NutritionX

# The Nutrition X—CHANGE

08

## CAFFEINE AND SPORTS PERFORMANCE

A detailed look at the effect of caffeine intake on athletic performance

Dr. Neil Clarke

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## Practical Implications

+ Caffeine ingestion can be ergogenic for endurance, high-intensity and resistance exercise, as well as team sports. The beneficial effect is generally independent of training status, habitual caffeine intake, and sex.

+ The ingestion of caffeine at doses of between 3 and 6 mg·kg$^{-1}$ body mass appears to offer the most ergogenic benefit. However, when starting to use caffeine it is prudent to begin with a lower dose (~1.5 to 3 mg·kg$^{-1}$ body mass) in order to minimise the chances of side effects. Furthermore, higher doses (>6 mg·kg$^{-1}$ body mass) do not appear to offer any additional performance benefits, and may increase the risk of side effects.

+ Many so-called 'energy drinks' contain an amount of caffeine of around 100-250 mg, which for an 80 kg athlete is ~1.5-3 mg·kg$^{-1}$ body mass. Low doses of caffeine do offer a performance benefit, although it is not clear if this performance benefit is greater than, or even equal to, that offered by caffeine doses between 3-6 mg·kg$^{-1}$ body mass.

+ The response to caffeine ingestion is individual; those wishing to use caffeine should trial it in training or 'friendly' fixtures first before moving to actual competitions, in order to minimise any adverse effects.

+ Caffeine is traditionally administered in capsules or tablets, but, coffee, sports and energy drinks, gum, gels, bars and dissolvable mouth strips have all been demonstrated to improve performance. However, mouth rinsing with caffeine and aerosols appears less likely to improve performance.

## Background

Although it has no nutritional value, caffeine (1,3,7-trimethylxanthine) is consumed daily by approximately 80% of the world's population (Ogawa and Ueki, 2007). In chemical terms, caffeine is a pure alkaloid, which means it is a basic and organic plant-derived substance, and is an odourless white powder soluble in both water and lipids, and characterized by a bitter taste (Guest et al., 2021). Typically, caffeine is ingested most frequently in the form of a beverage such as coffee, soft drinks and tea, although the consumption of many functional beverages, such as energy drinks, has increased during the past two decades (Bailey et al., 2014). It is important to recognise that the caffeine content in foods and drinks varies considerably between products.

Caffeine was added to the list of banned substances by the International Olympic Committee (IOC) in 1984 and the World Anti-Doping Agency (WADA) in 2000. The IOC and WADA subsequently removed the classification of caffeine as a "controlled" substance in 2004. Having said that, caffeine is still monitored by WADA, and athletes are encouraged to maintain a urine caffeine concentration below a limit of 12 μg·ml$^{-1}$ which corresponds to 10 mg·kg$^{-1}$ body mass of caffeine ingested over several hours. However, it is important to recognise that ~10 mg·kg$^{-1}$ body mass is significantly higher than the amounts reported to enhance performance (Guest et al., 2021), and raises the possibility of side effects (Burke, 2008). Since 2004 and the removal from the WADA list of banned substances, caffeine has become one of the most researched nutritional ergogenic aids. Consequently, caffeine is frequently taken by professional and amateur sports people in an attempt to facilitate improved performance during a wide range of activities such as intermittent exercise (e.g. football and racket sports), endurance exercise (e.g. running and cycling) and resistance exercise (e.g. weight lifting). In fact, recent data suggests that 76% of elite athletes ingest caffeine prior to competition (Aguilar-Navarro et al., 2019).

## Blood caffeine concentration

Caffeine is rapidly absorbed from the gastrointestinal tract, mainly from the small intestine but also in the stomach, and diffuses rapidly in other tissues. Following the ingestions of caffeine capsules, salivary caffeine concentration peaks after around 60 minutes (Liguori et al., 1997) and in plasma after about 1 hour (Kamimori et al., 2002). However, compared to caffeine capsules, caffeine chewing gums may be absorbed more quickly (Kamimori et al., 2002), and in fact, Liguori et al. (1997) reported that peak salivary caffeine concentration was faster and higher following coffee ingestion compared with a caffeine capsule. Figure 1 illustrates the changes in plasma caffeine concentrations over time with varying forms of caffeine. Please note that peak concentrations occur around 30-min after chewing gum, and around 60-min when ingested.

