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A 5-Year Systematic Review (01 November 2019 to 31 October 2024) Ergogenic Effects of Caffeine on Endurance and Strength Performance

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Abstract

Caffeine is common performance enhancing ergogenic aid. Though widely used, the extent of the effects of caffeine on individuals can vary due to individual variability in response to caffeine. This systematic review aims to provide a comprehensive analysis on caffeine's ergogenic effects on endurance and strength performance while examining the influence of individual factors on these outcomes. A literature search was conducted on PubMed for studies on caffeine on endurance and strength performance from 01 November 2019 to 31 October 2024. Forty out of 179 articles were included and categorized into three main themes: (i) caffeine's impact on endurance performance, (ii) its effects on strength performance, and (iii) individual factors influencing its ergogenic potential. Findings reveal that caffeine enhances both endurance and strength performance by improving key parameters, as well as via its role as an adenosine receptor antagonist and other peripheral parameters. However, performance outcomes are influenced by individual variabilities such as genetics, including CYP1A2, ADORA2A, and ACE polymorphisms, along with dosage, timing of ingestion, and habitual caffeine intake, contribute to inconsistent performance outcomes.

Keywords: Caffeine; Strength performance; Endurance performance; Enhancement; Genetics

Introduction

Caffeine is a potent stimulant and one of the most widely used ergogenic aids for enhancing physical performance and has demonstrated its positive effects on exercise performance, improving endurance and strength across various exercises and sports [1, 2]. Caffeine's ergogenic effects are primarily attributed to its primary action on the central nervous system, functioning as an adenosine receptor antagonist in the brain [2]. Due to its similar molecular structure to adenosine, caffeine can bind to these receptors, causing enhanced muscle fiber conduction velocity and motor unit recruitment, causing improvements in force production, delaying fatigue, and increasing cognitive and physical readiness to aid exercise performance [2, 3]. This is one of the main reasons for caffeine's popularity as it can influence various physiological mechanisms; such as, the increase of neurotransmitter release and decreasing perception of pain and fatigue; which are crucial factors that help with endurance [4]. In addition, caffeine exerts significant peripheral ergogenic benefits. These include inhibiting phosphodiesterase, facilitating calcium ion (Ca^{2+}) release from the sarcoplasmic reticulum, enhancing sodium-potassium pump activity, and antagonizing benzodiazepine receptors in skeletal muscle [2]. These mechanisms work together, improving performance through aerobic endurance, muscular strength, and power whilst reducing the subjective rating of perceived exertion (RPE) during exercise [3].

Caffeine is naturally present in plants like coffee, tea, and cocoa, but it can also be artificially added to foods and beverages [4]. While coffee, tea, and energy drinks are the most common sources of caffeine, it can also be ingested as capsules, pre-workout supplements or chewing gum, which might be more common during exercise [4]. Most research has suggested that the benefits of caffeine are typically observed when consumed at doses of 3 to 6 mg/kg of body weight approximately 60 minutes before exercise [2, 4]. Despite these general benefits, the effectiveness of caffeine in individuals can vary between individuals, influenced by factors often studied in isolation rather than comprehensively [5].

Twenty-five systematic reviews from 01 November 2019 to 31 October 2024 have been indexed in PubMed (see Existing SR in Supplementary materials) on the effects of caffeine and endurance performance but they are often focused on a single aspect; such as caffeine's effects on endurance, strength, fat oxidation, time-trial performance, high-intensity efforts, cardiopulmonary responses, or potential side effects. Therefore, this systematic review aims to provide a comprehensive review of caffeine's ergogenic effects on both endurance and physical performance, while also incorporating various individual factors that may influence these effects by combining evidence across studies.

Methods

A PubMed search was conducted on 28 October 2024 for studies published since 01 November 2019 regarding the effects of caffeine on endurance and performance. The search term (caffeine* AND endur* AND perform*) were used, with the following URL:

https://pubmed.ncbi.nlm.nih.gov/?term=caffeine+AND+endur*+AND+perform*&filter=dates.2019/11/1-2024/10/31. The following exclusion criteria were used: (A) Non-English language articles, (B) Non-full text articles, (C) Non-primary articles, (d) studies not on humans, (E) Non-blinded and placebo articles, (F) Not on pre-exercise caffeine ingestion articles, and (G) Not on caffeine effect on endurance and strength performance articles.

Results and Discussion

A total of 179 articles were retrieved from PubMed by using the search terms (Figure 1). After screening through the exclusion criteria, 40 studies are included and separated into three main themes. The three main themes are further divided into sub-themes (Table 1).

Theme 1: Caffeine and endurance performance

Caffeine is a popular ergogenic aid to improve endurance performance abilities. Numerous studies have demonstrated consistent improvements in performance following pre-exercise caffeine ingestion. For instance, the administration of 5 mg/kg of caffeine reliably improved cycling performance compared to a placebo, with similar benefits observed across two separate test days [4]. Coupled with its well-known ability to enhance both mental and physical performance, caffeine is seen as a reputable ergogenic aid, frequently used to improve endurance [7, 13].

