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Review

Caffeine—Not just a stimulant

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ABSTRACT

Objective: The beneficial effects of human caffeine consumption deserve clarification.
Methods: A detailed literature review was conducted and summarized.
Results: A large body of scientific evidence describes the beneficial effects of human caffeine consumption on a number of physiologic systems.
Conclusion: The consumption of moderate amounts of caffeine 1) increases energy availability, 2) increases daily energy expenditure, 3) decreases fatigue, 4) decreases the sense of effort associated with physical activity, 5) enhances physical performance, 6) enhances motor performance, 7) enhances cognitive performance, 8) increases alertness, wakefulness, and feelings of "energy," 9) decreases mental fatigue, 10) quickens reactions, 11) increases the accuracy of reactions, 12) increases the ability to concentrate and focus attention, 13) enhances short-term memory, 14) increases the ability to solve problems requiring reasoning, 15) increases the ability to make correct decisions, 16) enhances cognitive functioning capabilities and neuromuscular coordination, and 17) in otherwise healthy non-pregnant adults is safe.

Introduction

Considerations of the physiologic effects of caffeine typically are limited to presumptive "stimulant effects." Because the term *stimulant* often evokes emotionally pejorative reflexes, the distinction between "stimulant" and "non-stimulant" neurophysiologic responses to caffeine should be clarified. In fact, many of the human responses to caffeine extend beyond "stimulant effects" and evidence of such beneficial responses to caffeine consumption is abundant. In this era of evidence-based and science-based medical decision-making, this widely consumed phytonutrient deserves closer scrutiny.

Caffeine potentiates postsynaptic neurotransmission in the sympathetic nervous system

Caffeine (1,3,7-trimethylxanthine) is a plant alkaloid that increases the excitability of the adenosine-sensitive sympathetic nervous system [1,2]. Signals originating within the sympathetic nervous system produce transient increases in the cyclic adenosine monosphosphate concentration within the postsynaptic cells through which the signal is expressed [3]. By acting as a competitive antagonist of adenosine, caffeine inhibits the enzymatic degradation of cyclic adenosine monosphosphate by phosphodiesterases within the postsynaptic cell and the presence of caffeine may increase the strength of transmitted signals [4,5].

Caffeine increases resting energy expenditure

Human 24-h energy expenditure, sleeping metabolic rate, and resting awake metabolic rate all are proportional to the rate of sympathetic nerve activity and plasma norepinephrine concentration [3]. By potentiating sympathetic activity, caffeine stimulates fat lipolysis. For example, the ingestion of as little as 50 mg of caffeine by normal-weight, non-exercising, healthy men produced a significant increase in resting energy expenditure within 30 min of caffeine ingestion [5]. The increase persisted for at least 4 h and produced a significant 6% total increase in daily resting energy expenditure. Exercise-associated fatty acid oxidation also is increased by caffeine ingestion. When endurance-trained elite athletes performed at incrementally increasing work intensities after acute caffeine consumption, energy expenditure and fat oxidation increased disproportionately to increasing workload [6].

Caffeine increases endurance and enhances performance

In addition to its effects on energy production, caffeine increases serotonin concentrations in brainstem regions that

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have excitatory projections to spinal motor neurons, increasing the self-sustained firing of the skeletal muscle motor units that are enervated by these neurons [7]. By potentiating motor unit sensitivity to stimulation, caffeine postpones fatigue and increases human endurance [7]. For example, in a double-blind, randomized, placebo-controlled crossover study, the consumption of 100 mg of caffeine immediately before 2.5 h of cycling at 60% maximal effort significantly increased time to exhaustion in competitive cyclists [8]. Another group of healthy young men showed significantly smaller increases in heart rate, reflecting increased efficiency of energy utilization and decreased level of exertion, during a bout of submaximal exercise that began 30 min after the consumption of 90 to 150 mg of caffeine [9]. In its definitive 2001 report (*Caffeine for the Sustainment of Mental Task Performance. Formulations for Military Operations*), the Institute of Medicine Food and Nutrition Board Committee on Military Nutrition Research concluded that 150 mg of caffeine enhances physical endurance and the quality of physical performance [10].

