Turkish Journal of Sport and Exercise /Türk Spor ve Egzersiz Dergisi
http://dergipark.gov.tr/tsed
Year: 2021 - Volume: 23 - Issue:1 - Pages: 86-101
DOI: 10.15314/tsed.895754

Turkish Journal of Sport and Exercise
Türk Spor ve Egzersiz Dergisi
ISSN: 2147-5652
https://dergipark.org.tr/tr/pub/tsed

Effect Of Caffeine On Exercise Performance: Current Review

Yusuf BUZDAĞLI[1A], Aslıhan TEKiN[2B] ,Erdinç ŞIKTAR[1C], Günay ESKiCi[3D]

[1]*Department of Physical Education and Sport, Faculty of Sport Sciences, Erzurum Technical University, Erzurum, Turkey*

[2]*Nutrition and Dietetics Department, Graduate School of Winter Sports and Sport Sciences, Ataturk University, Erzurum, Turkey*

[3]*Department of Coaching Education, Faculty of Sport Sciences, Çanakkale Onsekiz Mart University, Çanakkale, Turkey*

Address Correspondence to Y. Buzdağlı: e-mail: yusuf.buzdagli@erzurum.edu.tr

(Received): 12/03/2021/ (Accepted): 30.04.2021

A:Orcid ID: 0000-0003-1809-5194 B:Orcid ID: 0000-0002-1760-5378 C:Orcid ID: 0000-0003-0387-3969 D:Orcid ID: 0000-0002-4349-4704

Abstract

Caffeine is an ergogenic supplement that has been attracting attention in the sports community for many years. It has been proven in many studies that coffee consumption has a positive effect on exercise performance. This study was conducted to (I) examine the effects of caffeine on exercise performance and different performance areas, (II) to provide comprehensive recommendations on the use of caffeine in sports and exercise, and (III) to identify existing gaps in the literature and to make key recommendations for future research. This current review article provides an analytical view of studies involving the use of caffeine for the physical, physiological, and cognitive performance of individuals, and discusses factors that may affect the ergogenic effects of caffeine on the different proposed activities. Within the scope of this review, previously published studies were searched using comprehensive keywords related to "caffeine" through "ELSEVIER Science Direct (SciVerse), Taylor & Francis, EBSCOhost-Academic Search Complete, PubMed and SpringerLink, Google Scholar" databases until January 2021. As a result, it has been reported that caffeine increases endurance performance by 2-4% and improves short-term and intense intensity exercise performance in highly trained individuals. The improving effect of caffeine on cognitive performance supports the use of caffeine as an ergogenic supplement. Caffeine has been shown to increase sympathetic nervous system activity and release fatty acids from adipose and / or intramuscular stores. This mechanism, which occurs indirectly through increased adrenaline levels, has the potential to increase the availability of fatty acids for oxidation and the resting metabolic rate. At the same time, it has been observed that caffeine does not cause dehydration and is a reliable ergogenic supplement in this respect. The ergogenic effect of caffeine should be clarified by focusing on questions such as at what time of the day caffeine consumption affects caffeine ergogenicity, the effect of age on caffeine ergogenicity, caffeine intake according to athlete's training level, and the importance of genotype in terms of caffeine consumption.

Keywords: Caffeine, Exercise, Athletic performance

INTRODUCTION

Caffeine is the world's most consumed psychoactive substance, naturally found in many plant species, including coffee, tea, and cocoa. Caffeine, which is added to many beverages such as energy drinks and whose consumption has increased day by day in the last two decades, is mostly consumed in the form of beverages such as coffee, soft drinks, and tea (1). In Western countries, approximately 90% of adults consume caffeine regularly, while daily caffeine consumption in US adult men and women is estimated to be 200 mg, according to 2009-2010 data (2, 3).

Caffeine is one of the most popular socially acceptable ergogenic supplements that has been used in athletic circles as an ergogenic aid or performance enhancer for years, because it is not doping and can be taken from natural sources. It is also a supplement with a long history of use for its ergogenic effects on performance. Caffeine intake has been very common among athletes, especially since 2004, when the World Anti-Doping Agency was removed from the in competition prohibited substances list. For example, 74% of urine samples collected between 2004 and 2008 and analyzed as part of doping control contained caffeine (4). Given the inconsistent evidence from primary research examining the effects of caffeine on exercise performance, several research groups have explored this issue using meta-analytical methods (5-8) . While these meta-analyzes generally report the ergogenic effects of caffeine on exercise performance, current studies should not focus solely on the effect of caffeine on exercise performance; He suggested that attention should also be paid to cognitive performance, caffeine use dosage and intake forms, fat metabolism, combined intakes of caffeine, caffeine consumption habits and effects on dehydration. Although many studies are investigating the effects of caffeine on overall health and exercise performance, recent research has shown that caffeine not only affects exercise performance, but also metabolic disorders, cognitive performance, consumption amount and forms, fat metabolism, combined intakes, caffeine consumption habits, and dehydration. It emphasizes the need to focus on the effects of caffeine (5, 9).

Responses in the organism with caffeine intake may vary from person to person. A person's genetic structure, consumption amount, individual's performance goal, type of sport performed, placebo effect, and caffeine intake form can affect the result. In addition, the health effects of caffeine have long been a topic of interest, and as noted by extensive research, caffeine remains an important dietary component for public health. It has also become ubiquitous in the sports world, where there is intense interest to better understand the effect of caffeine on various exercise performance. Thus, caffeine has been the focus of attention in the field of ergogenic aids and sports supplement research in recent years.

The purpose of this review is to reveal many aspects of caffeine's effect on exercise performance. In this direction, the results of the research on aerobic/anaerobic performance, strength/power performance, consumption amount and time, combined forms, caffeine consumption habits, and dehydration were evaluated and suggestions were made on the subject.

METHOD

Within the scope of this review, previously published studies were scanned through "ELSEVIER Science Direct (SciVerse), Taylor & Francis, EBSCOhost-Academic Search Complete, PubMed and SpringerLink, Google Scholar" until January 2021, "caffeine and exercise" for search, the keywords "caffeine and aerobic performance", "caffeine and resistance exercises", "caffeine and anaerobic performance", "caffeine and cognitive performance", "caffeine and supplements", "caffeine and dehydration", "caffeine consumption forms", "caffeine and doping", "caffeine metabolism", "caffeine and fat metabolism", "caffeine and doping", and "caffeine and consuming habits" were used.

Caffeine Metabolism

Caffeine is a purine alkaloid containing the methyl group at the 1,3,7 position, also called trimethylxanthin, and has a stimulating effect on the central nervous system (CNS). As a food additive, it can be produced synthetically for use in dietary supplements and pharmaceutical preparations where synthetic caffeine is the same as intrinsic or plant-derived caffeine. It has been defined as the most commonly consumed pharmacologically active food in the World (10).

Most of the biological effects of caffeine at the levels reached during normal consumption are due to its antagonizing the adenosine receptors, particularly the A1 and A2A receptors, and to a lesser extent the A2B and A3 receptors. A1 and A2A adenosine receptors affect various mechanisms found in large areas of the brain that are involved in the regulation of sleep, arousal, and cognition. Therefore, it is not surprising that caffeine as an adenosine receptor antagonistcan alter physiological and mental states. Central adenosine receptors affected by typical caffeine exposure (11). Because the caffeine molecule is chemically similar to the adenosine molecule, it binds to adenosine receptors. Since adenosine receptors are related to sleep, sleep is not felt if caffeine is attached to the receptors instead of adenosine. The sleep-disturbing effect of caffeine is due to this antagonist mechanism.