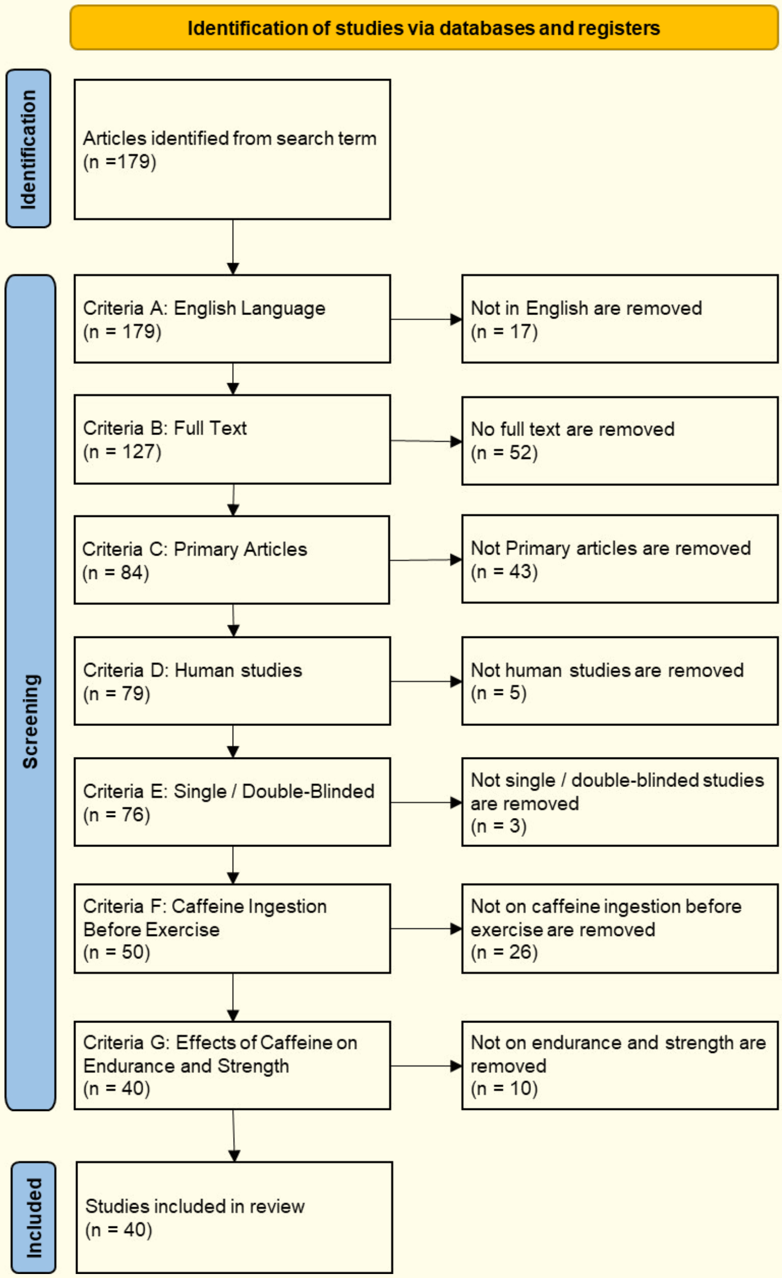

Figure 1: PRISMA Flowchart.

Themes	*Sub-Themes*	*References*
1: Caffeine and endurance performance	1.1: Time trials	[1, 4, 6-12]
	1.2: Time to exhaustion (TTE) & other physiological parameters	[7, 10, 13-22]
2: Caffeine and strength performance	2.1: Increased maximal strength	[2, 3, 15, 20, 23-26]
	2.2: Velocity-based training and power output	[23]
	2.3: Muscular endurance during resistance exercise	[3, 16, 18, 27-30]
3: Individual factors influencing caffeine's ergogenic effects	3.1: CYP1A2 Genotype, ADORA2A Genotype, ACE polymorphisms	[5, 22, 31-36]
	3.2: Dosage, timing and other factors	[9, 15, 22, 24, 28, 34, 37-40]

Table 1: Thematic Classification of the 40 Included Studies.

Theme 1.1: Caffeine and endurance performance - Time trials

Numerous studies have also consistently demonstrated that pre-exercise caffeine ingestion enhances time trial performance in both cycling and running [1, 4, 6-12]. In running time trials, studies indicate that participants consuming caffeine were able to cover greater distances compared to the placebo conditions [1, 7]. Notably, Dittrich et al. [7] reported a 18% improvement in performance, which was attributed to caffeine's ergogenic effects on the central nervous system, including reduced perceived effort and fatigue. Similarly, significant performance enhancements have been observed in cycling. For instance, Trujillo-Colmena et al. [4] explored the practical application of caffeine delivered via coffee in recreational cyclists during a cross-country cycling time trial. Their findings revealed that cyclists who ingested caffeinated coffee covered more distance within the same time frame compared to those consuming a placebo, highlighting caffeine's capacity to enhance endurance performance [4]. These improvements are likely due to caffeine's effects on various physiological and performance-related parameters, further reinforcing its utility as an endurance aid.

Firstly, caffeine's ability to improve performance has been related to its capacity to improve motor output entropy (MOEn), a measure of the central nervous system's adaptability to exercise-induced stressors [6, 8]. Studies by Ferreira Viana et al. [8] and Couto et al. [6] both support this mechanism, reporting faster completion times during their 4 km cycling time trials and increased power outputs after caffeine was ingested. Ferreira Viana et al. [8] observed a 1.8% reduction in completion time, along with an 8% increase in mean power output. These improvements were attributed to a 7% increase in MOEn post-caffeine ingestion, suggesting that caffeine enhances the central nervous system's ability to cope with exercise-induced perturbations [8]. These findings are further supported by Couto et al. [6], demonstrating that caffeine reduces the rate of fatigue development, enabling participants to sustain higher power outputs during closed-loop cycling tests and to perform longer in open-loop trials. This reduced fatigue rate likely reflects enhanced neuromuscular adaptability, as caffeine appears to mitigate fatigue-induced performance declines by supporting the physiological demands of prolonged exercise [8]. Together, backing caffeine's role in improving endurance capacities by enhancing both central nervous system adaptability and resistance to fatigue.

