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Effects of Caffeine on Physical and Cognitive Performance: A Review

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Abstract

Caffeine is one of the most consumed nutritional ergogenic supplements by athletes. In the literature, it is now widely accepted that caffeine taken 60 minutes before exercise improves performance. There are different methods of caffeine intake; caffeinated gum, coffee, anhydrous, and gel forms are among the most commonly used. Generally, the ergogenic effect sizes of different forms of caffeine consumption do not differ significantly. The effectiveness of caffeine doses of 3-6 mg/kg has been proven. However, in recent years, doses <3 mg/kg have also begun to be investigated, and some studies have reported positive effects. In addition, it can be stated from the literature that there is no difference in the responses of male and female athletes to caffeine. It can be argued that the distribution of the CYP1A2 gene allele (AA, AC), which is responsible for the metabolism of caffeine, may change the physical and cognitive responses to caffeine and that athletes should consider this factor

Key Words: Coffee, athletic, ergogenic, supplement

INTRODUCTION

Nutrition has been one of the main factors in the development of physical and cognitive performance, which is of great importance for the continuation of the generation throughout the evolutionary process, especially in the human species (55). The relationship of nutrition with physical-cognitive health and/or performance is of vital importance, especially for elite athletes. Although the cardiovascular and respiratory systems are thought to be the most important factors limiting exercise performance, saturation of nutrient stores and the athlete's nutritional diet are also among the main limiting factors (44). When viewed from a wider perspective, it can be said that 3 factors determine the upper limit of an elite athlete's performance: genetics, training and nutrition. Following the intake of macro and micro nutrients according to the training and competition period, the athlete can increase their physical and cognitive performance by planning their nutritional ergogenic aid intake.

Nutritional ergogenic (energy-generating) supplements are widely used by athletes and sedentary individuals for many different purposes (7).

Caffeine

Caffeine, creatine, beta alanine, bicarbonate, nitrate and carnitine are reported to be the main supplements that most affect performance and have proven benefits in the current literature (11). Dose, timing, consumption frequency, gender and genetics are the most important factors affecting the ergogenic effect size of the athlete's supplement consumption. Supplement consumed without paying attention to these parameters can cause more harm than good. Among them, caffeine is by far the most consumed supplement by athletes, and hundreds of scientific studies each year reveal its effects on performance (2). Caffeine, whose chemical name is 1,3,7-trimethylzantine, takes its name from its C8H10N4O2 formula and molecular structure. Today, 80% of the 2öşe2's population consumes an average of 200 miligrams (mg) or 3 cups of espresso per day, making caffeine the most consumed drink after water (61). Among these plants, coffee, tea, cocoa, yerba mate and cola plants contain the most caffeine. Caffeine consumed in the late hours makes us sleepless and increases the feeling of vitality, which is associated with binding to adenosine receptors and eliminating the purported effects of adenosine (2). Caffeine appears in the blood immediately after ingestion and peaks in approximately 45-90 minutes. Genetic differences are the most important factor affecting the metabolic rate of caffeine. 3 mg of caffeine per kilogram (kg) can increase blood levels to 15-20 micromoles per liter, 6 mg/kg caffeine to 40-50 micromoles and 9 mg/kg caffeine to 60-75 micromoles (52). Factors such as whether caffeine is taken at once or at intervals, gender, amount of muscle mass, frequency of habitual consumption are metabolic rate determinants and are among the factors that should be planned in use. In addition, the form in which caffeine is taken determines the rate of absorption. Different forms of caffeine are digested at different rates, although the total amount and velocity of digestion are the same (46). Caffeine, which is metabolized by the cytochrome P-450 liver enzyme and broken down into parasanthine (85%), theobramine (10%) and theophylline (5%), completes its half-life between 3.5 and 5 hours. It takes approximately 24 hours for caffeine to be completely eliminated from the whole body. However, it is known that the ergogenic effect does not last for 24 hours (9). Athletes who did not regularly consume caffeine significantly increased their aerobic endurance compared to placebo even 1, 3 and 5 hours after 5 mg/kg caffeine intake. Athletes whos regularly consume caffeine developed tolerance and their aerobic endurance increasd significantly after only 1 and 3 hours (9).

For the last 10 years, it has been thought that caffeine improves aerobic endurance, sprint-style activities and cognitive performance (executive functions, reaction time, attention) by adenosine receptor antagonism, and muscular performance types (strength, power, endurance) by increasing sodium/potassium pump activation (2, 60, 66). Since caffeine is molecularly similar to adenosine, it binds to adenosine receptors in the brain tissue, reducing the feeling of fatigue-increasing negative effects of adenosine on the nervous system. For example, caffeine blocks the A_{2a} receptor in the striatum, activating the D2 receptor of dopamine and increasing the triggering effect of dopamine on psychomotor activities (1, 30). Also, caffeine may act directly on muscle tissue. Carins et al. (1997) found that high doses of caffeine increase power production when potassium is inhibited. Another mechanism by which caffeine is effective may be that the increase in blood glucose level increases the sodium/potassium pump (60). It has been previously shown that elevated plasma glucose inhibits the deterioration of the electrical properties of the muscle fiber membrane (53). Increasing the activation of the sodium/potassium pump with caffeine intake may provide an increase in performance especially in high-intensity interval exercises and muscular endurance exercises consisting of repetitive contractions.

Topics to Consider in Caffeine Consumption

After decades of scientific research, it is now almost conclusively proven that caffeine improves athletic and cognitive performance (54). However, as in the use of all other nutritional ergogenic supplements, there are main issues to be considered by athletes in the consumption of caffeine. Athlete or trainer, in order not to cause more harm than good: it is of great importance to plan caffeine consumption by considering factors such as 3öşe, timing, gender, consumption frequency, side effect, training status, placebo effect, annual consumption periodization, genotype and chronotype (6). For now, although not for amateur athletes, anti-doping rules for athletes competing at national and international level are constantly updated by the World Anti-Doping Agency (WADA), and athletes are kept under strict monitoring. While aiming to increase sportive performance with the use of caffeine or another supplement, it is necessary to avoid use that can be considered as doping. Caffeine was first included in the list of banned substances by the International Olympic Committee in 1984 and by WADA in 2000. Exceeding a dose of 15 micrograms/milliliter in the urine was counted as doping. In 1985, this rate was reduced to 12 micrograms/milliliter (87). These limits were set to distinguish between the sociocultural use of caffeine and its use for sports performance enhancement. However, later scientific research has shown that caffeine can increase athletic and cognitive performance at much lower doses (77). That's why WADA has removed caffeine from its list of banned substances and added it to its list of monitored substances. Ironically, the amount of caffeine in urine samples taken from athletes in international competitions before 2004 was much higher than after 2004 (87).