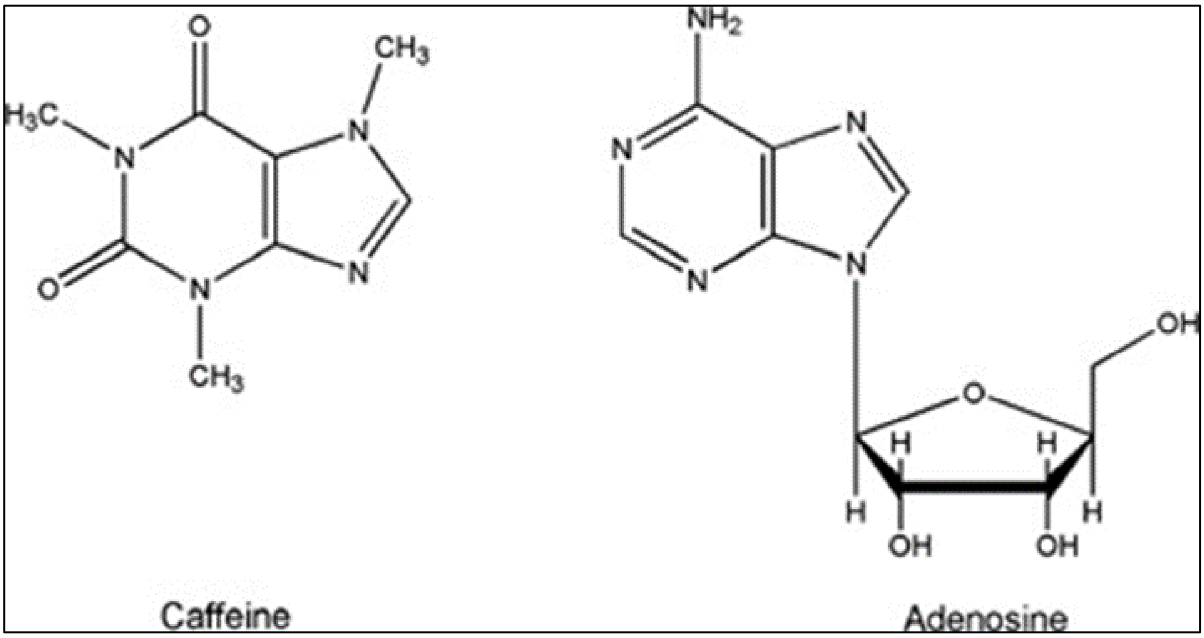

Figure 1. Chemical structures of caffeine and adenosine (12).

Caffeine is taken up and absorbed through food or synthetically. Once absorbed, it reaches all body cells. It then crosses the blood-brain barrier rapidly and is metabolized by the liver's P450 1A2 (CYP1A2) enzyme. Caffeine responses of individuals are different due to polymorphism in the CYP1A2 gene. After oral ingestion of caffeine, mostly in the form of coffee or tea, 99% is absorbed into the bloodstream from the gastrointestinal tract and peaks 30-60 minutes after eating. Caffeine absorption is between 45 and 80 minutes for caffeine-containing chewing gum, and 85-120 minutes for caffeine-containing capsules (13).

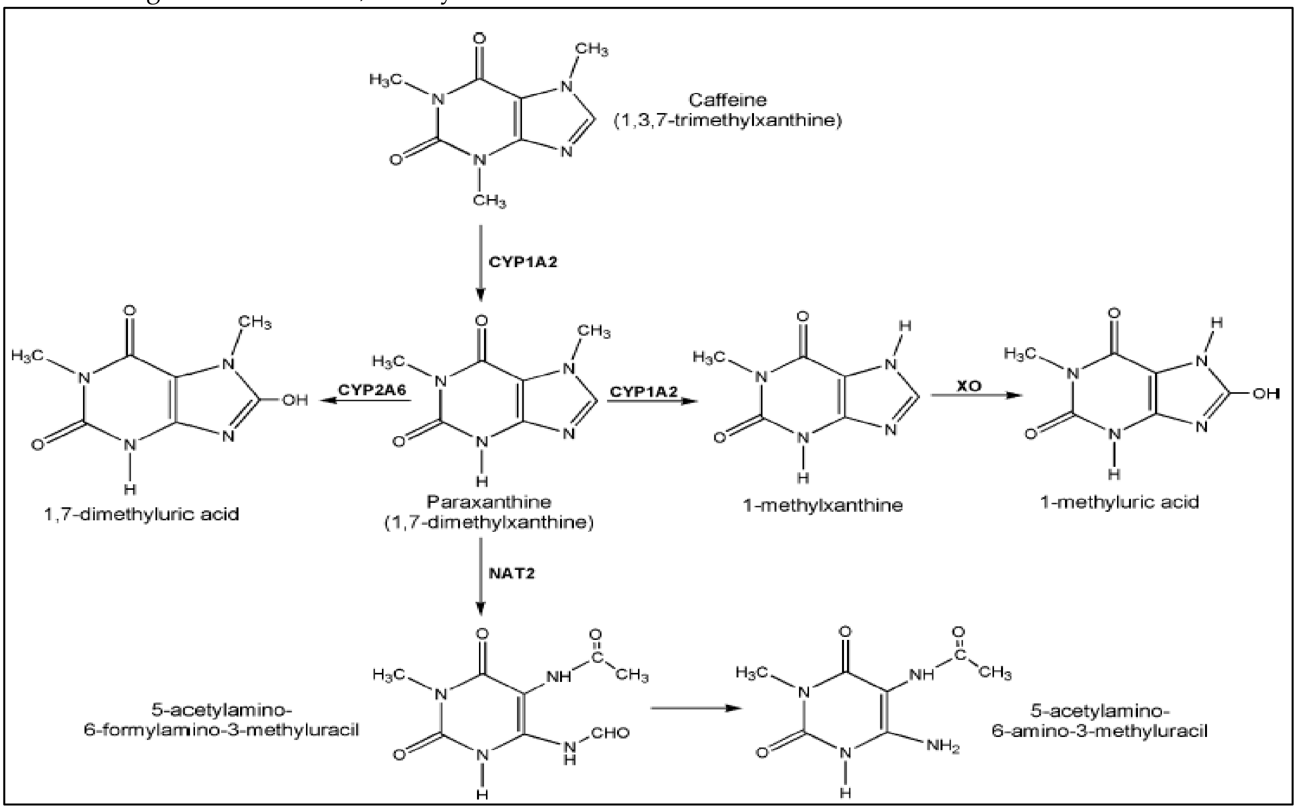

Figure 2. Main pathways in caffeine metabolism (12). Abbreviations: CYP1A2, cytochrome P450 1A2; CYP2A6, cytochrome P450 2A6; NAT2, N- acetyl transferase 2; XO, xanthine oxidase.

Table 1. Caffeine Amounts of Some Foods and Beverages

Food/Beverages	Amount	Caffeine (mg)
Cafe Latte /Cappuccino	200 mL	126
Filter Coffee / Black Coffee	200 mL	130
Espresso	200 mL	388
Nescafe	200 mL	62
Turkish Coffee	100 mL	58
Brewing Bag / Black Tea	100 mL	21
Green Tea	100 mL	15
Herbal Tea	240 mL	0
Redbull	250 mL	80
Energy Drinks	330 mL	100
Coffee With Milk	250 mL	158
Dark Chocolate	50 g	50
Hazelnut Chocolate	50 g	3
Chocolate Bar / Nougat	50 g	3
Chocolate Sauce	20 g	6
Chocolate Bar	50 g	9

Caffeine ergogenicity has effects on the muscle that can directly contribute. The most likely way that caffeine can benefit muscle contraction is through calcium ion (Ca^{2+}) mobilization, which facilitates force generation by each motor unit (15-17). Fatigue caused by the gradual reduction of Ca^{2+} release can be alleviated after caffeine intake (17, 18). Similarly; Caffeine, partially increased sodium/potassium pump activity (Na^+/K^+) potentially increases the stimulation-contraction matching required for muscle contraction (19). Caffeine appears to use its effects in various parts of the body, but the most solid evidence suggests that the main target is in the CNS, which is now considered the primary mechanism by which caffeine alters mental and physical performance (20). It is believed that caffeine exerts its effects on the CNS through antagonism of adenosine receptors and leads to increases in neurotransmitter release, motor unit firing rates, and pain suppression (21-23). Adenosine is involved in numerous physiological processes and plays a very important role as a homeostatic regulator and neuromodulator in the nervous system. The main known effects of adenosine are; It is to reduce the concentration of many neurotransmitters in the CNS, including serotonin, dopamine, acetylcholine, norepinephrine, and glutamate. Having a molecular structure similar to adenosine, caffeine binds to adenosine receptors after ingestion and therefore increases the concentration of these neurotransmitters (24, 25). This has positive effects on mood, alertness, focus, and mental vitality in most, if not all individuals (26-28). Caffeine can be used effectively to manipulate our mental state. It is widely consumed in the form of coffee to get rid of sleepiness. People avoid coffee consumption when they do not want their sleep to be affected negatively.

Caffeine and Exercise

The ergogenic potential of caffeine has been extensively studied in the sports and exercise science literature dating back to 1907 (29). The effect of caffeine on exercise performance can be listed as follows (30).