Theme 1.2: Caffeine and endurance performance - Time to exhaustion (TTE) & other physiological parameters

One of the reasons that caffeine improves endurance is due to its ergogenic effects on time to exhaustion (TTE). Several studies have seen that caffeine ingestion before exercise contributed to improvements in TTE. 2 Reports show an increase in TTE during treadmill tests after caffeine ingestion. [21] reported a 5.5% (19.4 seconds) increase in TTE, and Dittrich et al. [7] reported a 7.37-second increase. However, improvements are not only seen in treadmill tests, but Apostolidis et al. [13] also saw 53% improvements in TTE by caffeine in a simulated soccer protocol, and in another cycling test, Cristina-Souza et al. [14] observed a 14.4% improvement in endurance performance. Showing caffeine's ergogenic effect on improving TTE, as it can consistently delay fatigue even across various exercise modalities.

Caffeine intake also influences other physiological parameters associated with endurance, such as maximal fat oxidation (MFO), maximal oxygen uptake capacity (VO_2max), and the workload attained at the second ventilatory threshold (VT2). Caffeine ingestion can improve MFO during endurance exercise, as expressed in a study by Ramírez-Maldonado et al. [19] that showed improved mean MFO values after ingestion. MFO is one of the key parameters associated with endurance as it is a determinant of metabolic flexibility during exercise [19]. Higher fat oxidation rates translate to lower carbohydrate use during exercise, resulting in glycogen sparing in muscles and liver, allowing better endurance during exercise [19]. The body utilizes fat for energy, delaying fatigue by sparing glycogen stores in the body to optimise energy utilisation and preserve glycogen for critical phases of the exercise to delay fatigue hence enabling performance at a sustained pace for longer periods [19].

Ingestion of caffeine can also be seen to directly increase VO_2max [17, 21] or sustain the time spent at VO_2max [13, 14]. The study by Stadheim et al. [21] reported a 1.2% increase in VO_2max (from 75.8 to 76.7 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$) following caffeine ingestion in elite endurance athletes. This increase was attributed to enhanced ventilation (VEpeak) and heart rate (HRpeak), which resulted in an improvement in oxygen delivery and utilization [21]. Other studies noted that caffeine ingestion increased the time subjects were able to sustain exercise at their VO_2max levels [13, 14]. Cristina-Souza et al. [14] found that caffeine prolonged the time spent at VO_2max by 70%, allowing athletes to maintain maximal aerobic effort for longer durations. Similarly, Apostolidis et al. [13] also demonstrated caffeine's efficacy to maintain performance at submaximal intensities. The effect of prolonging the time spent at maximal intensity reflects that caffeine ingestion improves oxygen delivery and utilisation, allowing them to sustain exercise at higher levels for a longer period, improving endurance [13, 14].

Dittrich et al. [7] however shows contradicting results, showing no effect on VO_2max improvements. Although there have been contradicting findings on caffeine's ability to improve VO_2max improvements, this finding might not be significant to impact the erogenicity of caffeine on endurance as VO_2max itself is not the primary limiting factor in the endurance performance described in this study [7]. Instead, energy demand in this test relies on carbohydrate metabolism instead of VO_2max as human subjects in this study took part in short-term, high-intensity work at about 88% VO_2max efforts [7].

Evidence has also shown that caffeine's ergogenic effects on endurance are due to its ability to improve the workload attained at the second ventilatory threshold (VT2). During a cycling ramp test, participants ingested an acute intake of caffeine at a dose of 3 mg/kg of body mass [10]. Results showed that their workload at VT2 increased by 7.7 ± 9.7% as compared to placebo [10]. This suggests that caffeine can enhance performance during submaximal aerobic exercise by allowing individuals to exercise at a higher intensity before reaching the ventilatory threshold, therefore causing improvements in endurance [10].

Caffeine's ability to improve endurance during exercise is also often attributed to its potential to reduce the perception of effort (RPE), as it is linked to caffeine's role as an adenosine receptor antagonist in the central nervous system, which can create a sensation of lower exertion during exercise [7]. However, inconsistencies in findings about reduced ratings of perceived exertion (RPE) following caffeine ingestion suggest a more complex relationship. For instance, while one study conducted on soccer players reported significantly lower RPE levels in the caffeine group compared to the placebo group [13], several other studies have demonstrated no significant effect on RPE values despite improvements in muscular endurance and overall endurance performance [7, 15, 18, 20, 22]. These discrepancies may stem from factors such as differences in exercise modalities, the timing of RPE measurements, or variations in testing protocols.

Instead, the findings from these studies have highlighted that ergogenic effects from caffeine are due to other mechanisms rather than solely the reduction of RPE. Improved motor unit recruitment and altered pain perception are among the alternative explanations. For example, Lopes-Silva et al. [18] suggested that caffeine enhances phosphocreatine (PCr) replenishment during recovery intervals, maintaining energy supply via anaerobic alactic metabolism and therefore improving energy availability during exercise. Peripheral effects of caffeine, such as increased motor unit recruitment and calcium release from the sarcoplasmic reticulum, also contribute to enhanced muscle contractility and endurance [18]. Interestingly, Lopes-Silva et al. [18] noted that the unchanged RPE might reflect a suppressive effect of caffeine on the perception of effort. This phenomenon enables performance improvements without a corresponding increase in perceived exertion, underscoring the multifaceted ways caffeine influences endurance performance.

