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How Does Caffeine Enhance Athletic Performance? A Literature Review of Its Effects, Mechanisms of Action, Safety, Side Effects, and Sport- and Sex-Based Differences

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ABSTRACT

Introduction: Caffeine is a methylxanthine compound naturally found in coffee beans, tea leaves, and cocoa. It is among the most widely consumed psychoactive substances worldwide. Its primary mechanism of action involves antagonism of adenosine receptors within the central nervous system, resulting in reduced perception of fatigue and enhanced alertness. Caffeine's effects on the peripheral nervous system include increased intracellular calcium release and inhibition of phosphodiesterase activity, thereby enhancing muscle contractility and promoting utilization of energy substrates [1]. The metabolic effects of caffeine encompass multiple biochemical pathways [8]. Although caffeine exerts a multifactorial effect on aerobic performance its use should be carefully considered in the context of potential adverse effects [12]. Evidence derived from studies conducted in diverse athletic populations suggests that caffeine supplementation may represent an effective strategy for optimizing performance while preserving long-term athlete health.

Aim of the study :The aim of this study is to systematically analyze available literature regarding the effects of caffeine, its mechanisms of action, safety profile, adverse effects, and variability in response according to sport discipline and sex.

Material and Methods: Review and analysis of randomized clinical trials and clinical trials from 2010 to 2025 available on PubMed and Google Scholar.

Conclusions: The findings indicate that caffeine may serve as an effective ergogenic aid across a wide range of sports disciplines, provided that it is administered within safe dosage ranges tailored to individual needs—taking into account the specific characteristics of the discipline, athlete-related factors and individual tolerance [2]. Furthermore, current evidence indicates comparable magnitude of benefits in both female and male athletes across various disciplines [5], highlighting the broad applicability of caffeine as an ergogenic aid.

Keywords: *caffeine supplementation, sex-based differences, safety of supplementation, athletic performance, strength and power, ergogenic effects*

INTRODUCTION

Mechanisms of action of caffeine

The effects of caffeine on the central nervous system (CNS) are primarily attributed to its role as an antagonist of adenosine receptors, particularly the A1 and A2A subtypes [2]. By binding to these receptors, caffeine inhibits the suppressive action of adenosine on neuronal activity, resulting in increased concentrations of neurotransmitters such as dopamine, norepinephrine, acetylcholine, serotonin, and glutamate [1]. Consequently, neuronal excitability is enhanced, which is often perceived by athletes as increased energy levels and improved concentration during performance.

The elevated release of dopamine and norepinephrine may increase the firing frequency of motor neurons, potentially enhancing force production [7]. This neurochemical milieu may also influence the perception of effort through the activation of dopaminergic pathways associated with motivation [2].

The modulation of pain perception represents another significant aspect of CNS stimulation. Adenosine receptors are involved in the processing of nociceptive stimuli; therefore, their inhibition by caffeine contributes to a reduced perception of pain [1]. This attenuation of discomfort may enable individuals to sustain longer or more intense training sessions before voluntarily terminating exercise due to fatigue or pain. However, this analgesic effect may have implications for recovery, particularly if it promotes exceeding normal training thresholds without adequate rest.

Beyond receptor antagonism, caffeine also inhibits phosphodiesterase enzymes in CNS tissues [7], leading to increased intracellular levels of cyclic adenosine monophosphate (cAMP). Elevated cAMP concentrations enhance signal transduction pathways that regulate metabolic activity and neuronal responsiveness. Furthermore, phosphodiesterase inhibition is associated with increased calcium release from the sarcoplasmic reticulum, thereby influencing synaptic transmission in motor neurons and contributing to CNS involvement in movement execution [1].

The metabolic effects of caffeine involve multiple biochemical pathways and may influence both substrate utilization during exercise and post-exercise nutrient metabolism. One of the primary mechanisms is its function as a non-selective inhibitor of phosphodiesterase enzymes, which reduces the degradation of cyclic adenosine monophosphate (cAMP) [8], [9]. Elevated cAMP levels stimulate hormone-sensitive lipase activity, thereby promoting lipolysis in adipose tissue. The release of free fatty acids (FFA) into circulation provides an alternative energy source, particularly during prolonged aerobic exercise, where glycogen conservation is advantageous.