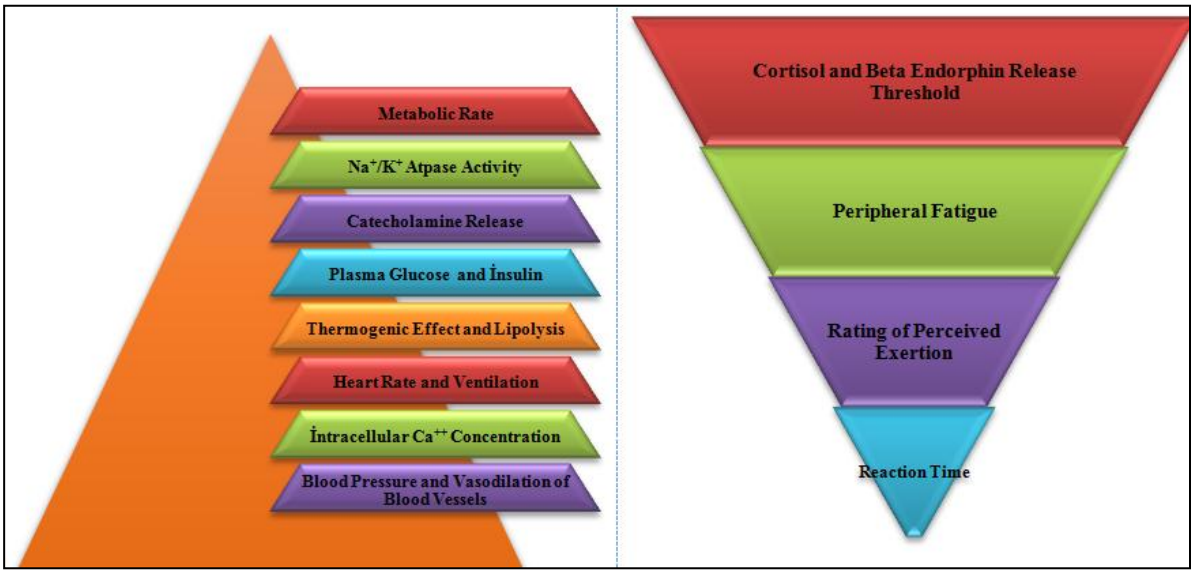

Figure 3. Caffeine and Performance Relationship. ∆: increased, ∇ : decreased

Effect of Caffeine on Aerobic Performance

Caffeine is an ergogenic aid preferred by athletes or active individuals in a wide variety of sports and activities involving aerobic endurance. A positive effect on performance has been proven in a variety of endurance sports, including cycling (31, 32), running (33, 34), cross-country skiing (35), and swimming (36).

Studies show that caffeine intake (eg, 3-9 mg / kg taken 30-90 minutes before exercise) can reduce carbohydrate use during exercise, thereby increasing endurance exercise capacity (37). In a study involving 8 trained cyclists and triathletes accustomed to consuming low doses of caffeine (≤300 mg / day), participants consumed beverages consisting of caffeine (5 mg / kg), instant coffee (5 mg/kg caffeine), instant decaffeinated coffee or placebo 1 h before exercise. The results of the study found that both caffeine (5 mg / kg) and coffee (5mg / kg caffeine) consumed 1 h before exercise could improve endurance exercise performance (38). In a study conducted on cyclists, it was determined that among those who consumed caffeinated coffee or decaffeinated coffee (6 mg / kg) 60 minutes before exercise, those who consumed caffeinated coffee had a positive effect on performance (39).

Many studies have shown that caffeine intake at the level of 3-6 mg / kg / day increases endurance by 2-4% (31, 32, 40, 41).

Effect of Caffeine on Anaerobic Performance

Anaerobic performance is a term of great importance for sports branches that are completed in a short time or require explosive force. Regular trainings cause an increase in the anaerobic performance of athletes. Athletes use a variety of ergogenic supplements to further increase anaerobic performance. Caffeine is of great importance in these ergogenic supplements.

In a study of 21 well-trained male participants, a gelatin capsule (30m; repeated at 35-second intervals) containing caffeine (5 mg / kg) and placebo (maltodextrin) taken 1 h before completing a multi-sprint trial was found to have an ergogenic effect on performance (42). In another study, it was determined that caffeine improves repetitive sprint performance but does not affect maximum strength and fatigue (43). In a study conducted by giving caffeine at a dose of 6 mg / kg to participants who are not trained in a particular sport, it was found that the maximal cycling speed of 2×60 seconds increased (44). In studies investigating the effect of caffeine given at the level of 5-6 mg / kg / day on anaerobic power in non-training individuals, it was found that performance did not change (45, 46) or increased (47).

Considering the studies that summarize the effectiveness of caffeine on short-term anaerobic exercises, it is seen that the use of caffeine in such exercises is less, and there is no consensus on the results. Therefore, it seems that more studies need to be performed on the relationship between caffeine and short-term exercise. In general, although the results are heterogeneous, it has been reported that caffeine supplementation at doses of 4-6 mg / kg on multiple and single sprint activities requiring high-intensity effort significantly increases performance in athletes with high training level while the same positive effect was not observed in participant groups with low training level.

The Effect of Caffeine on Strength Performance

Strength development through resistance training is an important component of conditioning programs for both fitness and competitive sports and activities. The most common consumption form preferred by individuals with or without training in strength studies is caffeine taken at the level of 3-6 mg / kg (2-11 mg / kg) 90 minutes before exercise in the form of pills or capsules. Although several studies have been published by ISSN (International Society of Sports Nutrition) since 2010, investigating the effects of caffeine on strength performance (48), some uncertainties persist in the performance enhancing effect of caffeine in activities involving muscle endurance, strength, and power.

Table 2. Investigations examining the effects of caffeine on exercise performance

References	Participants	Exercise Protocol	Cafe Dose	Conclusion
Grgic J et al. (49)	Resistance trained male (n=22)	1RM barbell bench press and leg press and 60% at 1RM again until exhaustion	**6 mg / kg**	↑ The total weight removed during the 60% 1RM trial was 11% and 12% higher for bench press and leg press with caffeine compared to placebo but still did not reach significance. ↔ The perceived intensity was similar to caffeine versus placebo at the end of resistance exercise. ↔ Acute caffeine intake did not significantly alter muscle strength or endurance during intense bench press or leg press exercise.
Norum M. et al. (50)	Resistance trained female (n=15)	Squats, bench press, countermovement jumps (CMJ) until exhaustion at 60% 1RM	**4 mg / kg**	↑ *Caffeine significantly improved repetitions in squats and bench press to exhaustion compared to placebo. ↑ *Caffeine significantly increased CMJ height and strength.
Goldstein E. et al. (51)	Resistance trained female (n=15)	1RM barbell bench press and repeat until exhaustion at 60% 1RM	**6 mg / kg**	↑ A significantly higher bench press maximum was seen with caffeine at 60% 1RM repeats with no significant difference between conditions. ↑ Systolic blood pressure was significantly higher after exercise with caffeine.
Timmins TD and Saunders DH (52)	Resistance trained male (n=16)	Maximal voluntary contraction; The isokinetic peak torque of knee extensors, ankle plantar flexors, elbow flexors and wrist flexors was measured at an angular velocity of 60 ° / s.	**6 mg / kg**	↑ Caffeine increased the maximal voluntary contractile strength in resistance training men, regardless of the position of the muscle group. ↑ Although the improvement in peak torque increased according to muscle group size, its effect was not clear.
Woolf K. et al. (53)	High-level fitness male team athlete (n = 18)	Leg press, chest press ve wingate testi	**5 mg / kg**	↑ With caffeine, the more total weight was lifted on the chest press and a higher peak strength was achieved during the Wingate test. ↔ No difference was found between caffeine and placebo for average strength, minimum strength, and power drop (Wingate test) on leg press. ↑ Higher insulin and glucose concentrations were observed after exercise with caffeine. ↑ Systolic blood pressure was significantly higher after exercise with caffeine. ↔ No difference was found between caffeine and placebo for free fatty acid concentrations, plasma lactate concentrations, cortisol concentrations, heart rate, and perceived intensity.
Beck TW. et al. (54)	Resistance trained male (n=31)	1RM bench press power and time to exhaustion at a speed corresponding to 85% of VO2max	**201 mg (2.1-3 mg / kg)**	↔ It was observed that caffeine did not contribute to the exercises.
Wilk M. et al. (55)	Male bodybuilding with caffeine habits (n = 16)	1RM strength test, muscle endurance at 50% 1RM	**9-11 mg / kg**	↔ It was observed that high-dose acute caffeine supplementation did not increase muscle strength or muscle endurance in athletes with caffeine habits.
Trevino MA. et al. (56)	Recreatively active male (n = 13)	3 maximum isometric muscle movements of the elbow flexors	**5-10 mg / kg**	↔ It was observed that caffeine supplementation did not provide an ergogenic effect for elbow flexors during isometric muscle movements.