Believing that one has made a positive attempt, without actually taking the active substance, the placebo effect, which has beneficial results, shows its effect in the ergogenic use of caffeine as in medical sciences. Anderson et al. (2020) revealed that the wingate anaerobic test performance of athletes can be increased with the placebo effect. Although there is not much research on whether the training status of athletes affects the ergogenic effect size of caffeine, Apostolidis et al. (2020) classified the neuromuscular and cardiorespiratory performances of twenty football players as high and moderate and examined the effect of 6 mg/kg caffeine on exhaustion time and vertical jump performances. In conclusion, athletes with high or moderate neuromuscular and cardiorespiratory endurance all significantly improved their performance with 6 mg/kg caffeine intake. As with any supplement, caffeine intake also has some side effects that vary individually. The most common side effects are; heart palpitations, nausea, headache, insomnia and anxiety (14). Caffeine taken especially before evening workouts can negatively affect the time to sleep and sleep quality (27). In addition, the increase in the frequency of caffeine consumption also increases the level of chronic anxiety, and this may cause instantaneous performance drops and defeat in some branches. Side effects, which are directly proportional to dose intake, can be reduced by using lower doses (64). Before the competition, the athletes can try different doses on themselves and observe the side effects. For many years, athletes and coaches have been aware that training should be periodized annually, monthly or weekly. In recent years, due to the fact that nutrition also affects training adaptation, it should be periodized according to the annual training period (44). In an article published in 2021, Pickering and Grgic (2021) reported that caffeine intake should also be planned according to training and feeding periods. Considering the importance of the competition for the athlete, the tolerance effect of caffeine can be reduced by avoiding or reducing caffeine intake in technical-tactical training sessions, and annual periodization can be planned according to the genotype of the athlete (67).

Dose

In the literature, caffeine taken under a dose of 3 mg/kg is classified as a low dose, a medium dose between 3 and 6 mg/kg, and a high dose if >6 mg/kg (40). After hundreds of studies, it has been shown that caffeine taken in low doses also improves performance (77). Caffeine taken in doses of 3-6 mg/kg provides a performance increase between 1% and 8% in aerobic exercises, team sports and exercises with high glycolytic activity demand (56). Pallares et al. (2013) reported that caffeine intake at doses of 3, 6 and 9 mg/kg significantly increased muscular strength, but a dose of 3 mg/kg could increase strength at low weights, and 9 mg/kg dose was effective for strength gain at higher weights. He also reported that although 9 mg/kg caffeine significantly improved power performance, it had some side effects that lasted for 24 hours. Spriet (2014) suggested that the performance-enhancing mechanism of low doses of caffeine is central rather than peripheral. Zhang et al. (2020) investigated the effects of low (3 mg/kg), medium (6 mg/kg) and high (9 mg/kg) doses of caffeine on cognitive performance and brain activations and found that 3 mg/kg dose was more effective in activating cognitive functions than 6 and 9 mg/kg doses. With the research done by Zhang et al. (2020), Spriet's (2014) hypothesis was confirmed and it was revealed that low doses of caffeine can stimulate the central nervous system. Doses higher than 3 mg/kg may be required to activate the peripheral mechanisms of caffeine. The dose of caffeine that should be consumed for acute performance improvement is related to the dose of caffeine consumed regularly (+2-3 months) (68). It has been reported that for an acute performance increase, the athlete should take slightly more caffeine than the dose of caffeine taken in training and competitions throughout the year. However, increasing the dose of caffeine determines the size of the side effects according to the individual athlete and sports branch. Some studies have suggested that increasing the dose of caffeine creates changes in oxidized substrates and increases fat burning, thus increasing the performance of long-term aerobic exercise by providing backup of muscle glycogen stores (22, 79). Studies on dose-response in the literature are generally between 3 and 6 mg/kg doses. More research is needed examining doses less than 3 mg/kg. In addition, performance responses to caffeine at the same doses may differ between genders (59). There is a need to examine the effects of very-low (≤ 3 mg/kg) caffeine intake on different performance parameters by directly comparing female and male athletes and measuring side effects. Also, no studies to date have investigated the effects of low, moderate, and high-dose caffeine intake on cognitive performance in male and female athletes. To make more suggestion, further research is needed in these topics.

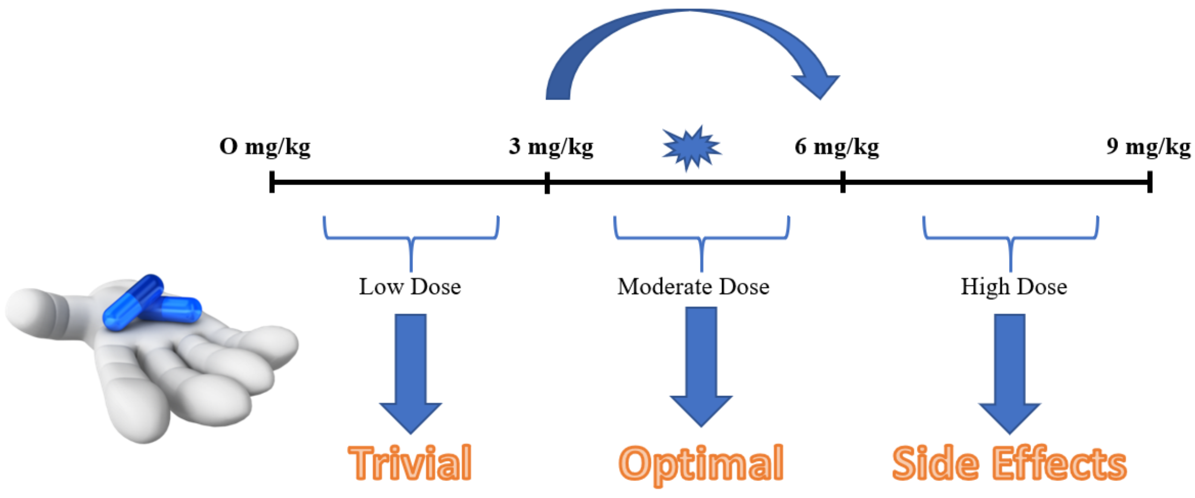

Figure 1. Dose response of caffeine

Gender

One of the main determinants of athletic performance is gender. Hormonal differences lead to gender differences in body composition, aerobic capacity and anaerobic threshold values (81). Therefore, gender-specific training and nutrition plans should be made. Although the effects of caffeine on sportive and cognitive performance are known, there is not much research directly comparing genders (36). Kaçoğlu (2019) reported that low-dose caffeine intake did not significantly increase 30-second wingate performance in adolescent female handball players, and that dose-response studies should be conducted in placebo-controlled in future studies. Skinner et al. (2019) investigated the effects of 3 mg/kg caffeine intake on time trial performance by directly comparing 16 male and 11 female elite cyclists and reported that 3 mg/kg caffeine significantly improved performance, but there was no difference between genders. Sabblah et al. (2015) examined the effects of 5 mg/kg caffeine intake on 1-repetition maximum (1RM) muscle strength and muscular endurance performances, and 10 male and 8 female athletes participated in the study. As a result, both male and female athletes significantly improved their 1RM performance in the caffeine trial, but muscular endurance performance increased only in males. The authors reported that the effects of different doses of caffeine intake on muscular performance should be compared between genders. In the literature review, no research to date has examined the effects of caffeine intake on cognitive performance by directly comparing genders. Since only 13% of the studies in the literature were conducted on women, recommendations regarding the use of caffeine cannot be considered accurate for female athletes directly (73). Also, the effects of low doses of caffeine have never been studied before in female athletes.

