

An unpublished observation in our laboratory, using 300 mg and 600 mg caffeine, indicated similar results for maximal torque as those of Bond et al.\textsuperscript{72}. Additionally, no difference in anaerobic muscle endurance was evident as a result of 15 repetitions at 300 degrees.s\textsuperscript{-1} in knee movement.

Reaction time and movement time

Several inconsistencies have been reported in studies investigating the effect of caffeine on reaction time and speed of movement. This matter is further complicated by differences in experimental protocol, subject tolerance and its variation in dose used in the experiments. An early study found that typing speed improved with 65–130 mg caffeine and that a dose of 390 mg caffeine resulted in poor performance and tremors\textsuperscript{73}. In a study using 300 mg caffeine, Thornton found faster reaction times compared with control\textsuperscript{74}. Wenzel and Rutledge reported dose-related improvements in simple reaction time and inverse relationships with complex reaction time as a result of 100 mg and 300 mg caffeine\textsuperscript{75}. Cheney, in two separate investigations, found 3.3, 3.6 mg kg caffeine ingestion brought about varied results in discriminatory reaction time and that a dose of 5 mg.kg\textsuperscript{-1} body weight always decreased reaction time\textsuperscript{76,77}.

Smith and others reported a significant facilitative effect on choice reaction time as a result of 200 mg caffeine\textsuperscript{78}. A recent investigation by this author noted significantly improved movement time and reaction time scores after administering 300 mg caffeine but found no significant improvements in either reaction or movement time following a 600 mg dose\textsuperscript{79}. The aforementioned study led to the conclusion that a dose response relationship might exist and that perhaps a saturation point of caffeine was reached with the higher dose\textsuperscript{80}.

Coordination

The scant literature regarding the effects of caffeine on motor coordination has produced largely negative results. Graf stated that caffeine ingestion resulted in undesirable effects on motor coordination\textsuperscript{81}. Goldstein and associates, utilizing a coordination test involving trace-drawing of vertical lines, found that 150 mg and 300 mg caffeine had 'no effect upon coordination, as measured by this test\textsuperscript{82}. Putz-Anderson and co-workers found a 'small but significant' improvement in a tracking test involving hand-eye coordination as a result of ingestion of 200 mg caffeine\textsuperscript{82}.

Differences in testing protocol and doses of caffeine may have accounted for this disparity. Perhaps the fact that 200–900 mg caffeine decreases hand steadiness predisposes a decrease in fine motor coordination\textsuperscript{78,94,95}. Certainly the study by Goldstein et al. would be influenced by a decrease in hand steadiness\textsuperscript{82}.

Influence of caffeine on vision

Putz-Anderson and associates concluded that a dose of 200 mg caffeine generated significant improvement in visual monitoring during a dual task of tone-detection and compensatory tracking\textsuperscript{83}. In an investigation on foveal simultaneous contrast using a small circular test field surrounded by an inducing annulus (multipole-field), Klemann and associates found that caffeine 'not only diminished the enhancement phenomenon but erased it\textsuperscript{96}'. Examining visual threshold, Diamond and Cole found that 1.5 and 3.0 grams of caffeine significantly decreased visual threshold luminance when compared with a control group\textsuperscript{97}. Diamond and Cole suggested that caffeine causes the 'on' visual pathways to become more sensitive to light and that the
threshold decreases correspondingly to the increase of the dose\(^9\).

With regard to perceptual-restructuring tasks, caffeine was found to impair performance in novel perceptual-restructuring tasks and to facilitate the performance task after it was no longer novel\(^9\). Administering doses of 32, 64, 128, and 256 mg caffeine, Lieberman et al. found significantly improved auditory vigilance and visual reaction time as a result of all of the higher doses of caffeine\(^9\). Additionally, no adverse effects were observed in a barrage of motor performance tests\(^9\).

**Mental alertness**

The stimulating properties of caffeine have traditionally been used to delay sleep and to promote alertness. One of the earliest investigations demonstrated that caffeine at moderately large doses stimulated mental activity\(^9\). Graf also concluded that caffeine was a strong neural stimulant suitable for improving physical and mental efficiency\(^9\). Goldstein administered 150–200 mg caffeine in an investigation of wakefulness and found: caffeine prolonged the time required to fall asleep; caffeine disturbed the soundness of sleep; and caffeine-tolerant individuals were distinctly less affected by the drug\(^9\). Another study involving caffeine and cognitive performance indicated caffeine to be effective in preventing attention lapses\(^9\).

However, disagreement regarding the effects of caffeine on mental activity and intellectual performance exists. Two studies reported no evidence that caffeine at moderate and moderately large doses stimulated mental activity\(^9\) and that caffeine had no effect on objectivity measured performance\(^9\). The latter investigation noted that some of the subjects indicated a feeling of nervousness rather than alertness.

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