Astorino TA. et al.(38)	Resistance trained male (n=22)	1RM bench press and leg press, repeat until it is exhausted at 60% 1RM	**6 mg / kg**	↔ Bench press and leg press 1RM, there was no significant increase in caffeine-boosted participants.
Glaister M. et al.(42)	Well-trained male (n = 21)	Multiple sprint test consisting of 12×30 m straight-line sprints repeated at 35 second intervals	**5 mg / kg**	↑ Caffeine has been shown to have ergogenic properties with the potential to benefit performance in both single and multiple sprint sports.
Trexler ET. et al.(43)	Well-trained male (n = 21)	Single reps for leg press and bench press at 80% of 1RM and repetitions to fatigue at 1RM	**300 mg (powder)** **303 mg (coffee)**	↑ It has been observed that caffeine can improve repetitive sprint performance. ↔ It was observed that caffeine did not affect repetitions for maximum strength and fatigue using both upper body and lower body exercises.
Crowe MJ. et al. (44)	Untrained male (n = 12), Untrained female (n = 5)	2 × 60 seconds maximal cycling	**6 mg / kg**	↓ It was observed that peak power was reached in a shorter time in the second of 2 × 60 seconds maximal cycling.
Collomp K. et al. (45)	Untrained male participating in non-specific sports activities only 2-3 h per week (n = 3), untrained female participating in non-specific sports activities only 2-3 h per week (n = 3)	30-second wingate test	**5 mg / kg**	↔ *Caffeine did not appear to cause a significant increase in performance for peak power or total work load.
Greer F. et al. (47)	Recreatively active male (n = 9)	30-second wingate test (2 separate sections, 4 minutes interval)	**6 mg / kg**	↓ The last two of the four wingate test showed a decrease in strength compared to the placebo. ↔ Caffeine did not appear to have a significant effect on blood lactate, O2 consumption, or aerobic additives at any time during the protocol. ↔ No ergogenic effects of caffeine on power output were observed during repetitive periods of short intense exercise.
Lorino AJ. et al. (46)	Untrained male (n = 16)	Agility run and 30-second Wingate test	**6 mg / kg**	↔ Caffeine did not seem to provide significantly better performance for agility running and the 30-second wingate test.

Bold text associated with reported trial outcomes; * delineates a significant change, ↔ = no improvement/change, ↑ = improved performance, ↓ = decreased, 1RM = repetitive maximal, VO_{2max} = maximum oxygen consumption

Forms of Caffeine

Although caffeine is often taken through beverages such as tea and coffee, it can be consumed in different forms to examine its effect on sports performance and to be consumed most beneficially. Caffeine in athletes; caffeinated bars and gels, caffeinated chewing gum, caffeinated energy drinks, caffeinated nasal and mouth aerosol sprays, and caffeinated mouthwashes.

Studies show that bars and gels containing 100 mg of caffeine improve cognitive function, exhaustion time, and time trial performance. Although plasma caffeine measurements are lacking in these studies, it can be assumed that the increases will mimic the findings obtained from caffeine tablet and coffee consumption (57-60). Since caffeinated bars and gels are key sources of caffeine for athletes during training and competition, and there are currently no studies examining female participants, more research is needed in this area. Studies show that caffeine in chewing gum at a dose of 200-300 mg is ergogenic when given before or during an endurance exercise in well-trained women and male cyclists (61). Current literature does not support the ergogenic effects of caffeine supplements administered in the form of energy drinks. However, additional studies are needed to examine the effectiveness of individual components of caffeinated energy drinks on performance (62).

The consumption of caffeine in the form of mouth and nasal sprays enables the stimulating physiological effect to begin very quickly. Caffeine is poured into the person's tongue in combination with a carrier and a breath freshener, as a liquid spray or directly into the person's tongue. It is rapidly absorbed from the intestinal buccal membrane. It has been suggested that caffeine mouthwash exerts its ergogenic effects by allowing caffeine molecules to bind to adenosine receptors in the mouth and inhibit adenosine competitively (63, 64). This interaction is thought to increase the permeability of the buccal mucosa and thus trigger caffeine absorption into the bloodstream (65). Another mechanism of action is mentioned to explain the performance benefits associated with caffeinated mouthwash. The oral cavity is decorated with bitter taste receptor cells, especially found in the oropharyngeal epithelium, and these have been shown to be activated when exposed to caffeine. It has been suggested that activation of these bitter taste receptors can activate taste neural pathways and ultimately stimulate brain regions associated with information processing and reward. Although it has been reported that caffeinated aerosol mouth and nasal sprays can stimulate nerves with direct brain connections and enter the blood through mucosal and pulmonary absorption, research on this condition is scarce (62).

The Effect of Caffeine on Cognitive Performance

For centuries, caffeine, usually taken in the form of coffee or tea, has been a popular tool for enhancing various aspects of mental or cognitive functions (28). In addition to exercise performance; Continuous cognitive function is also important because of the routine work requirements of caffeine. Although there is widespread scientific work on the behavioral effects of caffeine, some details regarding specific functional aspects remain controversial (66). While there is a general consensus that caffeine improves “lower” cognitive functions such as simple reaction time, the effects of caffeine on “higher” cognitive functions such as problem solving and decision making are often debated. This is partly because there are fewer published studies of higher-level cognitive function and the available ones differ greatly from the methods used (67).

Caffeine increases arousal in a dose-dependent manner; low doses can improve hedonic tone and reduce anxiety, while high doses can increase symptoms of anxiety, irritability, and tension (68). How caffeine affects performance depends in part on the level of arousal of the individuals studied, particularly the extent to which the participants were sleep deprived or how tired or well rested. One study evaluated the classic inverted-U hypothesis in terms of caffeine to what extent stimulation improves or impairs performance (69). According to the Yerkes-Dodson law, there is an empirical relationship between arousal and performance, such that low arousal is associated with poor performance, while increased physiological or mental arousal is associated with improved performance, but only to a range (70). When the arousal level increases too much, performance decreases. Thus, the individual's pre-dose arousal level before consuming caffeine will affect the effects observed (71). Giving a large dose of caffeine to a person who is seriously tired will improve performance because in this case caffeine promotes an appropriate level of arousal (i.e., caffeine advances the individual's stimulation towards the middle range of the Yerkes-Dodson curve). Conversely, giving the same dose to someone who is already well rested and highly aroused may decrease rather than improve performance because in this case caffeine produces an over-arousal state that will impair cognition according to the Yerkes-Dodson law (72).

Table 3. Investigations examining the effects of caffeine on cognitive performance

References	Participants	Cafe Dose		Conclusion
Brunyé TT. et al. (67)	University student male (n = 16) and female (n = 20)	100 mg 200 mg **400 mg**	↑ ↑ ↑	It was observed that caffeine improved participants' skills to use warning cues efficiently and to avoid the impact of information incompatible with the action. Caffeine has been shown to improve performance in tasks that require constant attention and attention. It has been observed that caffeine has different effects on visual attention networks as a function of dose, and these effects have implications for the interactions of caffeine, adenosine and dopamine in the brain areas that direct visual attention.
Hogervorst E. et al.(58)	Well-trained cyclist male (n = 24)	**100 mg**	↑ ↑	It was observed that caffeine increased speed in Rapid Visual Information Processing Tests. It was seen that complex cognitive ability increased significantly.
Antonio J. et al.(73)	In training men (n=11), in training women (n=9)	**4 mg/kg**	↓ ↑	The energy drinks psychomotor vigilance ensured a shorter average reaction time. Caffeine significantly improved psychomotor alertness performance, a constant attention task.
McLellan TM. et al. (74)	Soldier ((n=31)	**200 mg**	↑	Continuous alertness was maintained in the control, observation and exploratory vigilance task.
McLellan TM. et al. (75)	Soldier (n=20)	**600 mg**	↑	It was observed that the alertness increased.
Kamimori G. et al.(76)	Special Forces Operators (n=20)	**4×200 mg**	↑ ↔	It was observed that the response speed increased during sustained psychomotor speed, enhanced event perception, the number of correct responses to stimuli, and logical reasoning tests. No changes were observed in gun shooting.
Tikuisis P. et al.(77)	Soldier (n=20)	**400 mg** 100 mg	↑	There was an increase in the cognitive component of the gun shooting mission.
Zhang Y. et al.(78)	Fireman (n=10)	**400 mg**	↔	No changes were observed in perceived difficulty, mood reaction time, short-term memory and recall memory.
Share B. et al.(79)	Elite sniper male (n=7)	**2 mg / kg** **4 mg / kg**	↔	No difference was observed in shooting accuracy, response time, or target tracking time between groups.
Stuart GR. et al. (80)	Competitive Rugby players male (n=9)	**6 mg / kg**	↑	There was a significant increase in correct passing ability.
Karayigit, R. et al. (81)	Female athletes (n=17)	**3 mg / kg** **6 mg / kg**	↑	Caffeine has been shown to improve cognitive performance.
Khcharem A. et al.(82)	Recreational running (n=10)	**5 mg / kg**	↑ ↓	Caffeine was cognitively processed by applying the correct fine after complete sleep deprivation. Caffeine has been shown to affect cognitive performance by reacting after complete sleep deprivation.