Whether there is an ergogenic difference between the sexes of caffeinated coffee Clarke et al. (2019) and it was revealed that 3 mg/kg dose of caffeinated coffee significantly increased 5 km cycling time-trial in men and women. Most of the studies on caffeinated coffee in the literature are on aerobic endurance and men (2). Also, the effects of caffeinated coffee on the sprint performance of female athletes have never been investigated until now. However, for the first time, Karayiğit et al. (2021), investigated the effects of different doses of caffeinated coffee intake (3-6 mg/kg) on muscular endurance, cognitive performance and heart rate variability in female athletes. In conclusion, Karayiğit et al. (2021) found to improvement in muscular endurance and cognitive performance with both 3 and 6 mg/kg of caffeinated coffee intake. Further, these performance enhancements did not lead to a cardiovascular load which shown by heart rate variability parameters.

Time

The pre-exercise caffeine consumption timing is generally recommended as 60 minutes. Plasma level peaks at 60 minutes following caffeine intake (38). During 2-3 hours of high-intensity exercise, caffeine shows its effects more when fatigue begins to occur. In this regard, caffeine intake does not always need to be taken before exercise. Caffeine taken during exercise, just before the onset of fatigue, has been shown to increase time-trial performance more, especially as the exercise duration gets longer (74). According to the results of this research, it can be thought that caffeine may be more effective in marathon and cycling-style sports, in case of fatigue. The time of intake of caffeine is directly related to the form of caffeine consumed. For example, caffeine taken with gum or cola is digested faster than the anhydrous form taken in capsules, and therefore the intake time of caffeine taken with gum or cola should be 5-10 minutes before exercise (40). In a study conducted with caffeinated gum, it was shown that caffeinated gum improves performance just before exercise, but chewing it 1 or 2 hours before has no significant effect (71). Because caffeinated gum comes into direct contact with enzymes in the oral cavity, it may be digested faster and enter the bloodstream faster. This makes caffeinated gum attractive to some athletes. The same is not true for caffeinated coffee. Caffeinated coffee intake is the same as the timing of anhydrous caffeine intake. Trexler et al. (2015) reported that 3-5 mg/kg of caffeinated coffee or anhydrous caffeine taken 30 minutes ago did not increase lower-upper body 1RM strength and 80% 1RM strength muscular endurance performance. Kara et al. (2019) revealed that caffeine supplementation taken 60 and 120 minutes ago did not significantly affect performance in short-term high-intensity activities in amateur football players. Athletes can plan their own intake timing by trying the caffeine timing before in training.

Form

Athletes generally prefer anhydrous or coffee form for physical and cognitive performance increase (40). Caffeinated gum, aerosol, energy bars, gels and nasal sprays are some of them. Caffeinated chewing gum can be preferred by athletes during early morning training or competitions, as it is digested faster. When we think nationally, there is no sale of caffeinated gum and other forms in our country. Athletes in our country have to realize their caffeine intake with the consumption of caffeinated coffee. It is known that long-term coffee consumption significantly reduces the risk of chronic diseases (21). Along with the thousands of polyphenols and catechins it contains, coffee is consumed by people as a health and physical-cognitive performance enhancer and is socioculturally accepted. It has been shown that increasing the amount of caffeine consumed with coffee daily up to 400 mg does not have a negative effect on health (25). Denoeud et al. (2014) stated that the daily consumption of coffee in the world is 2.2 billion cups. In addition to containing caffeine, coffee also contains substances that have the potential to change the effects of caffeine in coffee, such as chlorogenic acid, ferulic acid, and caffeic acid (41). Whether these substances reduce the effects of caffeine has been examined by many studies. Richardson and Clarke (2016) examined the effects of 5 mg/kg anhydrous caffeine and caffeinated coffee intake on squat endurance performance of male athletes at 60% 1TM intensity and reported that both anhidrosis and coffee form significantly increased muscular endurance performance. But in another study, Clarke et al. (2016) revealed that lower doses (3 mg/kg) of caffeinated coffee and anhydrous caffeine did not significantly increase sprint performance. The authors suggested that the fact that the participant group consisted of untrained individuals could explain the ineffectiveness of caffeine. Much more recently, there have been many studies suggesting that caffeinated coffee significantly improves physical performance (18, 66).

Caffeine Consumption Frequency

It is known that caffeine’s “adenosine receptor antagonism” is the main mechanism in increasing sportive and cognitive performance (1, 88). However, physiologically, the organism develops an adaptation to long-term caffeine consumption, as it responds to any chronic condition. Although it has not been clarified exactly from which adenosine subreceptor (A_1, A_{2A}) sportive and cognitive performance arises, it has been reported that chronic caffeine consumption increases adenosine A_1 and A_{2A} receptor concentrations in the striatum and brain regions responsible for the coordination of voluntary movements (80, 29). Therefore, chronically consumed caffeine by athletes may lead to tolerance and affect performance responses resulting from acute caffeine intake. In the literature, there are conflicting studies on this subject. Irwin et al. (2011) reported that consumption of 3 mg/kg caffeine for 4 days followed by withdrawal had no significant effect on time-trial performance. In another study, male athletes who consumed 3 mg/kg caffeine for 4 weeks developed tolerance at the end of 4 weeks and could not acutely respond to caffeine in time-trial performance (8). The authors suggested that there was no significant difference in serum cortisol and prolactin hormones measured as central noradrenergic and dopaminergic indicators, and that tolerance may have arisen from another central nervous pathway. Similarly, in athletes who do not consume caffeine regularly, 3 mg/kg of caffeine intake per day was reported that sprint (49) and submaximal aerobic (70) exercise performance increased until the 18^{th} day, but significant decreases in the size of the response to caffeine occurred after the 18^{th} day. On the contrary, there are studies that describe the development of tolerance to caffeine responses as a myth and reveal that regular caffeine consumption has no effect on performance responses from acute caffeine intake (35, 23).