Hence, caffeine is a well-documented ergogenic aid that significantly enhances endurance performance through its central and peripheral mechanisms. The reviewed studies consistently highlight caffeine's ability to improve key parameters such as time to exhaustion (TTE), maximal fat oxidation (MFO), maximal oxygen uptake (VO_2max), workload at the second ventilatory threshold (VT2), and time trial performance. These physiological benefits are primarily attributed to caffeine's action as an adenosine receptor antagonist, leading to reduced fatigue perception, enhanced energy utilization, and improved neuromuscular function. Despite some inconsistencies, particularly in the effects on perceived exertion (RPE), the overarching evidence underscores caffeine's ability to improve endurance through both central and peripheral mechanisms. These findings highlight its relevance as a practical intervention for people seeking endurance performance enhancements.

Theme 2: Caffeine and strength performance

The role of caffeine as an ergogenic aid extends beyond endurance activities, with substantial evidence indicating its benefits for muscular strength and power. Here, the specific effects of caffeine on resistance exercise are explored, delving into the mechanisms by which caffeine enhances strength performance. While caffeine's impact on endurance is well-established, its influence on strength and power is equally significant in various aspects such as weightlifting, powerlifting, and other high-intensity, short-duration activities.

Caffeine exerts its ergogenic effects on strength performance through a combination of central, peripheral, and metabolic mechanisms. As an adenosine receptor antagonist, caffeine primarily impacts the central nervous system by increasing neural drive, enhancing motor unit recruitment, and reducing the perception of effort during high-intensity activities [36]. These effects can result in greater force output and improved physical performance during resistance exercise. Moreover, with caffeine's ability to modulate pain perception, it may enable athletes to push closer to their physiological limits during strength tasks, further contributing to its benefits.

On a peripheral level, caffeine influences muscle contractility by enhancing calcium ion release from the sarcoplasmic reticulum, which facilitates stronger and more sustained muscle contractions [36]. This mechanism may be particularly relevant in the context of maximal effort lifts or explosive power movements, where efficient and forceful contractions are critical for performance outcomes.

Caffeine may also exert a metabolic impact that benefits strength performance. It has been suggested that caffeine influences substrate utilization during resistance training, potentially favoring glycogen-sparing or optimizing energy availability for short-duration, high-intensity efforts [15]. Overall, showing that caffeine's multifaceted impact on strength performance underscores its value as an ergogenic aid for resistance training.

Theme 2.1: Caffeine and strength performance - Increased maximal strength

Maximum strength can be measured by one-repetition maximum (1RM) tests. Numerous studies demonstrate that caffeine ingestion before taking part in resistance training or exercise increased participant's 1RM in bench press and squat, proving that caffeine can increase maximal strength. For instance, Norum et al. [25] showed that a 4 mg/kg dose of caffeine increased 1RM in the squat by 4.5% (4.1 kg) and in the bench press by 3.3% (2.2 kg). Liu et al. [24] also reported that a 3 mg/kg dose of caffeine increased bench press 1RM by 7.58% and deep squat 1RM by 9.45% compared to a placebo. These improvements in strength appear to stem from caffeine's ability to stimulate the central nervous system (CNS), enhancing motor unit recruitment and muscle fiber conduction velocity [25].

However, while caffeine enhances strength in both upper and lower body exercises, studies suggest differential effects. Norum et al. [25] noted that caffeine yielded greater improvements in squat 1RM (4.5%) compared to bench press 1RM (3.3%), while Liu et al. [24] also saw that deep squat was improved by 9.45%, and bench press 1RM was improved by 7.58%. This may be due to larger muscle groups, such as the knee extensors, having a lower baseline muscle activation level (85-95%) compared to smaller muscle groups like the elbow flexors (90-99%), whereby lower baseline activation in larger muscles allows greater room for improvement via central nervous system stimulation [25]. Improvements could be seen in an isokinetic knee extension test, whereby caffeine supplementation significantly enhanced muscle strength [26]. Zart et al. [26] reported that during the test, there was a notable increase in maximum torque (+5.1%) and average torque (+4.2%), supporting that caffeine is an effective ergogenic aid in larger muscle groups such as the knee extensors.

Montalvo-Alonso et al. [2] further supported this by showing that caffeine (3 mg/kg) had particularly pronounced effects on lower body exercises, especially the back squat, at 50%-90% 1RM. Their study highlighted a significant ergogenic effect of caffeine on variables such as mean velocity (Vmean) and mean power (Wmean), particularly in larger muscle groups like the quadriceps [2]. In contrast, smaller muscle groups such as the elbow flexors did not show similar ergogenic effects [2].

These findings align with the understanding that muscle activation during maximal voluntary contraction (MVC) is typically lower in larger muscle groups like the quadriceps compared to smaller ones [2]. This suggests that caffeine's CNS-mediated effects by enhancing motor unit recruitment and muscle fiber conduction velocity may provide a greater boost in force production for larger muscle groups [2]. Despite caffeine's more pronounced impact on lower body strength, its efficacy in improving upper body strength is still well-supported. Other studies [3, 15, 20, 23] have all documented significant improvements in upper body 1RM, confirming caffeine's role as a reliable ergogenic aid for enhancing maximal strength across both upper and lower body exercises.