Caffeine increases mental energy

In addition to benefitting physical performance and endurance, caffeine directly supports the central nervous system. Magnetic resonance imaging evidence shows that cerebral blood flow is directly proportional to recent caffeine intake [11] and the acute consumption of 400 mg of caffeine has been shown by pulsed transcranial Doppler sonography to increase significantly blood flow through the middle and anterior cerebral arteries [12]. In addition, caffeine acutely increases the functioning efficiency of neuronal networks in the human cerebral cortex [13]. For example, 20 min after the consumption of 100 mg of caffeine and while performing a task requiring the use of working memory, subjects exhibited magnetic resonance imaging evidence of increased neuronal activity in a network of brain areas that are associated with attention-demanding cognitive functions [14]. Such increases in "mental energy" can produce increases in the functional capacity to engage in cognitively demanding tasks that can be expressed as increased vigilance, alertness, ability to concentrate, and ability to correctly choose among alternatives [15].

Caffeine enhances cognitive functioning

In many human studies, caffeine consumption has increased alertness, ability to concentrate, problem-solving ability, wakefulness, and feelings of "energy" [8,16–20]. The consumption of a single bolus of as little as 32 to 50 mg of caffeine has been observed to stimulate significant improvements in alertness and in the ability to concentrate in as little as 20 min [16,17]. Compared with the ineffectiveness of placebo, the consumption of 100 mg of caffeine 1 h before attending a 75-min university lecture significantly increased self-assessed postlecture wakefulness, mental clarity, feelings of being energetic, alertness, attentiveness, ability to concentrate, and state of mental arousal [18]. Even well-rested young adults have exhibited significantly increased mental alertness within 50 min of the consumption of 140 mg of caffeine [19]. A group of healthy volunteers responded to the consumption of 75 mg of caffeine with sustained performance on the critical flicker fusion test of overall central nervous system activity throughout the day and evening, with no performance decrement resulting from tiredness [20].

The benefits of caffeine consumption extend beyond "wakefulness" to other reflections of enhanced mental energy. For example, in a test of caffeine and acute exhaustion, previously well-rested and well-trained cyclists consumed placebo or 100 mg of caffeine immediately before cycling at 60% of maximal capacity for 2.5 h; after 2.5 h, the pre-exercise consumption of caffeine was associated with significantly faster and more accurate performance on tests of complex cognitive functions [8].

Cognitive functions, including the abilities to concentrate and to solve problems, are enhanced after caffeine consumption. For example, the findings of two prospective observational studies indicated that the habitual daily consumption of any caffeine decreased significantly the risk for "cognitive failures" ("forgetting where you put things," "loss of concentration," "making the wrong choice") [21,22].

In many placebo-controlled studies, placebo was ineffective, whereas the acute consumption of caffeine produced significant improvements in reaction time, accuracy of responses, ability to focus attention, working short-term memory, sentence-verification accuracy, ability to solve difficult problems requiring reasoning, mental fatigue, vigor, and alertness [23–28]. In one study, within 30 min of its ingestion, 40 mg of caffeine increased the ability to correctly match visual stimuli to motor responses; this effect was associated with increased event-related potentials in brain regions involved in visual processing, decision-making, and the application of selective attention [23]. In double-blind, placebo-controlled, randomized trials, the consumption of an average of 125 mg of caffeine [24] or of an average of 150 mg of caffeine [25] by healthy adults produced improved performance on tests of speed of responses and of the ability to recall number sequences when measured 30 min after caffeine ingestion. The magnitude of these improvements was even greater after the consumption of 250 mg of caffeine.

In other double-blind, placebo-controlled, randomized trials, the consumption of 75 mg of caffeine improved reaction time, vigilance, ability to focus attention, accuracy of responses, and ability to recall number sequences [26,27]. A group of young adult men responded to the acute consumption of 64 mg of caffeine with increases in the accuracy of responses coupled with decreases in reaction time [28]. In its definitive 2001 report (*Caffeine for the Sustainment of Mental Task Performance. Formulations for Military Operations*), the Institute of Medicine Food and Nutrition Board Committee on Military Nutrition Research concluded that the consumption of 150 mg of caffeine enhances cognitive performance and that these effects can persist for as long as 10 h after consumption [10].