Additionally, caffeine ingestion increases plasma caffeine concentration in a dose-response manner (Figure 2), whereby high doses increase the possibility of side effects (Burke, 2008). Caffeine has a relatively long half-life of between 2.5 and 10 hours in adults (Magkos and Kavouras, 2005), although there is genetic variability in these times. Therefore, care should be taken when considering the timing of caffeine ingestion due to the potential negative effects on sleep.

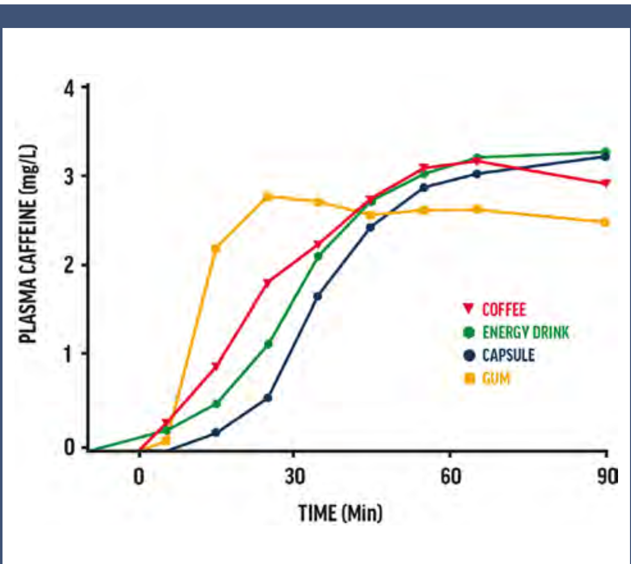


**Figure 1. Plasma caffeine concentration following ingestion of caffeine gum, caffeine capsules, an energy drink, and coffee, with each providing 200 mg of caffeine. Data is collated from (Liguori et al., 1997), (Kamimori et al., 2002) and (White et al., 2016)**

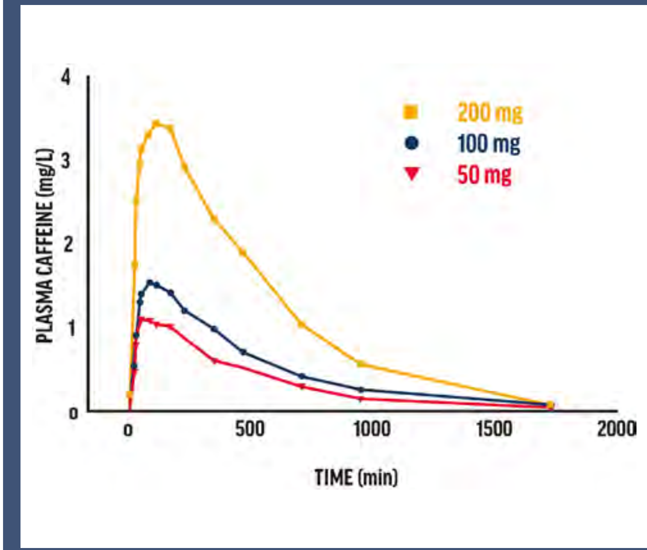


**Figure 2. Time course of plasma caffeine concentration following a 50-, 100- or 200-mg dose of caffeine delivered as a capsule to healthy male volunteers (Kamimori et al., 2002).**

## Mechanisms

The mechanisms by which caffeine exhibits an ergogenic effect are multifactorial in so far as caffeine is purported to affect brain (central factors) as well as muscle and adipose tissue (peripheral factors). Figure 3 is a schema outlining how caffeine may affect these tissues. For example, adenosine antagonism is a most probable mechanism with regard to central factors (McLellan et al., 2016), whereas other proposed performance-related effects such as enhanced calcium release from the sarcoplasmic reticulum (Rousseau et al., 1988) and improved skeletal muscle contractility (Williams, 1991) are obviously muscle-related factors. In addition, caffeine is proposed to stimulate fatty acid release from adipose tissue – either via enhanced adrenalin secretion or directly promoting activation of lipolysis. However, since caffeine interacts with many tissues, it is difficult to independently investigate its effects on the central and peripheral nervous systems, and metabolism (Spriet, 2014).