This difference between studies may be due to the training status of the participants, test differences, and most importantly, the different grouping of caffeine consumption frequency. Filip et al. (2020) stated that the regular caffeine consumption grouping differs a lot in the literature, and in future studies, those with <25-75 mg/day caffeine consumption are "low", those with 200-450 mg/day "moderate", and those with +450 mg/day stated that grouping them as "high" will ensure standardization and achieve more reliable results. In addition, Pickering and Kiely (2019) suggested that acutely ingesting more than the caffeine dose they regularly consume may eliminate the effect of tolerance. For this, athletes with different consumption frequencies need to be affected by different doses. Most of the tolerance studies in the literature are on aerobic endurance performance and men. In addition, the relationship between acute caffeinated coffee intake and tolerance has never been studied to date.

Genotype

Genetic differences determine how nutrients are metabolized, absorbed, and used. The gene-diet interaction, which has important effects on health and performance by affecting metabolic pathways, has now begun to be investigated a lot in the sports science literature (83). Caffeine is one of the most researched substances in the field of nutrigenomics. The individual differences in the effects of caffeine intake on sportive and cognitive performance led researchers to investigate genetic factors. The CYP1A2 and ADORA2A genes, which are responsible for the metabolism, sensitivity and response of caffeine, are among the most studied. Yücesoy (2017) examined the allele distribution of CYP1A2 genetic polymorphism in short and longdistance runners in his master thesis and reported that the gene allele that metabolizes caffeine more slowly is seen more. The study with the largest participant group to date, Guest et al. (2018), while all participants increased their endurance performance by 3% with 4 mg/kg caffeine intake, only participants with AA genotype (fast metabolism) responded significantly to 2 mg/kg caffeine intake. Similarly, in another study, participants with the AA genotype responded to caffeine, while those with CC genotypes did not (86). On the contrary, there are studies reporting that there is no difference in caffeine response between genotypes (3), and even only slow metabolisers with CC genotypes respond to caffeine (65). Although the effects of genetic factors on caffeine responses are not known for now, athletes can still plan individual caffeine intake by determining their CYP1A2 genotypes.

Caffeine Effects on Physical and Cognitive Performance

In Olympic competitions, even a 1-2% performance increase can lead to winning or losing a gold medal (15). Since elite athletes at the Olympic level are physiologically at the highest level of genetic potential, they have to create their training, recovery and nutrition plans by making use of all scientific methods. Nutritional supplements, such as caffeine, whose use is not prohibited and whose significant effects on performance have been proven, are almost “pebble on the beach” for athletes. The significant effects of 3-6 mg/kg caffeine intake on aerobic endurance have been demonstrated by dozens of studies in both male and female athletes (76). In the last 10 years, the effects of caffeine on muscular strength and muscular endurance performance have been studied more (84). As in aerobic endurance, many studies showing that caffeine intake at doses of 3-6 mg/kg significantly increases muscular endurance, in particular, have been included in systematic reviews and meta-analyses (31). However, it has been reported that the effects of 1TM on muscular strength performance should be investigated further (36). Men metabolize caffeine faster than women due to greater CYP1A2 activation (62), so performance responses may also differ. However, Skinner et al. (2019) and Clarke et al. (2019) reported that 3 mg/kg of caffeine intake increased aerobic endurance performance in men and women at the same rate. During strength and muscular endurance training, neural recovery is of great importance in order to maintain muscle performance after repetitive contractions. Although the gender differences in neural responses to resistance exercises are not well known, it is known that women are more resistant to fatigue and recover more quickly in low-intensity and slow-paced resistance exercises than men (42). Recently, it has been found that, despite the same level of neuromuscular fatigue in response to resistance training, there are different sex-specific cortico-motor regulation mechanisms in the corticospinal pathways (16). Since caffeine intake also increases performance by stimulating the central nervous system, its effects on strength and muscular endurance performance may differ between genders. While 5 mg/kg caffeine intake significantly increased the chest press 1RM strength performance in male and female athletes, it increased muscular endurance performance only in men (72). The authors reported that a similar protocol should be applied to subgroup muscles with larger muscle group size in future studies. Lara et al. (2021), on the other hand, performed the effect of caffeine intake on sprint performance for the first time by comparing the genders and reported that the 3 mg/kg dose significantly increased the 15 second adapted Wingate peak and mean power for both genders. Since the research group consisted of only those with “low” caffeine consumption frequency, it was reported that the answers of those with “medium” or “high” consumption frequency should be examined with the same protocol. Considering that after 20 days of caffeine intake, tolerance developed in the 15-second wingate performance responses to 3 mg/kg of anhydrous caffeine intake (49).

In the literature, the possible effects of caffeine consumption frequency on performance responses are mostly on aerobic endurance, and its effects on muscular performance have only been investigated a few times. Grgic and Mikuliç (2020) revealed that 3 mg/kg caffeine intake significantly increased 85% 1RM chest press endurance and wingate performance in male athletes with both low and high caffeine consumption frequency. In addition, it was reported that 3 and 6 mg/kg caffeine intake significantly increased chest press 1RM strength but had little effect on 50% 1RM muscular endurance performance in female athletes with high caffeine consumption (33). Similar findings revealed that 3, 6 and 9 mg/kg caffeine intakes did not increase chest press performance in male athletes with high consumption frequency (85). On the contrary, in a study on female athletes with low caffeine consumption frequency, 3 and 6 mg/kg caffeinated coffee significantly increased squat endurance performance but did not affect chest press performance (48). There is a need for research that directly compares the genders and examines the effects of caffeine intake at lower doses (<3 mg/kg) on lower and upper body strength and muscular endurance performance. In addition to exercise performance, the effects of caffeine intake on sports branch-specific performances, where cognitive performance is important, have recently been studied. In a systematic review, it was reported that caffeine doses up to 300 mg significantly increased different cognitive performance parameters (attention, alertness, reaction time) (57). In addition, studies in the literature report that caffeine intake increases both physical and cognitive performance more after sleep deprivation (51, 57). Contrary to physical performance, it has been reported that lower doses are more effective for cognitive performance increase, rather than high doses in one go (51). In this regard, the effects of low-dose caffeine intake on the cognitive performance of athletes should be compared with higher doses. The results of other studies measuring branch-specific cognitive performance differ. Foskett et al. (2009) reported that 6 mg/kg caffeine intake significantly increased cognitive performance parameters measured by ball control and accuracy in football players. Similar findings, also confirmed by Stuart et al. (2005). However, there are studies stating the opposite (13, 69). It is thought that the different results can be explained by the difference in the test protocols used (flanker, simon or stroop task), the participants and the amount of caffeine dose. In recent studies, studies have been published reporting that generally 3 and 6 mg/kg caffeine intakes increase the reaction time and accuracy rates and increase cognitive performance significantly. Duncan et al. (2019) reported that cognitive performance increased significantly in addition to increasing upper body wingate performance. The results of this research are important for sports branches such as wrestling, where both upper body performance and cognitive processes are important. Almost all of the above-mentioned studies are on men. Bottoms et al. (2013), in his study on 4 female and 7 male fencers, reported that 3 mg/kg caffeine intake had a significant effect on fencing skills, but did not increase cognitive performance. As far as is known, there is no other study examining the effects of caffeine intake on cognitive performance by comparing the genders and frequency of consumption of different doses of caffeine. Table 1 and 2 summarized the studies in these topics.