Caffeine increases neuromuscular coordination

In contrast to common misconceptions, moderate caffeine consumption contributes to enhanced neuromuscular coordination. For example, compared with placebo, the consumption of 200 mg of caffeine as coffee decreased significantly the number of "lane violations" committed by drivers during 90 min of nighttime driving at 80 mph on a public highway [29]. A similar improvement in performance was recorded during 30-min daytime driving simulations that began immediately after caffeine consumption (100 mg) [30]. In a placebo-controlled field trial, compared with placebo, the acute consumption of 200 mg of caffeine enabled US Navy SEAL trainees to sight a rifle and shoot more rapidly and accurately after 73 h of total sleep deprivation [31]. In another placebo-controlled field trial, compared with placebo, the consumption of 600 mg of caffeine over a period of 6 h after over 2 d of enforced sleep deprivation significantly improved the marksmanship of US Army infantrymen [32]. In its definitive 2001 report (*Caffeine for the*

Sustainment of Mental Task Performance. Formulations for Military Operations), the Institute of Medicine Food and Nutrition Board Committee on Military Nutrition Research concluded that single doses of caffeine containing up to 600 mg of caffeine enhance cognitive functioning capabilities and neuromuscular coordination [33].

After a rigorous preapproval process, on December 31, 2007, the Natural Health Products Directorate of Health Canada, an agency of the Canadian government, approved the inclusion of caffeine in dietary supplements intended to promote alertness, wakefulness, enhanced cognitive performance, endurance, decrease of fatigue, and enhanced motor performance [34]. The recommended intakes of caffeine are 100 to 200 mg, every 3 to 4 h, up to five times daily [34].

Caffeine elevates mood and relieves anxiety

Improvements in cognitive functioning capabilities are accompanied by improved mood, self-image, and overall "happiness" and less anxiety [27,35,36]. In a double-blind, placebo-controlled, randomized trial, the consumption of 75 mg of caffeine improved energetic mood [27]. In another double-blind, placebo-controlled, randomized trial, the consumption of 100 mg of caffeine decreased anxiety 30 min later in a group of healthy adults [35]. The results of another double-blind, placebo-controlled, randomized trial demonstrated that the consumption of 64 mg of caffeine produced significant improvements in vigor, feelings of inertia, despondency, hostility, imagination, and contentment 30 to 180 min after consumption [36]. In addition to these effects, the consumption of 128 mg of caffeine by these same subjects produced significant improvements in clearheadedness, listlessness, and efficiency of thought processes. The cognitive and emotional benefits of caffeine consumption increase in magnitude as the amount of acutely consumed caffeine increases [17,30,35–38], persist for at least 6 h after consumption [35], and may be more pronounced in individuals who habitually consume more than one 8-oz cup, can, or bottle of caffeine-containing beverages daily [39].

Caffeine consumption is safe

Moderate intakes of caffeine pose no health risks. The authors of a detailed review of the published literature (itself published in 2007) concluded that the routine daily consumption of up to 1000 mg of caffeine posed no risks to human health [40]. In fact, the findings of the Leisure World Cohort Study, in which 8644 elderly women and 4980 elderly men were studied for 23 y, indicated that the daily consumption of up to 400 mg of caffeine significantly decreased (by 10%) the risk of dying from any cause (relative risk ratio [RR] 0.90, 95% confidence interval [CI] 0.85–0.94) [41]. This significant risk decrease was not increased further or reversed by the routine daily consumption of more than 400 mg of caffeine. The results of a 14-y prospective observational study of men and women older than 70 y when the study began indicated that the risk of dying prematurely was decreased 4% by every cup of coffee consumed daily (95% CI 0–8) [42].

Meta-analysts have concluded that although weaker retrospective case-control studies tend to support the hypothesis that an increase in the risk for developing coronary heart disease is associated with chronic consumption of three or more cups of caffeinated coffee daily, more reliable prospective cohort studies have consistently found no association between any amount of coffee consumption and coronary heart disease [43]. In fact, an analysis of the data provided by the 44 005 male participants in the Health Professionals Follow-Up Study and the 84 488 female participants in the Nurses' Health Study demonstrated that even more than six cups of caffeinated coffee (equivalent to about 1000 mg of caffeine [44]) daily had no effect on the risk for developing coronary heart disease [45]. In addition, in 3497 men in the Health Professionals Follow-Up Study with type 2 diabetes, there was no relation between habitual coffee consumption and risk for developing cardiovascular disease [46]. In contrast, the combined data from the Health Professionals Follow-Up Study and the Nurses' Health Study indicated that the risks for dying prematurely from any cause and specifically from cardiovascular disease were significantly *inversely proportional* to chronic daily coffee consumption [47]. Furthermore, after 24 y of observation, the data from the Nurses' Health Study indicated that the risk of developing a stroke also was significantly *inversely proportional* to chronic daily coffee consumption [48]. In addition, data from 27 312 postmenopausal women who were observed for 15 y during the Iowa Women's Health Study demonstrated that any amount of habitually consumed caffeinated coffee *decreased* the risk of death from cardiovascular disease by 15% to 25% [49]. Consistent with these findings, the 10-y prospective Framingham Heart Study of men and women initially 65 to 96 y old found that the consumption of coffee halved the risks for heart valve disease (RR 0.57, 95% CI 0.34–0.96) and for death from coronary artery disease (RR 0.57, 95% CI 0.36–0.91) [50].