Theme 2.2: Caffeine and strength performance - Velocity-based training and power output

Caffeine's impact on strength performance is also evident in its ability to enhance velocity-based training and increase power output as seen from improvements in mean and peak bar velocity, peak force, and peak power output throughout a structured training [23]. The study's design, which involved 4 sets of 8 repetitions at 70% 1RM, closely mirrors common strength training practices, emphasizing its relevance to real-world scenarios [23]. This shows caffeine as an accessible and practical application for both athletes and recreational lifters aiming to enhance strength and power and demonstrates that it not only boosts maximal strength but also enhances performance in recreational resistance training.

Theme 2.3: Caffeine and strength performance - Muscular endurance during resistance exercise

A consistent trend across studies examining caffeine's impact on resistance exercise is its ability to enhance muscular endurance. Numerous studies have demonstrated improvements in the number of repetitions performed during both upper and lower body exercises following caffeine ingestion. For instance, Jones et al. [16] observed significant increases in repetitions during a leg press exercise, with muscular endurance improving by 23% and 36% at caffeine doses of 3 mg/kg and 6 mg/kg body weight, respectively. Similarly, enhancements in lower body muscular endurance have been reported in exercises such as squats [3, 28]. Comparable benefits have also been observed in upper body endurance, particularly in bench press performance [3, 18, 29, 30]. This improvement is consistent with prior literature, which attributes the effects to a combination of central and peripheral mechanisms, leading to improvements of the ability of muscles to sustain repeated contractions over a period of time or until exhaustion [27]. Hence, this presents caffeine's acute ergogenic effects on resistance exercise performance, specifically in enhancing muscular endurance which are effective across various muscle groups.

Thus, these effects on increase of maximal strength, velocity-based training and power output and endurance during resistance exercise shows caffeine's ergogenic ability for strength performance. It also shows the relevance of caffeine as a pre-exercise supplement for individuals aiming to optimize their performance in resistance or strength training. By ingesting caffeine prior to exercise, individuals may experience significant improvements in overall performance and strength, making it a valuable ergogenic aid.

Theme 3: Individual factors influencing caffeine's ergogenic effects

While caffeine is widely recognized as an ergogenic aid in improving endurance and strength, its effectiveness can vary from person to person due to various individual factors, leading to variability in responses. These factors can be broadly categorized into genetic, physiological, and lifestyle-related aspects. Genetic factors are variations in genes that code for proteins involved in caffeine metabolism and its mechanisms of action [5]. Variations in these genes can lead to significant differences in how people process caffeine and how their bodies react to it, which might in turn affect the extent to which they experience the performance-enhancing effects of caffeine [5].

Theme 3.1: Individual factors influencing caffeine's ergogenic effects - CYP1A2 genotype, ADORA2A genotype & angiotensin-converting enzyme (ACE) polymorphisms

The CYP1A2 gene encodes a cytochrome P450 enzyme that metabolizes approximately 95% of caffeine in the body by converting it into its primary metabolite, paraxanthine [5]. Variations in the single nucleotide polymorphism (SNP) rs762551 (-163 C>A) categorizes individuals into "fast" (AA genotype) or "slow" (AC/CC genotype) metabolizers [34]. This is a result of an A to C substitution at position 163 (-163 C>A) of SNP rs762551 in the CYP1A2 gene, which impacts the speed of caffeine metabolism [34]. "Fast" metabolizers are believed to benefit more from caffeine due to its capability to process caffeine more rapidly, resulting in faster availability of active metabolites [34]. This enhances the binding affinity of caffeine metabolites to these receptors, which may lead to quicker and more pronounced ergogenic responses [33, 34]. Conversely, "slow" metabolizers process caffeine at a slower rate, and have higher risks of adverse side effects [33]. The study by Carswell et al. [5] supports this mechanism, reporting that caffeine enhanced CYP1A2 "fast" metabolizers cognitive performance more than "slow" metabolizers, and that "fast" metabolizers showed a greater improvement in 40-km time trial performance. Similarly, Guest et al. [33] reported that a 4-mg·kg−1 dose of caffeine improved 10-km cycling performance in those with the AA genotype, who are "fast" metabolizers.

However, results are not consistent across all research. Guntoro Aji et al. [34] observed that while "fast" metabolizers showed increases in VO_2max when caffeine was consumed one or two hours before exercise, "slow" metabolizers experienced greater VO_2max increases when caffeine was ingested two hours before exercise. Other studies have contradicted the effectiveness of "fast" metabolizers, showing no differences in caffeine pharmacokinetics between "fast" and "slow" metabolizers [31]. For example, Glaister et al. [31] reported no differences in caffeine pharmacokinetics or performance outcomes between fast and slow metabolizers. Similarly, Spineli et al. [35] found that caffeine improved muscular endurance and aerobic performance in adolescent athletes irrespective of their CYP1A2 genotype. These inconsistencies could be due to independent factors from the different studies, indicating that further studies would be needed to draw further conclusions.