Table 1. Effects of caffeine on cognitive performance

Reference	Participant	Dose	Time	Form	Test	Result
Bottoms et al., 2013	4 female 7 male	3 mg/kg	90 min.	Anhydrous	Stroop Task	No effect
Duncan et al., 2019	12 males	5 mg/kg	60 min.	Anhydrous	Flanker Task	Beneficial
Foskett et al., 2009	12 males	6 mg/kg	60 min.	Anhydrous	Test Batery	Beneficial
Karayigit et al., 2021	17 females	3, 6 mg/kg	60 min.	Coffee	Flanker Task	Beneficial
Zhang et al., 2020	10 male	3, 6, 9 mg/kg	60 min.	Anhydrous	Stroop Task	Beneficial with 3 mg/kg

Table 2. Effects of caffeine on physical performance

Reference	Participant	Dose	Time	Form	Test	Result
Anderson et al., 2020	10 trained cyclists 9: male-1: female	280 mg	45 min.	Coffee	30 seconds Wingate	No effect
Apostolidis et al., 2020	20 male soccer player	6 mg/kg	75 min.	Anhydrous	Time to exhaustion	Beneficial
Clarke et al., 2016	12 recreationally active males	3 mg/kg	45 min.	Coffee and Anhydrous	Repeated sprint cycling	No effect
Clarke et al., 2018	13 trained male runners	3 mg/kg	60 min.	Coffee	1 mile race	Beneficial
Clarke et al., 2019	19 male – 19 female	3 mg/kg	60 min.	Coffee	5 km cycling time trial	Beneficial
Filip-Stachnik et al., 2021	21 resistance trained female	3 mg/kg 6 mg/kg	60 min.	Anhydrous	1-RM strength	Beneficial
Grgic et al., 2020	24 resistance trained male	3 mg/kg	60 min.	Anhydrous	Wingate Resistance Exercise	Beneficial
Kaçoğlu et al., 2019	18 female henbtol player	0,05 g/kg	60 min.	Coffee	30 seconds Wingate	No effect
Kara et al., 2019	12 male soccer player	6 mg/kg	60 min.	Anhydrous	Test Batery	No effect
Lara et al., 2021	10 female	3 mg/kg	60 min.	Anhydrous	15 seconds Wingate	Beneficial
Richardson et al., 2016	9 resistance trained male	5 mg/kg	60 min.	Coffee and Anhydrous	60% of 1RM endurance	Beneficial
Skinner et al., 2019	11 female-16 male trained cyclists	3 mg/kg	90 min.	Anhydrous	Cycling time-trial	Beneficial
Wilk et al., 2019	15 resistance trained males	3, 6 and 9 mg/kg	60 min.	Anhydrous	Resistance exercise	No effect

CONCLUSION

- Athletes can ingest caffeine via different forms such as gum, coffee, anhydrous, and aerosol. Caution must be given that each form have different digestion duration and time to peak caffeine levels in blood.
- Although differences appears individually, caffeine seems to be effective 45-90 minutes after ingestion. Nevertheless, athletes should try its caffeine intake timing in trainings to see the outcomes.
- Most of the researches in literature showed caffeine as an ergogenic doses between 3 and 6 mg/kg of caffeine. However, lower doses of caffeine (<3 mg/kg) is still being investigated and depending on athletes' habitual caffeine consumption level, some athletes may benefit from low doses.
- Caffeine has been shown to increase aerobic-muscular endurance performance and sprint type activities. However, muscular strength and power responses has not been investigated much and existing studies reported generally negative results.
- Caffeine has also some beneficial effects after vigorous exercise as an recovery agent especially in glycogen stores.
- Body composition and hormonal differences between genders are apparent, but caffeine seems to increase physical and cognitive performance in both men and women. However, it would be helpful for female athletes to consider menstruel cycle while consuming caffeine as an ergogenic aid.
- Athletes' genotype can also have an impact on caffeine ergogenicity. It may be a requirement for athlete to be aware of caffeine ingestion increase performance depending on genotype in some studies. Preferably, genotype tests can be done to know which allels (AA or AC) athletes have.
- Considering caffeine may lead to side effects in some athletes, placebo effect can then be used in this situations because this has been found to effective on sports performance with no adverse effects.
- Most importantly, literature also focused on this topic, caffeine may improve performance depending on individuals' habitual caffeine consumption level. It can be suggested that athletes can increase acute caffeine intake dose higher than their habitually usage to exclude this tolerance phenomenon.