In summary, the effects of caffeine involve a combination of receptor antagonism and broader physiological modulation, influencing neurotransmitter balance, pain perception, attentional processes, and motor unit activation. These interconnected mechanisms underpin the observed improvements in endurance performance, strength output in resistance exercise, and performance in sports requiring agility and rapid decision-making under conditions of physical exertion [2].

REVIEW OF LITERATURE

Differences in effects depending on type of sport

Caffeine in endurance sports

Endurance sports encompass activities in which the ability to sustain high-intensity effort over prolonged periods is a key determinant of competitive success and performance outcomes. Consequently, caffeine supplementation has attracted considerable scientific interest across various disciplines within this category, including swimming, running, and cycling [15].

Research findings indicate that professional cyclists who supplement with caffeine prior to stage races report maintaining higher riding intensity during later stages of competition, where fatigue would typically limit performance [2]. Similarly, soccer players demonstrate improved match performance following caffeine supplementation, covering greater distances at high speeds despite concurrently performing anaerobic sprints and skill-based actions [16].

In sports that require both aerobic support and intermittent high-intensity efforts—such as uphill segments during cycling stages or final accelerations in long-distance running—the ergogenic effects of caffeine appear particularly advantageous. In such contexts, caffeine’s capacity to enhance neuromuscular activation complements its role in sustaining aerobic endurance, resulting in cumulative benefits aligned with the demands of mixed-intensity performance [2].

Optimal utilization of caffeine supplementation therefore depends on its strategic integration, ensuring that enhanced performance coincides with critical moments of competition [17].

The form and timing of administration should be tailored to the specific sport and environmental conditions. In endurance events, the timing of caffeine ingestion relative to the onset and duration of competition represents a crucial factor [13].

Individual testing during training cycles is essential prior to incorporating caffeine into official routines of endurance athletes [3]. Furthermore, it should be noted that the effectiveness of caffeine is influenced by individual variability, including genetic differences in metabolism, physiological readiness (e.g., training status), environmental conditions, and the pharmacokinetics associated with the mode of administration [2], [12].

Caffeine in power based sport

In sports where short-duration, maximal efforts determine competitive outcomes, the effects of caffeine are primarily attributed to its ability to enhance neuromuscular activation, accelerate force development, and sustain high-intensity performance across repeated efforts. Such strength- and power-based sports include Olympic weightlifting, shot put, and short-distance sprinting. These disciplines differ fundamentally from endurance sports, as performance relies on the rapid recruitment of type II muscle fibers and the capacity to generate explosive power within a matter of seconds [4].

The ergogenic effects of caffeine are associated with more efficient motor unit recruitment, resulting from antagonism of adenosine receptors in both the central and peripheral nervous systems, combined with increased calcium release from the sarcoplasmic reticulum. This, in turn, enhances the rate of the actin–myosin cross-bridge cycle [9]. In practical terms, this is often reflected in greater jump height, faster sprint initiation, or increased barbell acceleration during the initial phase of a lift.

Evidence suggests that although the magnitude of caffeine's effect on maximal strength may be relatively modest, percentage improvements in muscular strength in the range of 2–7% can have a meaningful impact on rankings in strength-dominated sports [14]. Such small yet consistent benefits—for example, a slight increase in one-repetition maximum in exercises such as the bench press or squat—may ultimately determine medal positions.

It is also important to highlight the analgesic effects of caffeine, resulting from adenosine receptor blockade in the central nervous system. By increasing pain tolerance during maximal muscular contractions [9], caffeine may prolong the duration for which an athlete can sustain near-maximal force output without voluntarily terminating effort due to discomfort. In resistance training, this may translate into the ability to perform additional repetitions at a given load before technique deteriorates, thereby increasing total training volume within a session [6].

It should be noted that positive outcomes may be more pronounced in athletes who are well adapted to high-intensity training, where central nervous system stimulation can be more effectively utilized for additional motor unit recruitment during maximal efforts [3].

In summary, the role of caffeine becomes particularly significant in situations where outcomes are determined by minimal differences—characteristic of elite sport—where even marginal gains may decide podium placement or qualification status [2].