One of the most likely effects of caffeine is via its effect on adenosine. Adenosine, under normal conditions, promotes sleep and suppresses arousal. Adenosine acts upon $A^1$ and $A^2$ receptors, inhibiting the neuronal release of acetylcholine, noradrenaline (norepinephrine), dopamine, gamma-aminobutyric acid, and serotonin, which consequently has been shown to contribute to a sedative effect (Benowitz, 1990). As caffeine is similar in structure to adenosine (Kalmar, 2005), it easily crosses the blood brain

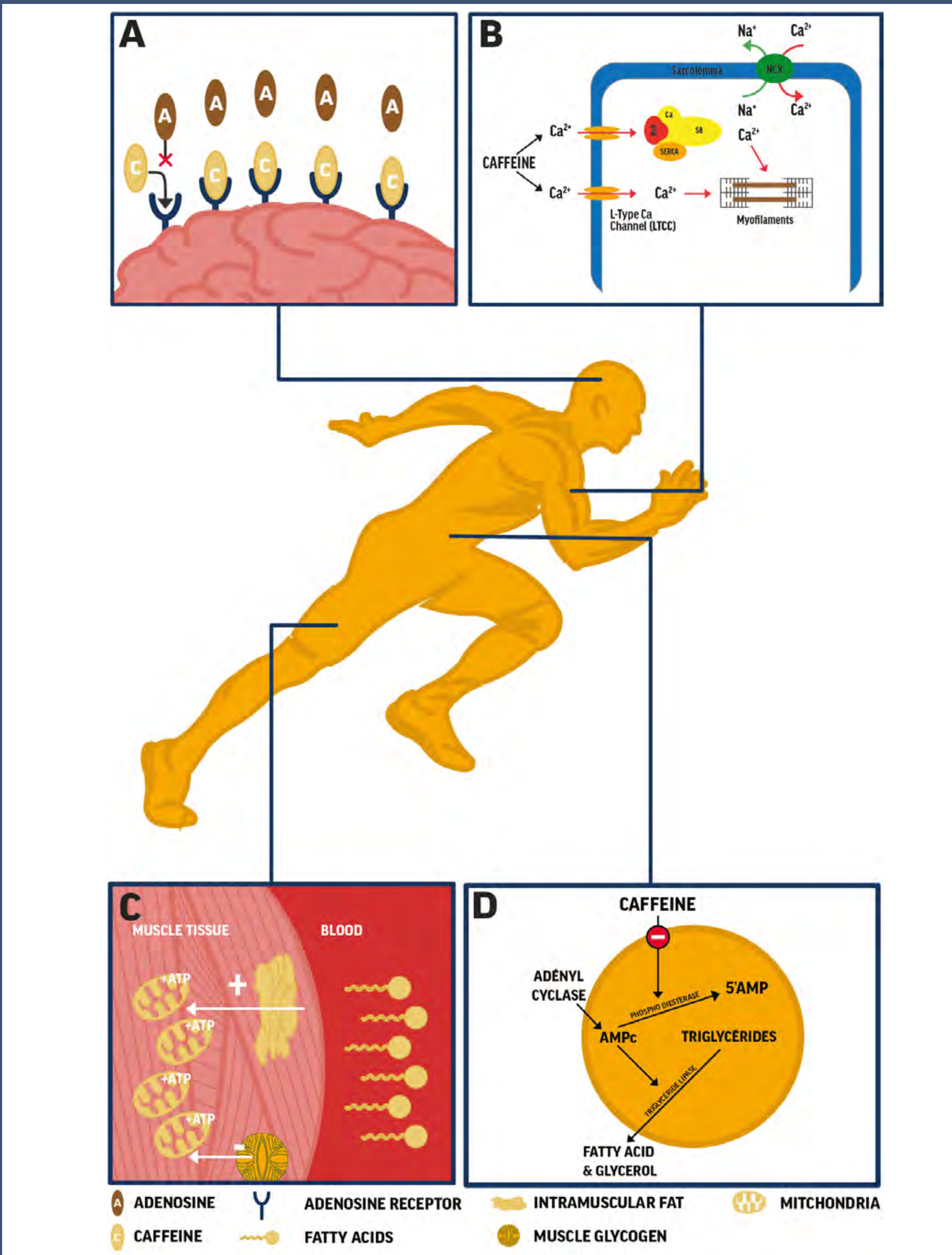


**Figure 3. Likely mechanisms of action of caffeine to increases in training capacities. (A) Antagonistic action of caffeine and its secondary metabolites to adenosine at its receptors in the Central Nervous System (CNS), increasing alertness and decreasing perceived exertion in exercise. (B) Increased release of calcium ions by a neuromuscular stimulus, enhancing contraction power in muscle fibres. (C) Effect of preserving muscle glycogen from a greater distribution of fatty acids in the bloodstream and energy use. (D) Promotion of adipose tissue lipolysis and greater release of fatty acids into the blood.**