Consistent with reports of the safety of moderate caffeine consumption, in a study of subjects in Costa Rica, the routine consumption of four or more cups of coffee (equivalent to about 500 mg of caffeine [44]) daily did not increase the risk of myocardial infarction in adults with otherwise overall increased risk for infarction [51,52]. Likewise, a study of survivors of non-fatal myocardial infarction conducted in the United States found that continued routine daily consumption of up to 14 cups of caffeinated coffee (equivalent to well over 1000 mg of caffeine [44]) had no effect on residual life span [53]. Similarly, putative potentiators of acute myocardial infarction (the cardiovascular responses to acute stress) were found to remain unaffected by caffeine consumption by healthy men [54].

The interactions between caffeine intake and blood pressure have been studied repeatedly. In an example of such studies, when healthy young men consumed a bolus of 300 mg of caffeine, they showed transient increases in systolic and diastolic blood pressures of 6.0 and 3.1 mmHg, respectively, that had resolved within 3 h [55]. Investigators performing a meta-analysis of well-conducted clinical trials that studied the putative effects of caffeinated coffee consumption on blood pressure and were published before 1997 calculated average increases in systolic and diastolic blood pressures of 2.4 and 1.2 mmHg, respectively, resulting from habitual consumption of five cups of caffeinated coffee, equivalent to more than 600 mg of caffeine [44], daily [56]. Investigators performing a similar meta-analysis of well-conducted clinical trials that studied the putative effects of caffeinated coffee consumption on blood pressure and were published before 2003 calculated average increases in systolic and diastolic blood pressures of 4.2 and 2.4 mmHg, respectively, resulting from habitual daily consumption of about 400 mg of caffeine [57]. The results of a clinical trial published after that meta-analysis appeared indicated that after 12 y of observation, the 155 594 originally normotensive women participating in Nurses' Health Studies I and II showed no association between caffeine intake or caffeinated coffee consumption and the development of hypertension [58].

In more recently published results, the acute consumption of 100 mg of caffeine had no effect on systolic blood pressure, diastolic blood pressure, heart rate, or measurements of cardiac ventricular function (peak systolic mitral annulus velocity, peak early diastolic mitral annulus velocity, peak late diastolic mitral annulus velocity, peak early diastolic transmitral flow, left atrioventricular plane displacement, peak systolic tricuspid annulus velocity, peak early diastolic tricuspid annulus velocity, peak late diastolic tricuspid annulus velocity, tricuspid annular plane systolic excursion) [59]. In college students with healthy cardiovascular systems, the acute consumption of 75 mg of caffeine was followed 30 min later by a significant *decrease* in resting heart rate [60]. Consistent with these findings, the chronic consumption of three or more cups of caffeinated coffee daily had no effect on resting heart rate, systolic blood pressure, diastolic blood pressure, aortic systolic blood pressure, or diastolic aortic blood pressure in subjects with untreated hypertension [61] (in contrast to the small, statistically significant, but clinically irrelevant increases that these investigators previously associated with caffeine intake in a cohort of subjects with normal blood pressures [62]), and even more than six cups of caffeinated coffee (equivalent to about 1000 mg of caffeine [44]) daily for 11 y had no effect on the risk for developing hypertension in 2985 men and 3383 women (the Doetinchem Cohort Study) [63]. The results of a recently published meta-analysis of 13 placebo-controlled human trials indicated that the consumption of at least 450 mg of caffeine within 24 h produced neither water retention nor diuresis [64], and the author of a recently completed systematic review of original research findings and of the results of previously published meta-analyses of those findings concluded that "there is no clear evidence for a causal relationship between caffeinated coffee and hypertension" [65]. The author of another recently completed systematic review of published epidemiologic studies concluded that "regular intake of caffeinated coffee does not increase the risk of hypertension" [66]. In fact, 4 wk of consumption of three to four cups of caffeinated coffee (equivalent to 500 to 600 mg of caffeine [46]) by individuals with hypertension produced significant *decreases* in systolic and diastolic blood pressures of 7 and 3 mmHg, respectively [67].