One other factor that could explain these inconsistencies could be due to the combined effects of genotypes. Guest et al. [33] examined the combined effects of CYP1A2 and HTR2A genotypes on caffeine's ergogenic potential and revealed that individuals with both the CYP1A2 AA genotype ("fast" metabolizers) and the HTR2A CC genotype ("slow" metabolizers, associated with lower serotonin receptor binding) exhibited the greatest performance improvement, with a 2.4-minute (12.6%) enhancement in 10-km cycling performance at a 4 mg/kg caffeine dose compared to placebo [33]. This effect may be attributed to reduced serotonin-mediated vasoconstriction in HTR2A CC individuals that allow better blood flow to active muscles during exercise, along with rapid caffeine metabolism in CYP1A2 AA individuals [33]. Both in synergy may explain the enhanced performance outcomes as having both CYP1A2 and HTR2A genotypes leads to optimization of the availability of active metabolites [33]. The CYP1A2 genotype alone may be insufficient to consistently produce ergogenic effects, but instead, the combination of both genotypes may provide clearer and more consistent results. Thus, further research with a multi-gene approach could be considered to aid in optimising the effects of caffeine.

Another genetic factor to consider when using caffeine as an ergogenic aid is the ADORA2A gene. They encode the A2A adenosine receptors, the primary targets of caffeine's action in the central nervous system [32]. However, it is mentioned that each individual's response to acute caffeine ingestion may vary due to polymorphic variations in the ADORA2A gene [32]. Research highlights that the rs5751876 single-nucleotide polymorphism (SNP) in the ADORA2A gene as a key determinant of caffeine sensitivity, where individuals are categorized as having "high" sensitivity (TT genotype) or "low" sensitivity (CT or CC genotypes) to caffeine [5]. It states that those who are ADORA2A C allele carriers tend to have higher habitual caffeine consumption, indicating that they might need higher caffeine doses to achieve a desired effect [32].

However, the evidence regarding the influence of the ADORA2A genotype on caffeine's ergogenic effects remains inconsistent. While Grgic, Pickering, et al. [32] reported that C allele carriers exhibited ergogenic responses to caffeine ingestion, other studies present conflicting findings. The study by Carswell et al. [5] observed no significant effect of the ADORA2A genotype on cognitive performance or caffeine metabolism. While similarly, Glaister et al. [31] found that caffeine's effects on exercise physiology and performance were not influenced by variations in the ADORA2A gene. Therefore, there are inconsistencies shown in the relationship between the ADORA2A genotype and caffeine's ergogenic effects, with no conclusive evidence to establish a definitive connection. These differing findings may stem from differences in study designs, including testing methods, participant demographics, and outcome measures, as highlighted by studies such as [5, 31, 32]. One key difference lies in the sex of participants. Both Glaister et al. [31] and Grgic, Pickering, et al. [32] focused exclusively on male participants, whereas Carswell et al. [5] included both males and females. This discrepancy is critical because sex-specific physiological differences could mean hormonal fluctuations and potential variations in caffeine metabolism that can influence performance outcomes [22]. Including both sexes and standardization would be essential for drawing a better definitive conclusion about caffeine's effects on performance across different ADORA2A genotypes. Another variation could be attributed to exercise modality. Glaister et al. [31] and Carswell et al. [5] employed cycling time trials, focusing on endurance performance, while [32] assessed caffeine's effects on power, muscular endurance, and sprinting. Different modalities of exercises, such as endurance-based exercises as compared to resistance and sprinting exercises place distinct physiological demands on the body's system, which potentially alters the extent to which caffeine enhances performance. Such differences might contribute to the variability in findings regarding the impact of the ADORA2A genotype on caffeine response. To clarify ADORA2A genotype's influence on caffeine's ergogenic effects, future research should prioritize standardization in key areas such as participant demographics and exercise modalities. Through standardized methodologies, it would help to present more lucrative findings on the role of ADORA2A polymorphisms in caffeine-related performance outcomes.

Angiotensin-converting enzyme (ACE) polymorphisms are another variation in the ACE gene that could influence physiological responses to exercise and caffeine. Specifically, the rs4340 variant of the ACE gene can affect an individual's response to caffeine [36]. It depends on whether the exercise is endurance- or strength-based due to the gene's impact on muscle fiber composition and the body's physiological response to caffeine [36].

The ACE gene encodes the angiotensin-converting enzyme, a key component of the renin-angiotensin system, which regulates blood pressure, fluid balance, and muscle fiber compositions [36]. The rs4340 polymorphism involves an insertion (I) or deletion (D) of a 287-base pair sequence, resulting in three genotypes: II, DI, and DD [36]. The II and DI genotypes are associated with a higher proportion of type I muscle fibers, characterized by high oxidative capacity and efficiency for prolonged, lower-intensity endurance exercise [36]. Conversely, the DD genotype has a higher proportion of type II muscle fibers, capable of generating greater force for strength and power activities, but fatigues quickly [36]. The study by Spineli et al. [36] highlights that individuals with II and DI genotypes show more significant positive responses to caffeine during endurance-based activities, while the DD genotype demonstrates less benefit in endurance tasks but may respond better to caffeine in strength-based exercises. For example, 84.6% of II genotype participants and 77.5% of DI participants exhibited improved endurance performance, heart rate, and perceived exertion after caffeine supplementation, compared to only 66.7% of DD participants [36]. These results have been consistent with the understanding that caffeine's effects are more pronounced in type I fibers during endurance activities, due to the positive correlation found between caffeine intake and endurance capacity in the II genotype. For individuals with the II and DI genotypes looking to enhance endurance performance, caffeine supplementation might show a greater effect. Meanwhile, those with the DD genotype may not benefit as much from caffeine in endurance-based exercises, but its effects could be more prevalent in a strength-based context. Hence these show that ACE polymorphisms play a part in affecting how individuals might respond to caffeine. Understanding ACE polymorphisms could be significant for individuals seeking to optimize performance, where caffeine supplementation could be tailored to maximize benefits based on their goals. However, it is worth noting that the sources do not provide information on how the DD genotype is impacted by caffeine in strength or power activities, thus there would need to be more research done on how the effects of caffeine could vary between these genotypes for a strength-based training approach.