barrier where it is distributed into intracellular fluid (Arnaud, 1987). Caffeine then facilitates central effects by antagonising adenosine receptors (Ribeiro and Sebastião, 2010) found throughout the body (Benowitz, 1990). Caffeine non-selectively blocks both adenosine receptors and competitively inhibits the action of adenosine, leading to an increase in neurotransmitter release, enhanced motor unit firing rates, pain suppression, reduced fatigue and improved neuromuscular performance (Davis and Green, 2009, Graham, 2001). Therefore, adenosine receptor antagonism is the leading hypothesis as to how caffeine could have an ergogenic effect on anaerobic exercise performance (Davis and Green, 2009) (Figure 3A).

The preservation of muscle glycogen through the inhibition of phosphodiesterase (PDE) has also been proposed as one of the mechanisms by which caffeine can enhance exercise performance (Graham and Spriet, 1991). Figure 3D illustrates the effect of caffeine on preventing breakdown of c-AMP by inhibiting PDE (mainly in adipocytes). The elevation of c-AMP in the cell promotes lipolysis and hence greater production of fatty acids (FFA). The FFA is released into blood and then transported to muscle to be used as an energy source. The net effect is possibility of reduced reliance on muscle carbohydrate (CHO) use.

Caffeine is also purported to augment the release of adrenaline. Adrenaline promotes lipolysis in both adipocytes and in muscle cells mediated via increasing c-AMP production. In effect the end result is similar to that of inhibiting PDE. The observed adrenaline-induced enhanced FFA availability (Figure 3C) and oxidation after caffeine ingestion may result in subsequent glycogen sparing (Costill et al., 1978). However, although the proposals regarding increased availability of fatty acids and thereby reduced reliance on the limited muscle glycogen stores have merit, neither of these suggestions can explain the improved performance during short duration high-intensity exercise, when muscle glycogen availability is unlikely to be a limiting factor.

It has also been suggested that caffeine may increase force production by enhancing neuromuscular transmission (Figure 3B) and improving the ability to achieve maximal muscle activation (Williams, 1991). The proposal is that caffeine may enrich the sodium-potassium pump within skeletal muscle and enhance excitation-contraction coupling (Davis and Green, 2009), which aids improvements in intense bouts of physical performance (Mohr et al., 2011). Mohr et al. (2011) reported that caffeine lowered muscle interstitial potassium during intense exercise and thus the performance-enhancing effects during intense intermittent exercise may be associated with an improved interstitial potassium handling in the exercising muscles. Caffeine has also been shown to cause an increase in calcium mobilization from the sarcoplasmic reticulum in isolated muscle fibres (Rosser et al., 2009), which could result in improved muscle speed and strength. However, the dose of caffeine required to mobilize intracellular calcium is 500 times higher than that required to block adenosine receptors (Garrett and Griffiths, 1997). Therefore, although a strong argument can be made for the effects of caffeine on mobilizing calcium in vitro, in vivo it appears the physiological dose required to do this could be toxic (Davis and Green, 2009).

Another possible mechanism through which caffeine may improve performance is by increasing the secretion of β-endorphins (Laurent et al., 2000), which may, at least partially, explain the mechanism by which caffeine attenuates the pain sensation (Gliottoni and Motl, 2008) and rating of perceived exertion (Doherty and Smith, 2004) during exercise. Any factor which decreases the perceptions of effort is likely to improve performance. In addition, factors such as improved reaction time, cognition, and mood (Ali et al., 2016) are also likely to have a positive influence on performance. It should be pointed out that these factors are 'central' and so the effect of caffeine on adenosine is also highly probable. Thus, it is possible that a combination of these factors may be responsible for the increase in exercise performance after caffeine ingestion.

## Caffeine and Performance

Caffeine ingestion is well-established as an ergogenic aid for endurance (Ahrens et al., 2007), intermittent (Mohr et al., 2011), and resistance exercise (Richardson and Clarke, 2016). It may also be ergogenic for cognitive function, including attention and vigilance. In addition, caffeine can improve cognitive and physical performance in some individuals under conditions of sleep deprivation (Cook et al., 2011).