The US Food and Drug Administration has concluded that individuals who habitually consume caffeine develop tachyphylaxis—a diminishment of a response after the repetitive consumption of a pharmacologically active substance [68]. Based on published scientific evidence that any acute pressor effects of caffeine consumption cease after 1 to 2 wk of daily consumption, the US Food and Drug Administration concluded that "the available evidence shows that chronic use of caffeine has no effect on blood pressure that persists beyond 2 weeks" [68]. It should be noted that these studies, reports, and conclusions concern adults; although caffeine appears to be without adverse effects in children in daily amounts of up to 3 mg/kg of body weight, amounts of at least 5 mg/kg of body weight may increase resting blood pressure in children [69].

The data from the 27 312 postmenopausal women who were observed for 15 y during the Iowa Women's Health Study demonstrated that any amount of habitually consumed caffeinated coffee *decreased* the risk of death from any noncardiovascular inflammatory disease by about 30% ("any other inflammatory disease" was defined as any infectious disease, chronic neurodegenerative disease, type 1 diabetes, type 2 diabetes, respiratory tract disease, liver disease, renal failure, and rheumatic disease) [49]. Consistent with and possibly explaining this finding, serum concentrations of C-reactive protein have been reported to be inversely proportional to routine daily coffee consumption [70,71]. Similarly, the risk of developing gout, the most common form of inflammatory arthritis in men, was approximately halved by the daily consumption of six or more cups of caffeinated coffee (equivalent to $\geq$1000 mg of caffeine [44]; RR 0.41, 95% CI 0.19–0.88) [72]. After 24 y of observation, the combined data from the Nurses' Health Study and the Health Professionals Follow-Up Study indicated that there is no relation between habitual caffeine consumption and the risk for developing primary open-angle glaucoma [73].

Cancer risk may be decreased by caffeine consumption. Of the participants in the prospective observational Nurses' Health Study who never used oral contraceptives or postmenopausal steroid hormones, the risk of developing epithelial ovarian cancer was nearly halved by the daily consumption of more than 500 mg of caffeine (RR 0.65, 95% CI 0.46–0.92; and RR 0.57, 95% CI 0.36–0.91, respectively) [74]. The subcohort of all postmenopausal women also showed a 12% decrease in the risk of developing breast cancer (RR 0.88, 95% CI 0.79–0.97) [75]. Of all 29 060 postmenopausal women in the 18-y prospective Iowa Women's Health Study, regardless of hormone use, the incidence of ovarian cancer was not affected by chronic daily caffeine intake [76]. A similar finding of no relation between caffeine intake and risk for ovarian cancer was reported by investigators conducting a retrospective case-control study [77].

Concerns that caffeine consumption might predispose to or exascerbate existing type 2 diabetes have been fueled by a report that the acute ingestion of a bolus of 250 mg of caffeine added to a meal resulted in significantly higher postingestion increases in plasma concentrations of glucose and insulin than were produced by the meal itself in a small group of men and women with type 2 diabetes [78]. In contrast, in normoglycemic subjects, the acute ingestion of a bolus of 250 mg of caffeine added to each of two consecutive meals had no effect on 24-h integrated plasma glucose concentrations [79]. Furthermore, the daily consumption of 400 mg of caffeine for 7 d by healthy normoglycemic young adults did not affect fasting plasma glucose concentrations [80] and the chronic consumption of about 400 mg of caffeine daily did not cause increased hyperglycemia or hyperinsulinemia after an acute glucose challenge [81]. In addition, in a prospective study of 1744 previously non-diabetic pregnant women, the routine daily consumption of 6 to 10 cups of caffeinated coffee (equivalent to 1000 to 1500 mg of caffeine [44]) contributed to successful pregnancy outcomes by cutting in half the risk of developing gestational diabetes [82]. Consistent with this finding, the results of the 18-y prospective Nurses' Health Study and the 12-y prospective Health Professionals Follow-up Study indicated that the risk for developing type 2 diabetes *decreases* as habitual caffeine intake increases in men and women [83].