Bold text associated with reported trial outcomes; * delineates a significant change, ↔ = no improvement/change, ↑ = improved performance/change, ↓ = decreased, 1RM = repetitive maximal, VO_{2max} = maximum oxygen consumption

Caffeine and Fat Metabolism

The list of supplements that claim to increase or improve fat metabolism is long; The most popular supplements include caffeine, carnitine, green tea, conjugated linoleic acid, forskolin, chromium, seaweed, and fucoxanthin (83). Much of the interest in caffeine's effects on metabolism stems from exercise physiology studies in the 1970s. Early research by Costill et al. Showed that taking caffeine (coffee and pure caffeine) before a workout significantly increases fat oxidation rates and performance (84). Essig et al. also reported a shift in substrate metabolism from carbohydrate to fat during exercise following caffeine intake, accompanied by a slight increase in serum plasma fatty acid concentrations (85). The theory is that caffeine activates fat and preserves muscle glycogen, resulting in increased performance. Later, these two effects separated from each other and it was reported that the ergogenic effect of caffeine was mostly due to central mechanisms. Thus, caffeine has been shown to increase sympathetic nervous system activity and release fatty acids from adipose and / or intramuscular stores. This mechanism, which occurs indirectly through increased adrenaline levels, has the potential to increase the availability of fatty acids for oxidation. Caffeine also has a direct effect on lipolysis. Acheson et al found that administration of high doses of caffeine (8 mg / kg) significantly increased the resting metabolic rate (RMR) [20 kJ / (m2*h)] within 3 h after eating (86). Dulloo et al. reported that even low doses of caffeine (100 mg) have the potential to cause a thermogenic effect at rest. Over a period of 150 minutes, RMR increased by 3-4% in both lean and obese individuals. In the same study, the RMR (8-11% increase) was further increased when caffeine was taken at repeated doses (2 h intervals over 12 h) (87). It is not known whether this increase is due to increased fat oxidation, increased carbohydrate oxidation, or both. It has been emphasized before that the finding that caffeine can increase fat oxidation is not new. Although there are a few studies that support this result, there are also studies showing that the cafe does not affect on fat oxidation. These results, on the other hand, spoil a general opinion on the subject. The different results can be explained by the exercise intensity or the participant population used in the studies.

Caffeine and Hydration

Dehydration refers to an imbalance in fluid dynamics (water and electrolyte balance) when fluid consumption fails to meet the needs of our body (88). In a study where participants exercised at 70-75% VO2max until their self-determined exhaustion, participants were given 5 mg / kg caffeine 2 h and half an h before exercise, followed by 2.5 mg / kg caffeine, respectively. There was no difference in dehydration in the caffeine group compared with placebo (89). In a study, just before running exercise, participants completed the 10-second mouthwash protocol with 300 mg of caffeine or placebo diluted in 25mL of water, and caffeine mouthwash did not change hydration status or sweat rate after a 10km run (90). In a study examining the effects of caffeine at different ambient temperatures (12 and 33°C), participants who performed endurance cycling exercises were provided 3 mg / kg of caffeine 60 minutes before and after exercise. Sweating rates differed between 12 and 33°C, but no difference was observed when comparing caffeine versus placebo (91). In addition, when the ISSN's review on caffeine and performance, published in 2010, was examined, it was observed that there was no change in urine and blood volume during the resting period, and the amount of sweat during exercise was not different in both cases (48). In a study of 50 men who drink coffee regularly, there was no difference in the volume of urine produced over 24 h, despite caffeine intake of 240 mg or more per day. In this study, participants consumed 4x200 ml of water and coffee containing 4 mg / kg of caffeine for 3 days (doses ranged from 204 to 453 mg of caffeine). Post-study data also revealed that there was no difference between the two groups for blood and urine markers of measured hydration level (92). Indeed, when caffeine intake is 200-450 mg or 2.5-4 mg / kg per day, there is no diuretic effect due to caffeine consumption. It should also be remembered that people who do not drink coffee regularly or have not had coffee for a certain period of time are more likely to temporarily respond to caffeine. On the other hand, regular caffeine intake develops a higher tolerance to the diuretic effect, even at higher doses.

The Effect of Caffeine Consumption Habit on Performance

Quantifying habitual caffeine intake is difficult to quantify, which is problematic for studies aiming to compare performance results following habitual caffeine intake with unconventional caffeine users. This concern is highlighted by reports that vary widely in the caffeine content of commonly consumed beverages. Taking into account the daily caffeine intake of all subjects enrolled in a given study is the standard procedure for a research protocol. The purpose of determining such dietary information is to determine whether caffeine consumption has an effect on performance and whether this result is different between a person who regularly consumes caffeine or not. Bell et al. Studied the effect of moderate doses of caffeine on subjects defined as the user (300 mg / day) and non-user (50 mg / day). The results showed an increase in performance for both groups; however, the effect of supplementation lasted approximately three h longer in subjects identified as non-users (93). Similarly, in a study describing caffeine habits among participants, there was no statistical difference for VO2max between groups (participants participated in a boost exercise protocol), but there was a significant difference in ventilation and heart rate for people who did not habitually caffeine at rest (94). In addition, another study reported no significant difference between caffeine users and those who did not, except for an increase in plasma epinephrine during exercise for caffeine naïve subjects compared with placebo (95).

Optimal Timing of Caffeine Supplement

Because plasma caffeine levels typically peak within 60 minutes of intake (96, 97), the timing of caffeine consumption relative to exercise should be considered. In a study where a 40 km time trial performance was performed, participants were given 6 mg / kg of caffeine 1 h before or just before exercise. Caffeine consumed 60 minutes before exercise resulted in significant improvements in the 40 km trail performance. The ergogenic effect of caffeine was found to be unrelated to the highest concentration of caffeine in the blood at the start of endurance exercise (98). In a study in which caffeine was provided in the chewing gum at 75% VO2max 5 minutes, 60 minutes, and 120 minutes before 15 minutes of cycling exercise, caffeine applied in the chewing gum increased performance when applied immediately before, not 1 or 2 h before exercise (61). In a study conducted to examine the effect of caffeine supplementation on cycling performance of 3 km more, at what time of the day it occurred, it was observed that caffeine was more effective in exercise performed before 10:00 than in exercise performed after 10:00. The greater effectiveness of caffeine in the morning may be attributed to the higher activity of the CYP1A2 enzyme in the morning than in the evening (99). In a study to determine the optimal timing of caffeine intake, participants were provided with 6 mg / kg of caffeine 30 minutes, 60 minutes, and 120 minutes before exercise. Caffeine timing before exercise provided the most consistent ergogenic benefits 1 h earlier compared to other time points, especially compared to 2 h (100). One study in which 5 mg / kg of caffeine was provided 1 h, 3 h, and 6 h before exercise concluded that the increase in performance was seen only when caffeine was taken 1 and 3 h before (93). In a study by Cox et al., 6 mg / kg of caffeine was provided in capsule form 1 h before exercise and six doses of 1 mg / kg caffeine every 20 minutes during exercise, with the significant difference being achieved with caffeine taken before exercise (101). Unlike other studies, in a study in which low (100 mg) and medium (200 mg) doses of caffeine were provided towards the end of the exercise, both doses given late were found to improve performance (102). Studies conducted for the optimal timing of caffeine intake are inconsistent. The uncertainty of the results may be due to the form of caffeine used, the individual characteristics of the participants, and the different caffeine consumption habits.