While sporting performance is more than just a physiological construct, many of the interventions that are researched tend to be physiological. The majority of the research on caffeine to date typically focuses on the ingestion of 3 to 8 mg·kg$^{-1}$ body mass of anhydrous caffeine, and uses predominantly men. Whilst it does not appear that the sex of the individual is likely to alter their metabolism of caffeine (Graham, 2001), and thus the ergogenic potential, there is a lack of research examining the ergogenic effect of caffeine on women. However, Skinner et al. (2019) recently reported that caffeine ingestion improved the time taken to complete a set amount of work (75% of peak sustainable power output) in men (5%) and women (4%) by similar magnitudes. Similarly, Clarke et al. (2019b) reported that ingesting coffee providing 3 mg·kg$^{-1}$ body mass of caffeine improved 5 km cycling time trial performance in men and women by approximately 9 seconds and 6 seconds compared with placebo and control respectively. Low doses of caffeine (<3 mg·kg$^{-1}$ body mass of caffeine,) are also ergogenic and are associated with few, if any, side effects, although this has been less well studied (Spriet, 2014). Larger caffeine doses (≥9 mg·kg$^{-1}$ body mass) do not appear to increase the performance benefit (Bruce et al., 2000) and are more likely to increase the risk of negative side effects, including nausea, anxiety, insomnia and restlessness (Burke, 2008).

## Caffeine and endurance activities

Studies investigating the effects of caffeine ingestion on endurance have primarily use two different protocols, time to exhaustion (in effect tests of capacity) or time trials (in effect test of performance). Cycling has been the most common form of exercise investigated, while running, Nordic skiing, rowing, triathlon and swimming have also been investigated and report positive effects of caffeine ingestion. A recent meta-analysis (Southward et al., 2018) reported that caffeine has a small but obvious improvement on endurance performance when taken in moderate doses (3 to 6 mg·kg$^{-1}$ body mass) as well as an increase in mean power output (3%) and time-trial completion time (2%). For example, the ingestion of 3 mg·kg−1 body mass of caffeine 90 minutes prior to an endurance cycle time trial improved performance by 4% in well-trained male cyclists. (Desbrow et al., 2012). It is also worth noting that in this study doubling the dose from 3 to 6 mg·kg−1 body mass did not offer any additional improvements in performance. Furthermore Skinner et al. (2019) reported that following the ingestion of 3 mg·kg$^{-1}$ body mass of caffeine, the magnitude of the performance enhancement during endurance exercise observed in women (4.3%) was similar to that of men (4.6%), suggesting that the current recommendations for caffeine intake are equally applicable to men and women. However, it is important to recognise that differences in the responses to caffeine ingestion were reported, with some studies suggesting no performance benefits of consuming caffeine, albeit in the heat (Cohen et al., 1996, Roelands et al., 2011).

Caffeine ingestion late in exercise has also been reported to be beneficial (Talanian and Spriet, 2016). The participants cycled for two hours followed by a time trial that lasted approximately 30 minutes. At 80 minutes of cycling, participants ingested either a low (1.5 mg·kg$^{-1}$ body mass) or moderate (3 mg·kg$^{-1}$ body mass) dose of caffeine. Both doses of caffeine improved the time trial performance compared with a placebo, with the moderate dose improving performance to a greater extent than the low dose. However, if employing this strategy, it is probably prudent to consume caffeine 40 to 60 minutes before the required time point e.g. a steep mountain.

## Caffeine and high intensity activities

The majority of research into caffeine as an ergonomic aid has focused on endurance exercise, although there is also evidence to suggest that caffeine positively affects short-term high-intensity performance (Graham, 2001). A number of studies report improvements in short-term high-intensity performance following caffeine ingestion (Bruce et al., 2000, Glaister et al., 2015, Wiles et al., 2006). For example, Jodra et al. (2020) reported that ingesting 6 mg·kg$^{-1}$ body mass of caffeine improved average power, peak power and the time needed to reach peak power during a Wingate test in elite and trained-recreational athletes. Similarly, Doherty et al. (2004) demonstrated that high-intensity cycling performance can be increased following moderate caffeine ingestion. The mean power output during the all-out effort was increased following the ingestion of 5 mg·kg$^{-1}$ body mass of caffeine compared with placebo (794 ± 164 W. 750 ± 163 W). Combined, these results suggest that high-intensity cycling performance can be increased following moderate caffeine ingestion. However, in contrast, Paton et al. (2001) reported that caffiene had no effect on repeated sprint performance and Greer et al. (1998) suggested that caffeine diminished exercise performance with no beneficial effect on peak power and a negative effect in the latter bouts. These observations may be due to the greater variability in performance typically observed in untrained participants. Therefore, overall, based on the data provided, particularly in trained individuals, caffeine supplementation appears to be beneficial for high-intensity exercise performance.