REFERENCES

1. Aguiar A.S., Speck, A.E., Canas, P.M., Cunha, R.A. (2020). Neuronal adenosine A_{2A} receptors signal ergogenic effects of caffeine. *Scientific Reports,* 10, 13414.
2. Akça, F., Aras, D., Arslan, E. (2018). Kafein, etki mekanizmaları ve fiziksel performansa etkileri. *Spormetre*, 16(1), 1-12.
3. Algrain Haya, A.T.R.M., Carrillo, A.E., Ryan, E.J., Chuk-ho, K., Lettan, R.B., Ryan, E.J. (2016). The effects of a polymorphism in the cytochrome P450 CYP1A2 gene on performance enhancement with caffeine in recreational cyclists. *Journal of Caffeine Research*, 6(1), 34-39.
4. Anderson, D.E., German, R.E., Harrison, M.E., Bourassa, K.N., Taylor, C.E. (2020). Real and perceived effects of caffeine on sprint cycling in experienced cyclists. *Journal of Strength and Conditioning Research*, 34(4), 929-933.
5. Apostolidis, A., Mougios, V., Smilios, I., Frangous, M., Hadjicharalambou, M. (2020). Caffeine supplementation is ergogenic in soccer players independent of cardiorespiratory or neuromuscular fitness levels. *Journal of the International Society of Sports Nutrition*, 17, 31.
6. Bayraktar, F., Taşkıran, A. (2019). Kafein tüketimi ve atletik performans. *Journal of Health and Sport Sciences*, 2(2), 24-33.
7. Bayram, H.M., Ozturkcan, S.A. (2020). Sporcularda ergojenik destekler. *Türkiye Klinikleri Sağlık Bilimleri Dergisi,* 5(3), 641-652.
8. Beaumont, R., Cordery, P., Funnell, M., Mears, S., James, L., Watson, P. (2017). Chronic ingestion of a low dose of caffeine induces tolerance to the performance benefits of caffeine. *Journal of Sports Sciences*, 35(19), 1920-1927.
9. Bell, D.G., Mclellan, T.M. (2002). Exercise endurance 1, 3, and 6 h after caffeine ingestion in caffeine users and nonusers. *Journal of Applied Physiology.* 93(4), 1227-1234.
10. Bottoms, L., Greenhalgh, A., Gregory, K. (2013). The effect of caffeine ingestion on skill maintenance and fatigue in epee fencers. *Journal of Sports Sciences,* 31(10), 1091-9.
11. Burke, L.M. (2017). Practical issues in evidence-based use of performance supplements: supplement interactions, repeated use and individual responses. *Sports Medicine,* 47, 79-100.
12. Cairns, S.P., Hing, W.A., Slack, J.R., Mills, R.G., Loiselle, D.S. (1997). Different effects of raised $[K^+]$ on membrane potential and contraction in mouse fast and slow-twitch muscle. *American Journal of Physiology Cell Physiology*, 273,598-611.
13. Chia, J.S., Barrett, L.A., Chow, J.Y., Burns, S.F. (2017). Effects of caffeine supplementation on performance in ball games. *Sports Medicine,* 47(12), 2453-2471.
14. Childs, E., Hohoff, C., Deckert, J., Xu, K., Badner, J., With, H. (2008). Association between ADORA2A and DRD2 polymorphisms and caffeine-induced anxiety. *Neuropsychopharmacology,* 33(12), 1694-1702.
15. Christensen, P.M., Shirai, Y., Ritz, C., Nordborg, N.B. (2017). Caffeine and bicarbonate for speed. A meta-analysis of legal supplements potential for improving intense endurance exercise performance. *Frontiers in Physiology,* 8, 240.

16. Christopher, L., Hendy, A., Vanderwesthuizen, D., Teo, W.P. (2018). The modulation of corticospinal excitability and inhibition following acute resistance exercise in males and females. *European Journal of Sport Science,* 18(7), 984-993.
17. Clarke N, Baxter, H., Fajemilua, E., Jones, V., Oxford, S., Richardson, D.L., Wyatt, C., Mundy, P. (2016). Coffee and caffeine ingestion have little effect on repeated sprint cycling in relatively untrained males. *Sports.* 4, 45.
18. Clarke, N.D., Richardson, D.L., Thie, J., Taylor, R. (2018). Coffee ingestion enhances 1-mile running race performance. *Nutrients,* 13, 789-794.
19. Clarke, N.D., Kirwan, N.A., Richardson, D.L. (2019). Coffee ingestion improves 5 km cycling performance in men and women by a similar magnitude. *Nutrients*, 11, 2575.
20. Clarke, N.D., Richardson, D.L. (2016). Effect of coffee and caffeine ingestion on resistance exercise performance. *Journal of Strength and Conditioning Research.* 30(10), 2892-2900.
21. Cornelis, M.C. (2019). The impact of caffeine and coffee on human health. *Nutrients,* 11, 416.
22. Cruz, R.S.D.O., De Aguiar, R.A., Turnes, T., Guglielmo, L.G.A., Beneke, R., Caputo, F. (2015). Caffeine affects time to exhaustion and substrate oxidation during cycling at maximal lactate steady state. *Nutrients*, 7, 5254-5264.
23. Del Coso, J., Lara, B., Ruiz-Moreno, C., Salinero, J.J. (2019). Challenging the myth of non-response to the ergogenic effects of caffeine ingestion on exercise performance. *Nutrients,* 11, 732.
24. Denoeud, F., Carretero-Paulet, L., Dereeper, A., Droc, G., Guyot, R., Pietrella, M., Aury, J.M. (2014). The coffee genome provides insight into the convergent evolution of caffeine biosynthesis. *Science,* 345(6201), 1181-1184.
25. Doepker, C., Wikoff, D. (2018). Key findings and implications of a recent systematic review of the potential adverse effects of caffeine consumption in healthy adults, pregnant women, adolescents, and children. *Nutrients,* 10(10), 1536.
26. Duncan, M.J., Dobell, A.P., Caygill, C.L., Eyre, E., Tallis, J. (2019). The effect of acute caffeine ingestion on upper body anaerobic exercise and cognitive performance. *European Journal of Sport Science,* 19(1), 103-111.
27. Dunican, I.C., Higgins, C.C., Jones, M.J., Clarke, M.W., Murray, K., Dawson, B., Caldwell, J.A., Halson, S.L.,
28. Eastwood, P.R. (2018). Caffeine use in a super rugby game and its relationship to post – game sleep. *European Journal of Sport Science,* 18(4), 513-523.
29. El Yacoubi, M., Ledent, C., Menard, J.F., Parmentier, M., Costentin, J., Vaugeois, J.M. (2000). The stimulant effects of caffeine on locomotor behaviour in mice are mediated through its blockade of adenosine A (2A) receptors. *British Journal of Pharmacology,* 129(7), 1465-1473.
30. Ferre, S. (2016). Mechanisms of the psychostimulant effects of caffiene: implications for substance use disorder. *Psychopharmacology,* 233(10), 1963-1979.
31. Ferreira, T.T., Farrias Da Silva, J.V., Bueno, N.B. (2020). Effects of caffeine supplementation on muscle endurance, maximum strength, and perceived exertion in adults submitted to strength training: a systematic review and meta-analyses. *Critical Reviews in Food Science and Nutrition,* 61(15), 2587-2600.