Caffeine and Doping

The World Anti-Doping Agency (WADA) explains what substances considered doping are in its annual statement. Until 2004, caffeine was also an ergogenic aid that was considered among these substances. However, WADA removed caffeine from the prohibited list as of 2004. It has been shown that caffeine supplementation in the 3-6 mg / kg range in training athletes can significantly improve both endurance and high-intensity performance. The International Olympic Committee sets an allowable limit for 12 µg of caffeine per ml of urine (103, 104). Approximately one hour before the competition, the caffeine dose in the range of 9-13 mg / kg will reach the maximum urine concentration permitted for competition (103). However, it should be kept in mind that caffeine consumption and urine concentration are dependent on factors such as gender and body weight (105). Consuming 6-8 cups of coffee containing approximately 100 mg of caffeine per cup results in the maximum permissible urine concentration (104, 105). According to The National Collegiate Athletic Association, urine concentrations in excess of 15µg/ml after the competition are considered illegal (106). WADA, on the other hand, does not consider caffeine a ban, but has included it in the list of must-watch in athletic competition.

CONCLUSION

The scientific literature on caffeine supplements is extensive. It is clear that caffeine is indeed ergogenic for sports performance, but specific to the athlete's condition, the intensity, duration, and type of exercise. Therefore, after reviewing the available literature, the following conclusions can be drawn:

• Caffeine is one of the most preferred ergogenic supplements by athletes after being removed from the prohibited list by WADA as of 2004.

• Caffeine makes the person feel more vigorous thanks to the antagonist effect it creates with adenosine.

Most of the studies have used a protocol in which caffeine is taken 60 minutes before the performance to ensure optimal absorption.

• It has been observed that moderate (3-6 mg / kg) caffeine intake contributes to sports performance in strength / strength exercises and long-term exercises.

• In the studies conducted, caffeine; Its use in caffeinated bars and gels, caffeinated chewing gum, caffeinated energy drinks, caffeinated nasal and mouth aerosol sprays, and caffeinated mouthwashes have been shown to have additional benefit potential depending on the type of exercise.

• When the effect of caffeine on cognitive performance was examined, it was seen that 200-300 mg of caffeine consumption positively affected cognitive performance, improved psychomotor alertness reaction time, and mood.

• It has been observed that pre-exercise caffeine consumption supports fat metabolism and increases the use of fat as a substrate in energy metabolism, in addition to increasing the resting metabolic rate.

• Scientific literature suggests that 2.5-4 mg / kg caffeine intake does not cause diuresis, contrary to what is known.

• While recommending caffeine supplements to athletes, individual recommendations should be made, keeping in mind that caffeine consumption habits may affect the ergogenicity of caffeine.

• Caffeine supplementation at doses of 4-6 mg / kg on multiple and single sprint activities requiring high intensity efforts is suitable for use as it significantly increases performance in athletes with high training levels.

• Considering the positive effect of caffeine on fat metabolism, it is appropriate to use it before exercise in athletes who aim to lose weight and / or burn fat.

• The positive effects of caffeine supplementation on cognitive performance can be evaluated particularly in professions where cognitive alertness is important, such as military personnel or firemen.

• In future studies, the ergogenic effect of caffeine should be clarified by focusing on questions such as (I) what time of the day caffeine consumption affects caffeine ergogenicity, (II) what is the importance of genotype in terms of caffeine consumption, (III) what is the effect of age on caffeine ergogenicity, (IV) does caffeine ergogenicity vary according to athlete's training level.

REFERENCES.

1. Bailey RL, Saldanha LG, Gahche JJ, Dwyer JT. Estimating caffeine intake from energy drinks and dietary supplements in the United States. Nutrition reviews. 2014;72(suppl_1):9-13.
2. Fulgoni III VL, Keast DR, Lieberman HR. Trends in intake and sources of caffeine in the diets of US adults: 2001–2010. The American journal of clinical nutrition. 2015;101(5):1081-7.
3. Rybak ME, Sternberg MR, Pao C-I, Ahluwalia N, Pfeiffer CM. Urine excretion of caffeine and select caffeine metabolites is common in the US population and associated with caffeine intake 1, 2, 3, 4. 2015.
4. Del Coso J, Muñoz G, Muñoz-Guerra J. Prevalence of caffeine use in elite athletes following its removal from the World Anti-Doping Agency list of banned substances. Applied physiology, nutrition, and metabolism. 2011;36(4):555-61.
5. Caldeira D, Martins C, Alves LB, Pereira H, Ferreira JJ, Costa J. Caffeine does not increase the risk of atrial fibrillation: a systematic review and meta-analysis of observational studies. Heart. 2013;99(19):1383-9.
6. Jiang W, Wu Y, Jiang X. Coffee and caffeine intake and breast cancer risk: an updated dose–response meta-analysis of 37 published studies. Gynecologic oncology. 2013;129(3):620-9.
7. Jiang X, Zhang D, Jiang W. Coffee and caffeine intake and incidence of type 2 diabetes mellitus: a meta-analysis of prospective studies. European journal of nutrition. 2014;53(1):25-38.
8. Wikoff D, Welsh BT, Henderson R, Brorby GP, Britt J, Myers E, et al. Systematic review of the potential adverse effects of caffeine consumption in healthy adults, pregnant women, adolescents, and children. Food and Chemical Toxicology. 2017;109:585-648.
9. Christensen PM, Shirai Y, Ritz C, Nordsborg NB. Caffeine and bicarbonate for speed. A meta-analysis of legal supplements potential for improving intense endurance exercise performance. Frontiers in physiology. 2017;8:240.
10. Pray L, Yaktine AL, Pankevich D. Caffeine in food and dietary supplements: examining safety. Workshop summary. Caffeine in food and dietary supplements: examining safety Workshop summary; 2014: National Academies Press; 2014.
11. Sebastião AM, Rei N, Ribeiro JA. Amyotrophic lateral sclerosis (ALS) and adenosine receptors. Frontiers in pharmacology. 2018;9:267.
12. Higdon JV, Frei B. Coffee and health: a review of recent human research. Critical reviews in food science and nutrition. 2006;46(2):101-23.
13. Kamimori GH, Karyekar CS, Otterstetter R, Cox DS, Balkin TJ, Belenky GL, et al. The rate of absorption and relative bioavailability of caffeine administered in chewing gum versus capsules to normal healthy volunteers. International journal of pharmaceutics. 2002;234(1-2):159-67.
14. Mitchell DC, Knight CA, Hockenberry J, Teplansky R, Hartman TJ. Beverage caffeine intakes in the US. Food and Chemical Toxicology. 2014;63:136-42.
15. Cureton KJ, Warren GL, Millard-Stafford ML, Wingo JE, Trilk J, Buyckx M. Caffeinated sports drink: ergogenic effects and possible mechanisms. International journal of sport nutrition and exercise metabolism. 2007;17(1):35-55.
16. Salamone JD, Farrar AM, Font L, Patel V, Schlar DE, Nunes EJ, et al. Differential actions of adenosine A1 and A2A antagonists on the effort-related effects of dopamine D2 antagonism. Behavioural brain research. 2009;201(1):216-22.
17. Tarnopolsky M, Cupido C. Caffeine potentiates low frequency skeletal muscle force in habitual and nonhabitual caffeine consumers. Journal of applied physiology. 2000;89(5):1719-24.
18. Allen DG, Lamb GD, Westerblad H. Impaired calcium release during fatigue. Journal of applied physiology. 2008;104(1):296-305.