## Caffeine and strength activities

Although much of the data produced on anaerobic exercise is equivocal, there are several studies that have exhibited enhanced resistance exercise performance following ingestion of caffeine. Woolf et al. (2008) demonstrated that in competitive athletes, 5 $mg{\cdot}kg^{-1}$ body mass of caffeine increased the total weight lifted for a chest press exercise. Similarly, Beck et al. (2006) observed a significant improvement in bench press one-repetition maximum (1-RM) performance when supplementing with caffeine compared to a placebo. Interestingly, they observed no significant increases in leg extension 1-RM or total weight lifted for leg extensions and bench press repetitions. In addition, Richardson and Clarke (2016) reported that during resistance exercise, the total weight lifted during back squats was 22% higher following the ingestion of coffee, providing 5 $mg{\cdot}kg^{-1}$ body mass of caffeine than compared with a placebo. Following this trend, a recent meta-analysis reported significant ergogenic effects of caffeine ingestion on maximal muscle strength of upper body and muscle power (Grgic et al., 2018). Therefore, the ingestion of caffeine prior to resistance exercise appears to increase both maximal strength and muscular endurance and could be a useful pre-exercise intervention.

## Caffeine and team sports

In relation to team sports, Salinero et al. (2019) revealed that caffeine increased single and repeated jump, single and repeated sprint velocity, and reduced the time to complete agility tests. Furthermore, the ingestion of 2 to 6 $mg{\cdot}kg^{-1}$ body mass of caffeine has been reported to increase repeated sprint and jump performance (Gant et al., 2010), reactive agility (Duvnjak-Zaknich et al., 2011), jump height (Ellis et al., 2019) and passing accuracy (Foskett et al., 2009) during intermittent exercise protocols, replicating the physical demands of soccer. Finally, during team sport matches, caffeine has also been reported to increase total running distance, distance covered at sprint velocity, and the number of sprints (Salinero et al., 2019). Therefore, it can be concluded that the acute ingestion of a moderate dose of caffeine had a small but significant positive effect on several aspects related to physical performance in team sports.

## Cognitive performance

In addition to the well-established ergogenic effect of caffeine on physical performance, caffeine ingestion can also improve cognitive performance, especially in those who are sleep-deprived. For example, Cook et al. (2011) reported that caffeine doses of 1 and 5 $mg{\cdot}kg^{-1}$ body mass alleviated the decrements in performance during a repeated rugby passing skill in elite rugby players following sleep restriction. These benefits have also been explored in military personnel; for example, caffeine was administered to SEAL trainees after three days of sleep deprivation and produced improvements in visual vigilance, choice reaction time, repeated acquisition (a test of learning and memory), and reduced self-reported fatigue and sleepiness, with a caffeine dose of 200 mg appearing to be optimal (Lieberman et al., 2002) (Figure 4). In virtually all studies of capacity where caffeine has been employed there is an invariable attenuation of the RPE score when compared with placebo i.e. participants report that the work effort is perceived lighter / less with caffeine than placebo (Doherty and Smith, 2005). Spriet (2014) concluded that low doses of caffeine (approximately 200 mg) improved cognitive processes associated with exercise including vigilance, alertness, and mood. Finally, in