The safety of caffeine during pregnancy remains controversial. Although the results of a Danish study of 1150 singleton pregnancies indicated that three or more cups of coffee consumed during pregnancy have no effect on neonatal birthweight or the length of human gestation [84], other investigators reported that routine daily consumption of more than 300 mg of caffeine during gestation increased slightly the risk of fetal growth restriction [85] and others observed a significantly increased risk of miscarriage in pregnant women who consumed more than 200 mg of caffeine daily [86]. The results of another observational study suggested that maternal consumption of more than 400 mg (but not less) of caffeine daily during gestation may increase the risk of delivering a male infant with neonatal cryptorchidism [87]. The results of another observational study suggested that

maternal consumption of caffeine daily during gestation does not affect the risk of delivering a baby with spina bifida, anencephaly, or encephalocele [88].

The potential for habitual caffeine consumption to be associated with the neurologic phenomena of dependence, tolerance, and withdrawal might suggest the presence of a relation between chronic caffeine consumption and psychiatric sequelae. However, an analysis of differences within several thousand pairs of monozygotic twins demonstrated that the routine daily consumption of up to 3000 mg of caffeine did not increase the likelihood of developing major depression, generalized anxiety disorder, panic disorder, adult antisocial personality disorder, alcohol dependence, or of engaging in drug abuse [89]. Nonetheless, clinicians have reported that caffeine consumption may excacerbate anxiety in children and adolescents who have been diagnosed with major depressive disorder [90] and in adults with panic disorder, generalized social anxiety disorder, or performance social anxiety disorder [91]. In contrast, adults free of these conditions did not have artificially induced panic attacks 45 min after consuming 480 mg of caffeine [91].

The results of a prospective observational study of 4197 women and 2820 men 65 y and older (the French Three City Study) indicated that the routine daily consumption of three or more cups of caffeinated coffee attenuated the aging-associated declines in verbal retrieval and visuospatial memory [92]. Another 21-y study of initially middle-aged men and women (the Cardiovascular Risk Factors, Aging and Dementia [CAIDE] Study) found that compared with subjects routinely consuming less than 300 mg of caffeine daily, those subjects routinely consuming 400 to 650 mg daily showed a significantly lower incidence of clinical dementia (RR 0.30, 95% CI 0.10–0.93) [93]. Furthermore, the protective effect was greatest in the oldest subjects. Interestingly, in a cross-sectional study, the risk of developing Parkinson's disease was found to be inversely proportional to routine caffeine intakes [94], and in a 22-y prospective observational study of men and women initially 50 to 79 y old it was found that the risk for Parkinson's disease was cut dramatically by the routine consumption of at least 10 cups of coffee (RR 0.26, 95% CI 0.07–0.99) [95].

The results of a 16-y prospective study of 116 363 women (the Nurses' Health Study II) indicated that the daily consumption of 400 mg of caffeine or more had no effect on the risk of seizure or epilepsy [96]. The results of the cross-sectional Nord-Trondelag Health Survey of 50 483 adult Norwegian men and women demonstrated that the prevalence of headache was independent of daily routine caffeine consumption [97].

The results of two prospective observational studies indicated that habitual caffeine intake is not related to the risks for angina, diabetes, myocardial infarction, hypertension, or depression [22]. Furthermore, the acute consumption of 600 or 800 mg of caffeine at one time did not produce side effects or adverse reactions [98–101]. In its definitive 2001 report (*Caffeine for the Sustainment of Mental Task Performance. Formulations for Military Operations*), the Institute of Medicine Food and Nutrition Board Committee on Military Nutrition Research concluded that single doses of up to 600 mg of caffeine do not produce neuromuscular manifestations ("jitters") [34].

Conclusions

The foregoing publicly available scientific evidence substantiates the conclusions that the consumption of moderate amounts of caffeine 1) increases energy availability, 2) increases daily energy expenditure, 3) decreases fatigue, 4) decreases the sense of effort associated with physical activity, 5) enhances physical performance, 6) enhances motor performance, 7) enhances cognitive performance, 8) increases alertness, wakefulness, and feelings of "energy," 9) decreases mental fatigue, 10) quickens reactions, 11) increases the accuracy of reactions, 12) increases the ability to concentrate and focus attention, 13) enhances short-term memory, 14) increases the ability to solve problems requiring reasoning, 15) increases the ability to make correct decisions, 16) enhances cognitive functioning capabilities and neuromuscular coordination, and 17) in otherwise healthy non-pregnant adults is safe.

Research focused away from any ergogenic properties of caffeine and concentrated on this nutrient's beneficial influences on human physiology and health can only accelerate the removal of any stigma associated with caffeine by the modern medical community. Unfortunately, the current patent-based commercially funded system and the novelty-based government-funded systems in the United States will continue to delay progress in this promising area.

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