19. Lindinger MI, Graham TE, Spriet LL. Caffeine attenuates the exercise-induced increase in plasma [K+] in humans. Journal of Applied Physiology. 1993;74(3):1149-55.
20. Meeusen R, Roelands B, Spriet LL. Caffeine, exercise and the brain. Limits of Human Endurance: Karger Publishers; 2013. p. 1-12.
21. Black CD, Waddell DE, Gonglach AR. Caffeine's Ergogenic Effects on Cycling: Neuromuscular and Perceptual Factors. Medicine and science in sports and exercise. 2015;47(6):1145-58.
22. Gonglach AR, Ade CJ, Bemben MG, Larson RD, Black CD. Muscle Pain as a Regulator of Cycling Intensity: Effect of Caffeine Ingestion. Medicine and science in sports and exercise. 2016;48(2):287-96.
23. Motl RW, O'connor PJ, Tubandt L, Puetz T, Ely MR. Effect of caffeine on leg muscle pain during cycling exercise among females. Medicine and science in sports and exercise. 2006;38(3):598-604.
24. Fredholm BB, Bättig K, Holmén J, Nehlig A, Zvartau EE. Actions of caffeine in the brain with special reference to factors that contribute to its widespread use. Pharmacological reviews. 1999;51(1):83-133.
25. Fredholm BB, Chen J-F, Cunha RA, Svenningsson P, Vaugeois J-M. Adenosine and brain function. Int Rev Neurobiol. 2005;63(1):191-270.
26. Meeusen R, Watson P, Hasegawa H, Roelands B, Piacentini MF. Central fatigue. Sports Medicine. 2006;36(10):881-909.
27. Nehlig A. Interindividual differences in caffeine metabolism and factors driving caffeine consumption. Pharmacological reviews. 2018;70(2):384-411.
28. Snel J, Lorist MM. Effects of caffeine on sleep and cognition. Progress in brain research: Elsevier; 2011. p. 105-17.
29. Rivers W, Webber H. The action of caffeine on the capacity for muscular work. The Journal of physiology. 1907;36(1):33.
30. Bayraktar F, Taşkıran A. Kafein Tüketimi ve Atletik Performans. Journal of Health and Sport Sciences. 2019;2(2):24-33.
31. Desbrow B, Biddulph C, Devlin B, Grant GD, Anoopkumar-Dukie S, Leveritt MD. The effects of different doses of caffeine on endurance cycling time trial performance. Journal of sports sciences. 2012;30(2):115-20.
32. Guest N, Corey P, Vescovi J, El-Sohemy A. Caffeine, CYP1A2 genotype, and endurance performance in athletes. Medicine & Science in Sports & Exercise. 2018;50(8):1570-8.
33. Evans M, Tierney P, Gray N, Hawe G, Macken M, Egan B. Acute ingestion of caffeinated chewing gum improves repeated sprint performance of team sport athletes with low habitual caffeine consumption. International journal of sport nutrition and exercise metabolism. 2018;28(3):221-7.
34. O'Rourke MP, O'Brien BJ, Knez WL, Paton CD. Caffeine has a small effect on 5-km running performance of well-trained and recreational runners. Journal of Science and Medicine in Sport. 2008;11(2):231-3.
35. Stadheim HK, Nossum EM, Olsen R, Spencer M, Jensen J. Caffeine improves performance in double poling during acute exposure to 2,000-m altitude. Journal of applied physiology. 2015;119(12):1501-9.
36. Lara B, Ruiz-Vicente D, Areces F, Abián-Vicén J, Salinero JJ, Gonzalez-Millán C, et al. Acute consumption of a caffeinated energy drink enhances aspects of performance in sprint swimmers. British Journal of Nutrition. 2015;114(6):908-14.
37. Grgic J, Trexler ET, Lazinica B, Pedisic Z. Effects of caffeine intake on muscle strength and power: a systematic review and meta-analysis. Journal of the International Society of Sports Nutrition. 2018;15(1):11.
38. Astorino TA, Rohmann RL, Firth K. Effect of caffeine ingestion on one-repetition maximum muscular strength. European journal of applied physiology. 2008;102(2):127-32.
39. Demura S, Yamada T, Terasawa N. Effect of coffee ingestion on physiological responses and ratings of perceived exertion during submaximal endurance exercise. Perceptual and motor skills. 2007;105(3_suppl):1109-16.
40. Shen JG, Brooks MB, Cincotta J, Manjourides JD. Establishing a relationship between the effect of caffeine and duration of endurance athletic time trial events: A systematic review and meta-analysis. Journal of science and medicine in sport. 2019;22(2):232-8.
41. Southward K, Rutherfurd-Markwick KJ, Ali A. The effect of acute caffeine ingestion on endurance performance: a systematic review and meta–analysis. Sports Medicine. 2018;48(8):1913-28.
42. Glaister M, Howatson G, Abraham CS, Lockey RA, Goodwin JE, Foley P, et al. Caffeine supplementation and multiple sprint running performance. Medicine & Science in Sports & Exercise. 2008;40(10):1835-40.
43. Trexler ET, Smith-Ryan AE, Roelofs EJ, Hirsch KR, Mock MG. Effects of coffee and caffeine anhydrous on strength and sprint performance. European journal of sport science. 2016;16(6):702-10.
44. Crowe MJ, Leicht AS, Spinks WL. Physiological and cognitive responses to caffeine during repeated, high-intensity exercise. International journal of sport nutrition and exercise metabolism. 2006;16(5):528-44.
45. Collomp K, Ahmaidi S, Audran M, Chanal J-L, Prefaut C. Effects of caffeine ingestion on performance and anaerobic metabolism during the Wingate test. International journal of sports medicine. 1991;12(05):439-43.
46. Lorino AJ, Lloyd LK, Crixell SH, Walker JL. The effects of caffeine on athletic agility. Journal of Strength and Conditioning Research. 2006;20(4):851.
47. Greer F, McLean C, Graham T. Caffeine, performance, and metabolism during repeated Wingate exercise tests. Journal of applied physiology. 1998;85(4):1502-8.
48. Goldstein ER, Ziegenfuss T, Kalman D, Kreider R, Campbell B, Wilborn C, et al. International society of sports nutrition position stand: caffeine and performance. Journal of the International Society of Sports Nutrition. 2010;7(1):1-15.
49. Grgic J, Mikulic P. Caffeine ingestion acutely enhances muscular strength and power but not muscular endurance in resistance-trained men. European journal of sport science. 2017;17(8):1029-36.
50. Norum M, Risvang LC, Bjørnsen T, Dimitriou L, Rønning PO, Bjørgen M, et al. Caffeine increases strength and power performance in resistance-trained females during early follicular phase. Scandinavian Journal of Medicine & Science in Sports. 2020;30(11):2116-29.
51. Goldstein E, Jacobs PL, Whitehurst M, Penhollow T, Antonio J. Caffeine enhances upper body strength in resistance-trained women. Journal of the International Society of Sports Nutrition. 2010;7(1):1-6.
52. Timmins TD, Saunders DH. Effect of caffeine ingestion on maximal voluntary contraction strength in upper-and lower-body muscle groups. The Journal of Strength & Conditioning Research. 2014;28(11):3239-44.
53. Woolf K, Bidwell WK, Carlson AG. The effect of caffeine as an ergogenic aid in anaerobic exercise. International journal of sport nutrition and exercise metabolism. 2008;18(4):412-29.
54. Beck TW, Housh TJ, Malek MH, Mielke M, Hendrix R. The acute effects of a caffeine-containing supplement on bench press strength and time to running exhaustion. The Journal of Strength & Conditioning Research. 2008;22(5):1654-8.