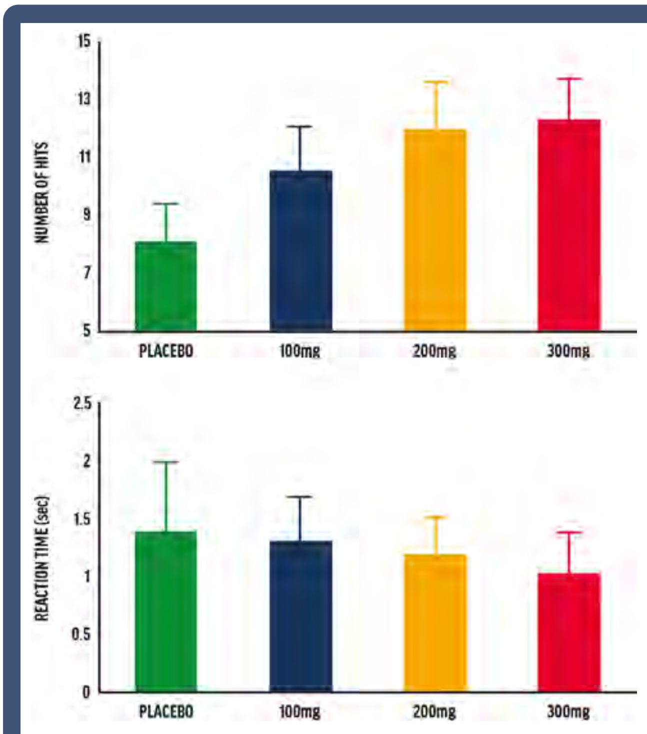


**Figure 4. The effect of caffeine dose on the number of correct hits (maximum of 20) and response time during a visual vigilance task presented during the 73rd hour of 'Hell Week'. (From Lieberman et al., 2002)**

sports such as tennis (Hornery et al., 2007) and golf (Mumford et al., 2016) that require concentration and skill, caffeine ingestion has been shown to increased hitting velocity and accuracy, and overall playing success, possibly due to improved reaction time and mental alertness. However, the important to remember that it is a low dose, as larger doses e.g. 300 mg have to reported to result in impaired accuracy, possibly due to increased muscle tremor and postural sway (Nygaard et al., 2019)

## Fat Oxidation

Studies in the late 1970s (Costill et al., 1978) reported that caffeine ingestion can increase the mobilisation of fatty acids, which when released from adipose tissue, is transported to the muscle and possibly used as fuel. However, it is not always the case that an elevation in blood fatty acids necessarily leads to an increase in fat oxidation, although some studies have reported an increase in fat oxidation with this elevation in fatty acids (Giles and Maclaren, 1984). A recent meta-analysis concluded that a pre-exercise intake of a moderate dose of caffeine may effectively increase fat utilization during submaximal aerobic exercise when performed after a fasting period (Collado-Mateo et al., 2020). For example, a pre-exercise intake of 3 $mg·kg^{-1}$ body mass of caffeine increased fat utilization from approximately 19 grams an hour with a placebo to 25 grams with caffeine during an hour of submaximal cycling (Ruiz-Moreno et al., 2020). Caffeine ingestion promotes lipolysis, due to a greater release of adrenaline and these fatty acids are then released into the blood and transported to muscle to be used as energy during subsequent exercise (Giles and Maclaren, 1984). So, it appears that caffeine may boost fat oxidation ('fat burning') when ingested before an exercise bout. However, a high carbohydrate meal consumed prior to caffeine ingestion reduces the serum caffeine concentration and delays the time to peak concentration (Skinner et al., 2013), which reduces the potential for fat oxidation (Giles and Maclaren, 1984). Furthermore, there are a few points to consider. It is important to note that the effects may have been increased due to this exercise being performed with no breakfast, when fat oxidation is naturally higher, and carbohydrate negates the efficacy of caffeine. Additionally, the ability of caffeine to enhance fat oxidation during exercise tends to be higher in sedentary or untrained individuals rather than trained and recreational athletes (Collado-Mateo et al., 2020). Finally, although caffeine ingestion might increase fat oxidation, it needs to be stated that weight loss will only occur when in a negative energy balance, i.e. the energy expended exceeds energy intake.