32. Filip, A., Wilk, M., Krzytofik, M., Del Coso, J. (2020). Inconsistency in the ergogenic effect of caffeine in athletes who regularly consume caffeine: is it due to the disparity in the criteria that defines habitual caffeine intake?. *Nutrients,* 12, 1087.
33. Filip-Stachnik, A., Wilk, M., Krzytofik, M., Lulinska, E., Tufano, J.J., Zajac, A., Stastny, P., Del Coso, J. (2021). The effects of different doses of caffeine on maximal strength and strength-endurance in women habituated to caffeine. *Journal of International Society of Sports Nutrition,* 18(1), 25.
34. Foskett, A., Ali, A., Gant, N. (2009). Caffeine enhances cognitive function and skill performance during simulated soccer acitivity. *International Journal of Sports Nutrition and Exercise Metabolism,* 19(4), 410-423.
35. Gonçalves, L.S., Painelli, V.S., Yamaguchi, G., Oliveira, L.F., Saunders, B., Silva, R.P., Maciel, E., Artioli, G.G., Roschel, H., Gualano, B. (2017). Dispelling the myth that habitual caffeine consumption influences the performance response to acute caffeine supplementation. *Journal of Applied Physiology,* 123(1), 213-220.
36. Grgic J, Grgic I, Pickering C, Schoenfeld Bj, Bishop Dj, Pedisic Z (2019). Wake up and smell the coffee: caffeine supplementation and exercise performance-an umbrella review of 21 published meta-analyses. British Journal of Sports Medicine, 11: 681-688.
37. Grgic, J., Mikulic, P. (2020). Acute effects of caffeine supplementation on resistance exercise, jumping, and wingate performance: no influence of habitual caffeine intake. *European Journal of Sport Science, 21(8), 1165-1175.*
38. Graham, T.E. (2001). Caffeine and exercise: metabolism, endurance and performance. *Sports medicine,* 31(11), 785-807.
39. Guest, N., Corey, P., Vesconi, J., El-Sohemy, A. (2018). Caffeine, CYP1A2 genotype, and endurance performance in athletes. *Medicine and Science in Sport and Exercise,* 50(8), 1570-1578.
40. Guest, N.S., Vandusseldrop, T.A., Nelson, M.T., Grgic, J., Schoenfeld, B.J., Jenkinds, N.D.M., Arent, S.M., Antonio, J., Stout, J.R., Trexler, E.T., Smith-Ryan, A.E., Goldstein, E.R., Kalman, D.S., Campbell, B.I. (2021). International society of sport nutrition position stand: caffeine and exercise performance. *Journal of the International Society of Sports Nutrition,* 18(1), 1.
41. Hall, S., Desbrow, B., Anoopkumar-Dukie, S., Davey, A.K., Arora, D., Mcdermott, C., Grant, G.D. (2015). A review of the bioactivity of coffee, caffeine and key coffee constituents on inflammatory responses linked to depression. *Food Research International,* 76(3), 626-636.
42. Hunter, S.K. (2016). The relevance of sex differences in performance fatigability. *Medicine and Science in Sports and Exercise*, 48(11), 2247-2256.
43. Irwin, C., Desbrow, B., Ellis, A., O’Keeffe, B., Grant, G., Leveritt, M. (2011). Caffeine withdrawal and high-intensity endurance cycling performance. *Journal of Sports Sciences.* 29(5), 509-515.
44. Jeukendrup, A.E. (2017). Periodized nutrition for athletes. *Sports Medicine,* 47, 51-63.
45. Kaçoğlu, C. (2019). Adölesan kız hentbolcularda, düşük doz kahve tüketiminin anaerobik performansa akut etkileri. *Türkiye Klinikleri Spor Bilimleri Dergisi,* 11(3), 97-107.
46. Kamimori, G.H., Karyekar, C.S., Otterstetter, R., Cox, D.S., Balkin, T.J., Belenky, G.L., Eddington, N.D. (2002). The rate of absortion and relative bioavailability of caffeine administered in chewing gum

versus capsules to normal healthy vounteers. *International Journal of Pharmaceutics*, 234(1-2), 159-167.

47. Kara, Z., Taşkın, H., Erkmen, N., Baştürk, D. (2019). Kafein takviyesinin kısa süreli yüksek yoğunluklu egzersize etkisi: kafein alım zamanı. *Spor ve Performans Araştırmaları Dergisi,* 10(1), 31-43.
48. Karayigit, R., Naderi, A., Akça, F., Gomez Da Cruz, C.J., Sarshin, A., Yasli, B.C., Ersöz, G., Kaviani, M. (2021). Effects of different doses of caffeinated coffee on muscular endurance, cognitive performance and cardiac autonomic modulation in caffeine naive female athletes. *Nutrients*, 13, 2.
49. Lara, B., Ruiz-Moreno, C., Salinero, J.J., Del Coso, J. (2019). Time course of tolerance to the performance benefits of caffeine. *Plos One*, 14(1), e0210275.
50. Lara, B., Salinero, J.J., Giraldez-Costos, V., Del Coso, J. (2021). Similar ergogenic effect of caffeine on anaerobic performance in men and women athletes. *European Journal of Nutrition,* online ahead of print.
51. Liebherman, H.R., Tharion, W.J., Shukitt-Hale, B., Speckman, K.L., Tulley, R. (2002). Effects of caffeine, sleep loss and stress on cognitive performance and mood during U.S. Navy Seal training. *Psychopharmacology,* 164(3), 250-261.
52. Magkos, F., Kavarous, S.T. (2005). Caffeine use in sports, pharmacokinetics in man, and cellular mechanisms of action. *Critical Reviews in Food Science and Nutrition*. 45(7-8), 535-562.
53. Marcil, M., Karelis, A.D., Peronet, F., Gardier, P.F. (2005). Glucose infusion attenuates fatigue without sparing glycogen in rat soleus muscle during prolonged electrical stimulation in situ. *European Journal of Applied Physiology,* 93(5-6), 569-574.
54. Martins, G.L., Guilherme, J.P.L.F., Ferreira, L.H.B., Souza-Junior, T.P., Lancha, A.H. (2020). Caffeine and exercise performance: possible directions for definitive findings. *Frontiers in Sports and Active Living, 2,* 574854.
55. Mattson, M.P. (2012). Evolutionary aspects of human exercise-born to run purposefully. *Ageing Research Reviews,* 11(3), 347-352.
56. Maughan, R.J., Burke, L.M., Dvorak, J., Larson-Meyer D.E., Peeling, P., Philips, S.M. (2018). IOC consensus statement: dietary supplements and the high-performance athlete. *International Journal of Sport Nutrition and Exercise Metabolism*, 28(2), 104-125.
57. Mclellan, T.M., Kamimori, G.H., Voss, D.M., Tate, C., Smith, S.J. (2007). Caffeine effects on physical and cognitive performance during sustained operations. *Aviation Space Environmental Medicine,* 78(9), 871-877.
58. Mclellan, T.M., Caldwell, J.A., Liebherman, H.R. (2016). A review of caffeine's effects of cognitive, physical and occupational performance. *Nueroscience&Biobehavioral reviews,* 71, 294-312.
59. Mielgo-Ayuso, J., Marques-Jimenez, D., Refoyo, I., Del Coso, J., Leon-Guereno, P., Calleja-Gonzalez, J. (2019). Effect of caffeine supplementation on sports performance based on differences between sexes: a systematic review. *Nutrients,* 11, 2313.
60. Mohr, M., Nielsen, J.J., Bangsbo, J. (2011). Caffeine intake improves intense intermittent exercise performance and reduces muscle interstitial potassium accumulation. *Journal of Applied Physiology,* 111(5), 1372-1379.