55. Wilk M, Krzysztofik M, Filip A, Zajac A, Del Coso J. The effects of high doses of caffeine on maximal strength and muscular endurance in athletes habituated to caffeine. Nutrients. 2019;11(8):1912.
56. Trevino MA, Coburn JW, Brown LE, Judelson DA, Malek MH. Acute effects of caffeine on strength and muscle activation of the elbow flexors. The Journal of Strength & Conditioning Research. 2015;29(2):513-20.
57. Cooper R, Naclerio F, Allgrove J, Larumbe-Zabala E. Effects of a carbohydrate and caffeine gel on intermittent sprint performance in recreationally trained males. European journal of sport science. 2014;14(4):353-61.
58. Hogervorst E, Bandelow S, Schmitt J, Jentjens R, Oliveira M, Allgrove J, et al. Caffeine improves physical and cognitive performance during exhaustive exercise. Medicine & Science in Sports & Exercise. 2008;40(10):1841-51.
59. Newton R, Broughton L, Lind M, Morrison P, Rogers H, Bradbrook I. Plasma and salivary pharmacokinetics of caffeine in man. European journal of clinical pharmacology. 1981;21(1):45-52.
60. Scott AT, O'Leary T, Walker S, Owen R. Improvement of 2000-m rowing performance with caffeinated carbohydrate-gel ingestion. International Journal of Sports Physiology and Performance. 2015;10(4):464-8.
61. Ryan EJ, Kim C-H, Fickes EJ, Williamson M, Muller MD, Barkley JE, et al. Caffeine gum and cycling performance: a timing study. The Journal of Strength & Conditioning Research. 2013;27(1):259-64.
62. Wickham KA, Spriet LL. Administration of caffeine in alternate forms. Sports Medicine. 2018;48(1):79-91.
63. Beaven CM, Maulder P, Pooley A, Kilduff L, Cook C. Effects of caffeine and carbohydrate mouth rinses on repeated sprint performance. Applied Physiology, Nutrition, and Metabolism. 2013;38(6):633-7.
64. Clarke ND, Kornilios E, Richardson DL. Carbohydrate and caffeine mouth rinses do not affect maximum strength and muscular endurance performance. The Journal of Strength & Conditioning Research. 2015;29(10):2926-31.
65. Rubinstein I, Chandilawa R, Dagar S, Hong D, Gao X-P. Adenosine A1 receptors mediate plasma exudation from the oral mucosa. Journal of Applied Physiology. 2001;91(2):552-60.
66. Smith AP. Practical Implications. Diet, brain, behavior: Practical implications. 2011:271.
67. Brunyé TT, Mahoney CR, Lieberman HR, Taylor HA. Caffeine modulates attention network function. Brain and cognition. 2010;72(2):181-8.
68. Stafford LD, Rusted J, Yeomans MR. Caffeine, mood and performance: a selective review. Caffeine and Activation Theory: Effects on Health and Behavior Boca Raton, FL: Taylor and Francis. 2007;2007:284-310.
69. Nehlig A. Is caffeine a cognitive enhancer? Journal of Alzheimer's Disease. 2010;20(s1):S85-S94.
70. Yerkes RM, Dodson JD. The relation of strength of stimulus to rapidity of habit-formation. Punishment: Issues and experiments. 1908:27-41.
71. Wood S, Sage JR, Shuman T, Anagnostaras SG. Psychostimulants and cognition: a continuum of behavioral and cognitive activation. Pharmacological reviews. 2014;66(1):193-221.
72. Harvanko AM, Derbyshire KL, Schreiber LR, Grant JE. The effect of self-regulated caffeine use on cognition in young adults. Human Psychopharmacology: Clinical and Experimental. 2015;30(2):123-30.
73. Antonio J, Kenyon M, Horn C, Jiannine L, Carson C, Ellerbroek A, et al. The Effects of an Energy Drink on Psychomotor Vigilance in Trained Individuals. Journal of Functional Morphology and Kinesiology. 2019;4(3):47.
74. McLellan TM, Kamimori GH, Voss DM, Bell DG, Cole KG, Johnson D. Caffeine maintains vigilance and improves run times during night operations for Special Forces. Aviation, space, and environmental medicine. 2005;76(7):647-54.
75. McLellan TM, Kamimori GH, Voss DM, Tate C, Smith SJ. Caffeine effects on physical and cognitive performance during sustained operations. Aviation, space, and environmental medicine. 2007;78(9):871-7.
76. Kamimori GH, McLellan TM, Tate CM, Voss DM, Niro P, Lieberman HR. Caffeine improves reaction time, vigilance and logical reasoning during extended periods with restricted opportunities for sleep. Psychopharmacology. 2015;232(12):2031-42.
77. Tikuisis P, Keefe AA, McLellan TM, Kamimori G. Caffeine restores engagement speed but not shooting precision following 22 h of active wakefulness. Aviation, space, and environmental medicine. 2004;75(9):771-6.
78. Zhang Y, Balilionis G, Casaru C, Geary C, Schumacker RE, Neggers YH, et al. Effects of caffeine and menthol on cognition and mood during simulated firefighting in the heat. Applied ergonomics. 2014;45(3):510-4.
79. Share B, Sanders N, Kemp J. Caffeine and performance in clay target shooting. Journal of sports sciences. 2009;27(6):661-6.
80. Stuart GR, Hopkins WG, Cook C, Cairns SP. Multiple effects of caffeine on simulated high-intensity team-sport performance. Medicine and science in sports and exercise. 2005;37(11):1998.
81. Karayigit R, Naderi A, Akca F, Cruz CJGd, Sarshin A, Yasli BC, et al. Effects of Different Doses of Caffeinated Coffee on Muscular Endurance, Cognitive Performance, and Cardiac Autonomic Modulation in Caffeine Naive Female Athletes. Nutrients. 2021;13(1):2.
82. Khcharem A, Souissi M, Atheymen R, Ben Mahmoud L, Sahnoun Z. Effects of caffeine ingestion on 8-km run performance and cognitive function after 26 hours of sleep deprivation. Biological Rhythm Research. 2020:1-11.
83. Jeukendrup A, Randell R. Fat burners: nutrition supplements that increase fat metabolism. Obesity reviews. 2011;12(10):841-51.
84. Costill D, Dalsky GP, Fink W. Effects of caffeine ingestion on metabolism and exercise performance. Medicine and science in sports. 1978;10(3):155-8.
85. Essig D, Costill D, Van Handel P. Effects of caffeine ingestion on utilization of muscle glycogen and lipid during leg ergometer cycling. International Journal of Sports Medicine. 1980;1(02):86-90.
86. Acheson KJ, Zahorska-Markiewicz B, Pittet P, Anantharaman K, Jéquier E. Caffeine and coffee: their influence on metabolic rate and substrate utilization in normal weight and obese individuals. The American journal of clinical nutrition. 1980;33(5):989-97.
87. Dulloo A, Geissler C, Horton T, Collins A, Miller D. Normal caffeine consumption: influence on thermogenesis and daily energy expenditure in lean and postobese human volunteers. The American journal of clinical nutrition. 1989;49(1):44-50.
88. Ulupinar S, Özbay S, Gençoğlu C. Siklet Sporlarında Dehidrasyon ve Hiponatremi. Ulusal Spor Bilimleri Dergisi. 2020;4(2):103-15.
89. Falk B, Burstein R, Rosenblum J, Shapiro Y, Zylber-Katz E, Bashan N. Effects of caffeine ingestion on body fluid balance and thermoregulation during exercise. Canadian Journal of Physiology and Pharmacology. 1990;68(7):889-92.
90. Gonzalez AM, Guimarães V, Figueiredo N, Queiroz M, Gentil P, Mota JF, et al. Acute Caffeine Mouth Rinse Does Not

Change the Hydration Status following a 10 km Run in Recreationally Trained Runners. BioMed Research International. 2020;2020.

91. Ganio MS, Johnson EC, Klau JF, Anderson JM, Casa DJ, Maresh CM, et al. Effect of ambient temperature on caffeine ergogenicity during endurance exercise. European journal of applied physiology. 2011;111(6):1135-46.
92. Killer SC, Blannin AK, Jeukendrup AE. No evidence of dehydration with moderate daily coffee intake: a counterbalanced cross-over study in a free-living population. PloS one. 2014;9(1):e84154.
93. Bell DG, McLellan TM. Exercise endurance 1, 3, and 6 h after caffeine ingestion in caffeine users and nonusers. Journal of applied physiology. 2002;93(4):1227-34.
94. Dodd S, Brooks E, Powers S, Tulley R. The effects of caffeine on graded exercise performance in caffeine naive versus habituated subjects. European journal of applied physiology and occupational physiology. 1991;62(6):424-9.
95. Van Soeren M, Sathasivam P, Spriet L, Graham T. Caffeine metabolism and epinephrine responses during exercise in users and nonusers. Journal of Applied Physiology. 1993;75(2):805-12.
96. Benowitz NL. Clinical pharmacology of caffeine. Annual review of medicine. 1990;41(1):277-88.
97. Graham T, Spriet L. Performance and metabolic responses to a high caffeine dose during prolonged exercise. Journal of applied physiology. 1991;71(6):2292-8.
98. Skinner TL, Jenkins DG, Taaffe DR, Leveritt MD, Coombes JS. Coinciding exercise with peak serum caffeine does not improve cycling performance. Journal of science and medicine in sport. 2013;16(1):54-9.
99. Pataky M, Womack C, Saunders M, Goffe J, D'lugos A, El-Sohemy A, et al. Caffeine and 3-km cycling performance: Effects of mouth rinsing, genotype, and time of day. Scandinavian journal of medicine & science in sports. 2016;26(6):613-9.
100. Harty PS, Zabriskie HA, Stecker RA, Currier BS, Tinsley GM, Surowiec K, et al. Caffeine Timing Improves Lower-Body Muscular Performance: A Randomized Trial. Frontiers in Nutrition. 2020;7:270.
101. Cox GR, Desbrow B, Montgomery PG, Anderson ME, Bruce CR, Macrides TA, et al. Effect of different protocols of caffeine intake on metabolism and endurance performance. Journal of Applied Physiology. 2002.
102. Talanian JL, Spriet LL. Low and moderate doses of caffeine late in exercise improve performance in trained cyclists. Applied Physiology, Nutrition, and Metabolism. 2016;41(8):850-5.
103. Graham TE. Caffeine and exercise. Sports medicine. 2001;31(11):785-807.
104. Spriet LL. Exercise and sport performance with low doses of caffeine. Sports medicine. 2014;44(2):175-84.
105. Ellender L, Linder MM. Sports pharmacology and ergogenic aids. Primary care. 2005;32(1):277-92.
106. Botnick I. Honoring Trademarks: The Battle to Preserve Native American Imagery in the National Collegiate Athletic Association. J Marshall Rev Intell Prop L. 2007;7:735.