Genetic differences may therefore help to explain the inter-individual variability in response to caffeine, that highlights the need for personalized sports nutrition strategies. Genetic variations, particularly in genes like CYP1A2, ADORA2A, and ACE, contribute to the diverse responses individuals exhibit towards caffeine, emphasizing that nutrition or supplementation strategies should be personalized. A "one-size-fits-all" approach to caffeine supplementation is inadequate and could lead to suboptimal or even negative outcomes for some individuals, hence genetic differences could be a crucial factor for consideration.

Theme 3.2: Individual factors influencing caffeine's ergogenic effects - Dosage, timing & other factors

The general dose recommendations of caffeine as an ergogenic aid range between 3 and 6 mg/kg of body mass [37]. While it is commonly assumed that higher doses lead to greater performance benefits, studies suggest that lower doses can still provide measurable effects. For example, Grgic, Sabol, et al. [37] found that a 2 mg/kg dose of caffeine enhanced lower-body strength but not upper-body strength, Waller et al. [22] reported improved maximal force production during a lower-body muscular endurance test with a 1.5 mg/kg dose. These findings indicate that intake below the recommended dose of 3 mg/kg can still be effective, particularly for lower-body exercises making it a viable option for individuals seeking ergogenic effects without higher intake levels. Meanwhile, for higher caffeine doses within the recommended range, performance benefits can also be observed. Karayigit et al. [38] compared the effects of 3 mg/kg and 6 mg/kg doses on lower-body muscular endurance and found similar performance-enhancing effects without a significant difference between them. This indicates that a moderate dose of 3 mg/kg would be sufficient for performance improvements, reducing the need for higher doses in some cases. Filip-Stachnik et al. [15] also reported a dose-response relationship in resistance-trained women, where a 3 mg/kg dose increased one-repetition maximum (1RM) bench press strength by 3.5%, while a 6 mg/kg dose improved it by 6.9%. Additionally, the 6 mg/kg dose significantly increased time under tension (TUT) by 17.6%, highlighting its benefits for sustaining muscle contractions during strength-endurance tasks [15]. Positive dose-response effects of caffeine are further highlighted by Grgic, Sabol, et al. [37], demonstrating that caffeine doses of 2, 4, and 6 mg/kg progressively improved upper-body strength, with improvements of +1.6 kg at 4 mg/kg and +2.1 kg at 6 mg/kg. This shows that while moderate doses are effective, higher doses may provide greater benefits, particularly for athletes aiming to optimize maximal strength or sustain muscle contractions for extended durations. This concludes that the effects of caffeine on performance are influenced by dosage, with benefits observed at both low and high doses. Due to the dose-response effects of caffeine, moderate doses of 3 mg/kg may suffice for significant performance improvements, but increasing the dose to 6 mg/kg can provide additional advantages, particularly in maximal strength tasks. Therefore, individualization should be considered when using caffeine as an ergogenic aid, due to the possibility of varying responses in different individuals.

Another important factor to consider when using caffeine as an ergogenic aid is the timing of caffeine ingestion. It is generally known that caffeine has an ergogenic effect on exercise when consumed before exercise [11]. However, the optimal timing of caffeine is not a one-size-fits-all recommendation, as different factors can affect its reaction. The most common timing for caffeine ingestion is about 30 to 60 minutes before exercise, frequently used across the studies [15]. This time frame is suggested to allow peak plasma caffeine levels to coincide with the start of activity [25]. Many studies use a 60-minute pre-exercise timing for ingestion as it aligns with recommendations in sports nutrition guidelines that suggest using caffeine one hour before exercise, to allow for sufficient absorption and onset of ergogenic effects [9].

However, optimal timing can vary due to individual factors such as caffeine metabolism and genetic differences. For example, the study by Guntoro Aji et al. [34] reported that fast metabolizers benefit from consuming caffeine about one hour before exercise, but slow metabolizers saw a greater improvement when caffeine was consumed two hours before exercise. This suggests that slow metabolizers may benefit from a longer pre-exercise timing window to allow for a sufficient accumulation of caffeine metabolites, for greater improvements [34]. This shows how optimal ingestion of caffeine varies across individuals due to reasons such as metabolic differences and genetic variations, affecting the ergogenic effects of caffeine.

Several studies have also explored the possibility of influence of habitual caffeine intake on its ergogenic effects. Regular consumption may attenuate caffeine's performance-enhancing benefits, due to the upregulation of adenosine receptors that diminishes caffeine's ability to block these receptors and consequently reducing its overall effect on the body [15]. However, other studies have found no significant impact of habitual caffeine consumption on the acute performance benefits of caffeine. For instance, Grgic & Mikulic et al. [28] reported no significant correlation between habitual caffeine intake (low vs. moderate-to-high users) and exercise performance outcomes. Similarly, Morales et al. [9] demonstrated that cyclists who consumed 6 mg/kg of caffeine for four consecutive days, despite being moderate-to-high caffeine consumers, did not develop tolerance to caffeine's ergogenic effects. Instead, acute intake continued to enhance their physiological, metabolic, and performance parameters [9]. These findings suggest that while habitual caffeine use may theoretically reduce its ergogenic effects, the evidence remains inconclusive, with current studies indicating that regular caffeine consumers still experience performance benefits despite acute caffeine ingestion.