Sex Differences in the Effects of Caffeine

Studies examining whether the ergogenic effects of caffeine differ between sexes have produced mixed findings. Some controlled experiments indicate similar improvements in endurance, maximal strength, and cognitive function in both men and women following caffeine ingestion [8], whereas others report subtle differences [13].

The primary enzymatic pathway responsible for caffeine metabolism in the liver involves the cytochrome P450 1A2 (CYP1A2) enzyme, whose activity tends to be lower in women—particularly in those using oral contraceptives or during specific phases of the menstrual cycle. Reduced CYP1A2 activity may slow caffeine clearance, prolonging its presence in plasma and thereby potentially altering both the magnitude and duration of its ergogenic effects.

Moreover, fluctuations in estradiol levels may further influence this process, potentially increasing sensitivity to lower doses during phases of the cycle characterized by elevated hormone levels.

Psychophysiological aspects should also be considered. Some studies suggest that self-reported positive sensations following caffeine ingestion are more frequently observed in men [8]. These differences indicate that the psychological interpretation of caffeine's effects may vary between sexes and may, in turn, influence pacing strategies or perceived readiness for competition.

Despite these metabolic differences, studies examining plasma caffeine concentrations indicate generally similar absorption patterns in both sexes when standardized doses of approximately 3 mg/kg body mass are administered. This suggests that the benefits associated with central nervous system stimulation may be largely comparable between men and women. In endurance tests, such as rowing or time-to-exhaustion running trials, performance improvements are typically observed in both sexes following caffeine ingestion [8].

In summary, although the fundamental ergogenic mechanisms of caffeine are shared between sexes, certain physiological differences related to hormonal fluctuations and enzyme activity may influence optimal supplementation strategies. The current body of evidence highlights the need for further research involving female participants. Until then, individualized approaches to dosing and timing during training remain the most appropriate strategy to account for variability in individual responses [13].

Individual Variability in Caffeine Response

Interindividual variability in the physiological response to caffeine can, to a significant extent, be explained by genetic factors. Of particular importance are polymorphisms in the *CYP1A2* gene, which encodes the cytochrome P450 1A2 enzyme responsible for approximately 95% of caffeine metabolism [2]. The AA genotype is associated with faster metabolism due to higher enzymatic activity, whereas AC and CC genotypes metabolize caffeine more slowly.

Individuals with the AA genotype tend to exhibit more pronounced performance benefits following moderate doses of caffeine, as rapid metabolism leads to the formation of active metabolites that may exert additional ergogenic effects beyond those of caffeine itself [13]. In contrast, athletes with the CC genotype, characterized by slower caffeine metabolism, may experience prolonged vasoconstriction induced by unmetabolized caffeine, which could potentially impair endurance performance due to sustained reductions in peripheral blood flow.

Beyond these two primary genes, evidence suggests that polymorphisms in dopaminergic genes (e.g., *DRD2*, *COMT*), adrenergic receptor genes (*ADRA1A*, *ADRA2B*, *ADRB1–3*), and genes related to energy metabolism (e.g., *AMPD1*) may also contribute to individual differences in caffeine responsiveness. This genetic diversity reflects the multisystem nature of caffeine's mechanisms of action [8].

Additional complexity arises from environmental influences. Circadian rhythms affect muscular performance, with peak torque values typically observed in the evening and the lowest values in the morning [13].

The application of genotyping in the planning of sports supplementation presents logistical challenges, including cost and the current inability to definitively determine which genetic variants consistently modify ergogenic outcomes—particularly in sports where marginal differences determine success. Nevertheless, by integrating controlled observation with individualized approaches, it is possible to effectively harness the ergogenic potential of caffeine despite genetically determined variability [2], [8], [13].

Side Effects and Safety of Caffeine Supplementation

Caffeine consumption is associated with both beneficial and adverse effects. It can influence vascular tone, cardiac performance, and heart rhythm, ranging from transient increases in blood pressure following ingestion to potential long-term correlations [8]. Acute elevations in systolic and diastolic blood pressure are consistently observed after sudden caffeine intake, typically peaking within one hour [8]. These increases may be clinically significant in populations with pre-existing hypertension or endothelial dysfunction [9].