61. Ogawa, N., Ueki, H. (2007). Clinical importance of caffeine dependence and abuse. *Psychiatry Clin Neurosci,* 61(3), 263-268.
62. Ou-Yang, D.S., Huang, S.L., Wang, W. (2000). Phenotypic polymorphism and gender-related differences of CYP1A2 activity in a Chinese population. *British Journal of Clinical pharmacology,* 49(2), 145-151.
63. Ryan, E.J., Kim, C.H., Fickes, E.J., Williamson, M., Muller, M.D., Barkley, J.E. (2013). Caffeine gum and cycling performance: a timing study. *Journal of Strength and Conditioning Research,* 27(1), 259-264.
64. Pallares, J.G., Fernandez-Elias, V.E., Ortega, J.F., Munoz, G., Munoz-Guerra J., Mora-Rodriguez, R. (2013). Neuromuscular responses to incremental caffeine doses: performance and side effects. *Medicine and Science in Sport and Exercise,* 45(11), 2184-2192.
65. Pataky, M.W., Womack, C.J., Saunders, M.J., Goffe, J.L., D'Lugos, A.C., El-Sohemy, A. (2016). Caffeine and 3-km cycling performance effects of mouth rinsing, genotype, and time of day. *Scandinavian Journal of Medicine and Science in Sports,* 26(6), 613-619.
66. Pickering, C., Grgic, J. (2019). Caffeine and exercise: what next?. *Sports Medicine,* 49(7), 1007-1030.
67. Pickering, C., Grgic, J. (2021). A time and a place: a framework for caffeine periodization throughout the sporting year. *Nutrition,* 82, 111046.
68. Pickering, C., & Kiely, J. (2019). Do non-responders to exercise exist—and if so, what should we do about them?. Sports Medicine, 49(1), 1-7.
69. Pontifex, K.J., Wallman, K.E., Dawson, B.T., Goodman, C. (2010). Effects of caffeine on repeated sprint ability, reactive agility time, sleep and next day performance. *Journal of Sports Medicine and Physical Fitness,* 50(4), 455-464.
70. Ruiz-Moreno, C., Lara, B., Gutierrez-Hellin, J., Gonzalez-Garcia, J., Del Coso, J. (2020). Time course and magnitude of tolerance to the ergogenic effect of caffeine on the second ventilatory threshold. *Life,* 10(12), 343.
71. Ryan Ej, Kım Ch, Fıckes Ej, Wıllıamson M, Muller Md, Barkley Je (2013). Journal of Strength and Conditioning Research, 27: 259-264.
72. Sabblah, S., Dizon, D., Bottoms, L. (2015). Sex differences on the acute effects of caffeine on maximal strength and muscular endurance. *Comperative Exercise Physiology,* 11(2), 89-94.
73. Salinero, J., Jimenez-Ormeno, E., Romero-Moraleda, B., Giraldez-Costas, V., Baltazar-Martins, G., Del Coso, J. (2019). More research is necessary to establish the ergogenic effect of caffeine in female athletes. *Nutrients,* 11, 1600.
74. Shen, JG, Brooks, M.B., Cincotta, J., Manjourides, J.D. (2019). 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,* 22(2), 232-238.
75. Skinner, T.L., Desbrow, B., Arapova, J., Schaumberg, M.A., Osborne, J., Grant, G.D., Aanookumar-Dukie, S., Leveritt, M.D. (2019). Women experience the same ergogenic response to caffeine as men. *Medicine and Science in Sport and Exercise,* 51(6), 1195-1202.
76. Southward, K., Rurtherfurd-Markwick, K.J., Ali, A. (2018). The effect of acute caffeine ingestion on endurance performance: a systematic review and meta-analysis. *Sports Medicine,* 48(8), 1913-1928.

77. Spriet, L.L. (2014). Exercise and sport performance with low doses of caffeine. *Sports Medicine*, Suppl 2, 175-184.
78. Stuart, G.R., Hopkins, W.G., Cook, C., Cairns, S.P. (2005). Multiple effects of caffeine on simulated high-intensity team-sport performance. *Medicine and Science in Sports and Exercise*, 37(11), 1998-2005.
79. Taylor, C., Higham, D., Close, G.L., Morton, J.P. (2011). The effect of adding caffeine to postexercise carbohydrate feeding on subsequent high-intensity interval-running capacity compared with carbohydrate alone. *International Journal of Sport Sutrition and Exercise Metabolism*, 21(5), 410-416.
80. Tepper, J.M., Wilson, C.J., Koös, T. (2008). Feedforward and feedback inhibition in neostriatal GABAergic spiny neurons. *Brain Research Reviews*, 58(2), 272-281.
81. Thibault, V., Guillaume, M., Berthelot, G., El Helou, N., Schaal, J., Quinquis, L., Nassif, H., Tafflet, M., Escolano, S., Hermine, O. (2010). Women and men in sport performance: the gender gap has not evolved since 1983. *Journal of Sports Science and Medicine*, 9(2), 214-223.
82. Trexler, E.T., Smith-Ryan, A.E., Roelofs, E.J., Hirsch, K.R., Mock, M.G. (2015). Effects of coffee and caffeine anhydrous on strength and sprint performance. *European Journal of Sport Science.* 16(6), 702-710.
83. Ulucan, K., Sercan, C., Eken B.F., Ulgut, D., Erel, S. (2016). Spor genetiği ve ace gen ilişkisi. *İnönü Üniversitesi Beden Eğitimi ve Spor Bilimleri Dergisi,* 3(2), 26-34.
84. Warren, G.L., Park, N.D., Maresca, R.D., Mckibans, K.I., Millard-Stafford, M.L. (2010). Effect of caffiene ingestioon muscular strength and endurance: a meta-alalysis. *Medicine and Science in Sport and Science.* 42(7), 1375-1387.
85. Wilk, M., Filip, A., Krzsytofik, M., Maszczy, A., Zajac, A. (2019). The acute effect of various doses of caffeine on power output and velocity during the bench press exercise among athletes habitually using caffeine. *Nutrients*, 11, 1465.
86. Womack, C.J., Saunders, M.J., Bechtel, M.K., Bolton, D.J., Martin, M., Luden, N.D. (2012). The influence of a CYP1A2 polymorphism on the ergogenic effects of caffeine. *Journal of International Society of Sport Nutrition,* 9(1), 438-452.
87. Van Thuyne, W., Delbeke, F.T. (2006). Distribution of caffeine levels in urine in different sports in relation to doping control before and after the removal of caffeine from the WADA doping list. *International Journal of Sports Medicine,* 27(9), 745-750.
88. Yang, C., Franciosi, S., Brown, R.E. (2013). Adenosine inhibits the excitatory synaptic inputs to basal forebrain cholinergic, GABAergic, and parvalbumin neurons in mice. *Frontiers in Neurology,* 4, 77.
89. Zhan, B., Liu, Y., Wang Xiaochun, W., Deng, Y., Zheng, X. (2020). Cognition and brain activation in response to various doses of caffeine: a near-infrared spectroscopy study. *Frontiers in Psychology,* 11, 1393.