General discussion

The studies above have shown that the ergogenic potential of caffeine ingestion is established to improve various aspects of exercise performance, such as endurance performance and in muscular strength. However, certain aspects can be considered as future directions about the research of caffeine as an ergogenic aid.

Although caffeine has been known to be widely used to enhance performance across various forms of exercise, its repeatable effects remain uncertain [1]. A study found that while caffeine can enhance muscular strength, power, and strength endurance, these effects are not consistently repeatable across trials [39]. This suggests that individuals may not experience the same performance-enhancing benefits each time caffeine is consumed. Hence there might still be certain contributing factors that are not yet factored in that could contribute to the variability in results, for example, mood, sleep, diet and lifestyle differences that may influence the body's response to caffeine.

Next, combination use of caffeine with other ergogenic aids also presents a possibility for enhancing performance. Athletes and individuals aiming to improve performance are highly likely to consume additional vitamins, supplements for bone and muscle health, and stimulants to further optimize muscle performance and recovery. Thus, understanding whether the combined use of such supplements enhances or diminishes caffeine's ergogenic potential would allow better personalisation and usage of ergogenic aids. Studies by Yun et al. [40] and Liu et al. [24] have highlighted the potential benefits of pairing caffeine with Rhodiola rosea, an adaptogen known for its performance-enhancing properties. Their research demonstrated a synergistic effect when caffeine was combined with Rhodiola rosea, leading to greater improvements in performance metrics compared to caffeine alone [24, 40]. These findings show that further research into the interactions between caffeine and other supplements could be further explored, as exploring possible combinations could unlock new strategies for maximizing performance benefits while ensuring safety and efficacy. Hence this is an area of research that holds significant potential for those seeking tailored approaches for ergogenic supplementation.

All the studies in this meta-analysis have documented caffeine ingestion from different sources, some of which are caffeine capsules, caffeinated coffee, and caffeine chewing gums. While these forms are commonly used in research to standardize caffeine administration, they may not fully reflect the diverse sources from which individuals may consume caffeine in real-world settings. Teas, cola beverages, and dark chocolate are popular examples of products containing caffeine, and they contribute significantly to daily caffeine intake for many people. This variability in caffeine sources introduces an additional layer of complexity when examining its ergogenic effects, as additional factors such as sugars present in these alternative sources could influence both the magnitude and the type of performance benefits. For instance, sugar present in cola beverages may interact with caffeine, potentially enhancing or attenuating its ergogenic effects. Furthermore, the method of caffeine delivery might influence individual responses. For example, caffeine from chewing gum is absorbed rapidly through the buccal mucosa that leads to quicker onset of effects, whereas caffeine in beverages or solid foods might have a longer absorption time [7]. Hence these differences that may contribute to the magnitude of the ergogenic effect of caffeine on individuals poses a potential factor that may be considered for future directions. Along with caffeine-containing products becoming more diverse, further research would be needed to evaluate the ergogenic potential of such alternative sources. This could provide valuable insights into whether these sources deliver comparable performance-enhancing benefits and allow for more practical caffeine supplementation strategies to optimise endurance and physical performance.

Lastly, future research could focus on the long-term adaptations of caffeine intake on the body, to investigate how prolonged caffeine use influences performance over time. Over an extended period, the body may adapt to caffeine's effects, potentially diminishing its ergogenic benefits due to tolerance development [10]. Understanding these long-term adaptations would be valuable to guide users to use caffeine strategically, whilst managing the frequency of intake to maximize caffeine's ergogenic benefits while minimizing tolerance. Hence future research could align to address such gaps, allowing further refinement of caffeine supplementation strategies to support consistent performance improvements across individuals.

Conclusion

This systematic review highlights that caffeine is a well-established ergogenic aid with the ability to enhance both endurance and strength performance. endurance is improved through key parameters such as time to exhaustion (TTE), maximal fat oxidation (MFO), maximal oxygen uptake (VO_2max), workload at the second ventilatory threshold (VT2), and time trial performance, largely attributed to its role as an adenosine receptor antagonist. Strength performance is also enhanced by increasing maximal strength, power output, and muscular endurance through central nervous system stimulation and improved muscle contractility. However, the ergogenic effects of caffeine are influenced by individual variabilities that contribute to inconsistencies in performance outcomes, underscoring the importance of personalized nutrition strategies for optimizing caffeine supplementation. While the evidence supports caffeine's efficacy in enhancing physical performance, gaps remain in understanding its long-term adaptations and its interactions with other ergogenic aids. Future research should explore these aspects, as well as the impact of different caffeine sources and delivery methods, to provide a more comprehensive understanding of caffeine's ergogenic potential. In conclusion, caffeine remains a valuable ergogenic aid for athletes and recreationally active individuals. However, the effectiveness of caffeine supplementation is highly individualized. Therefore, personalized strategies considering genetic makeup, lifestyle factors, and exercise modality are recommended to optimize performance outcomes.

Supplementary Materials

Supplementary materials for this review can be downloaded from https://bit.ly/Caffeine_SR.

Conflict of interest

No conflict of interest to declare.

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