Additional stress arising from sympathetic stimulation during caffeine-assisted exercise may elevate the risk of heat-related illnesses in inadequately hydrated athletes, particularly if caffeinated beverages replace water intake [18]. Habitual caffeine consumption has also been correlated with increased arterial stiffness, a recognized predictor of cardiovascular disease progression. Moreover, the analgesic effects of caffeine, resulting from its central nervous system activity, may mask early warning signals of potentially hazardous cardiac strain during prolonged exercise [2], [10].

Sleep disturbances represent one of the most consistently documented adverse effects of caffeine ingestion. The very neurochemical mechanisms responsible for caffeine's ergogenic and cognitive benefits directly interfere with processes regulating sleep onset, depth, and continuity [2]. The magnitude of these disruptions appears dose-dependent and is further influenced by the timing of ingestion relative to habitual sleep patterns; late afternoon or evening consumption generally produces more pronounced disturbances compared to morning intake [3]. Studies report an average reduction in total sleep duration of approximately 30 minutes on days when caffeine is consumed. Even minor deficits may accumulate over time, potentially impacting recovery.

Gastrointestinal discomfort is a relatively common adverse effect associated with caffeine intake. Symptoms can range from mild transient discomfort, such as stomach upset or acid reflux, to more severe manifestations, including nausea, diarrhea, or cramping, which can directly impair athletic performance [19]. These effects are primarily due to caffeine-induced stimulation of gastric acid and gastrin secretion, which may exacerbate reflux or gastric mucosal irritation, and to increased intestinal motility, which at high doses can produce unwanted effects during competition [20]. The form of caffeine administration, interactions with other supplements, and environmental conditions can modulate the likelihood and severity of gastrointestinal symptoms.

In summary, careful consideration of dose, form, and timing of caffeine ingestion, coupled with testing under training conditions, is essential to minimize risk while maintaining ergogenic benefits.

CONCLUSIONS

Caffeine has a wide range of performance-enhancing effects across different types of physical activity. It works by stimulating the central nervous system, changing metabolism, and improving neuromuscular function, all of which can help athletes perform better [2]. During long aerobic sessions, caffeine can make exercise feel easier, allowing athletes to maintain higher intensity with less perceived fatigue. In strength- and power-based sports, caffeine can increase maximal force and movement speed.

How well caffeine works depends on both its physiological effects and the specific demands of the sport. There are sex-related differences—for example, some women metabolize caffeine more slowly—so timing and dosage may need to be adjusted, and more research with female athletes is needed. For most healthy people, moderate caffeine doses are safe for the heart and blood pressure, though those not used to caffeine may see larger increases. Sleep disturbances and stomach issues can become more noticeable with higher doses, highlighting the importance of careful timing and testing.

Regular caffeine use can lead to tolerance, which may reduce its acute effects. Genetic differences, especially in the *CYP1A2* gene, also explain why some people respond differently.

To get the most benefit, athletes should consider dose, timing, form of intake, and individual factors like sex, genetics, habitual caffeine use, and environmental conditions. Testing caffeine during training helps find personal response patterns and tolerance levels, so performance improves without affecting technique or recovery. Staying hydrated is important, especially in hot conditions, to counteract caffeine's mild diuretic effect and keep the cardiovascular system stable [21]. Psychological factors, such as expectations, also play a role, influencing pacing and tactical decisions.

By tailoring caffeine use to these factors, athletes can improve endurance, strength, power, and even cognitive performance. This approach helps maintain a competitive edge while protecting health and long-term performance by using caffeine thoughtfully and individually [2], [3], [5].

Disclosure

Author's contribution

Conceptualization, M. Pacanowska-Trawnicka; methodology, M. Mrozek and M. Blecharczyk; software, A.Jakimowicz; check, A. Zielińska and Z. Kamińska; formal analysis, A. Jakimowicz and I. Zydlewski; investigation, A. Malcher ; resources, I. Zydlewski; data curation, M. Mrozek and A.Zielińska; writing - rough preparation, Z. Kamińska; writing - review and editing, A. Malcher; visualization, M. Mrozek; supervision, M. Pacanowska-Trawnicka; project administration, M. Pacanowska-Trawnicka;

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The authors deny any conflict of interest.

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