## Caffeine and Carbohydrate Ingestion

A number of studies suggest that combined caffeine and carbohydrate ingestion offers additive or synergistic performance benefits, or attenuate the effects of fatigue (Clarke and Duncan, 2016, Hulston and Jeukendrup, 2008, Roberts et al., 2010). For example, the co-ingestion of carbohydrate (40 $g·h^{-1}$) with caffeine (3 $mg·kg^{-1}$ body mass) compared to carbohydrate alone resulted in increased mean running speed, high-intensity running distance, and sprint performance in professional rugby league interchange players during simulated match play (Clarke et al., 2019a). One potential mechanism suggested for these benefits is faster intestinal absorption and subsequent increased exogenous carbohydrate oxidation rates during exercise following the ingestion of caffeine and carbohydrate compared with carbohydrate alone (Yeo et al., 2005). These effects may also be present post-exercise, with increased glycogen synthesis reported with caffeine and carbohydrate compared carbohydrate alone (Pedersen et al., 2008). However, other studies have reported similar exogenous carbohydrate oxidation rates during exercise (Hulston and Jeukendrup, 2008) and glycogen synthesis rates following exercise (Beelen et al., 2012) when carbohydrate was consumed with or without caffeine. In general, it appears that adding caffeine to carbohydrate is beneficial for performance, although the magnitude and nature of the benefit is yet to be fully elucidated. With regards to replenishing muscle glycogen, caffeine ingestion (8 $mg·kg^{-1}$ body mass) alongside carbohydrate (1 $g·kg^{-1}·h^{-1}$) has been reported to result in substantially higher rates of muscle glycogen storage over 4 h of recovery (Pedersen et al., 2008). However, Beelen et al. (2012) found no difference in muscle glycogen synthesis when caffeine (1.7 $mg·kg^{-1}.h^{-1}$) was added to large CHO feedings (1.2 $g·kg^{-1}·h^{-1}$) during a 6 h post-exercise recovery period. These findings suggest that a large dose of caffeine may be required to enhance muscle glycogen resynthesis and the question of practicality of using caffeine as a post-exercise refuelling aid. Therefore, the addition of caffeine may not be suitable if carbohydrate loading after evening (and possibly afternoon) competitions due to the potential to cause interruption to sleep.

## Alternative Forms of Caffeine

The traditional form of caffeine administration in research and athletic settings has been to ingest tablets or capsules with liquid. However, currently, there is growing evidence that caffeine administered in alternative forms, such as coffee (Clarke et al., 2018), and commercially available products such as chewing gums, bars, and gels can increase performance (Wickham and Spriet, 2018). Similarly, energy drinks have been reported to improve aerobic endurance and anaerobic performance on cycle ergometers, along with improvements in mental performance included choice reaction time, concentration and alertness (Alford et al., 2001). However, there is less compelling evidence for the use of aerosols or caffeine mouth rinses, although further research is warranted.

## Individual Variation

The responses to caffeine are often variable (Figure 5) and possibly affected by a number of factors such as training status, genotype and habitual caffeine use (Pickering and Grgic, 2019).

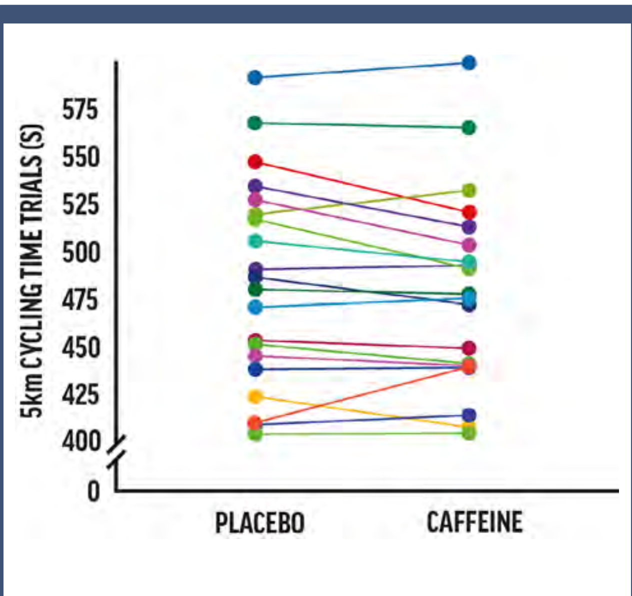


**Figure 5. Individual performance times during a 5 km time trial following the ingestion of 3 mg·kg$^{-1}$ body mass of caffeine or a placebo. These data highlight the individual responses to caffeine ingestion, and not everybody improves their performance following the ingestion of caffeine; 13 participants improved their performance with caffeine and 7 were slower.**

However, few investigations, for example Collomp et al. (1992) and O'Rourke et al. (2008), have included both trained and untrained subjects in their study design. Therefore, currently, it seems that trained and untrained individuals experience similar improvements in performance following caffeine ingestion; however, more research in this area is warranted (Guest et al., 2021). Two of the genes which are thought to have the largest impact on the ergogenicity of caffeine are CYP1A2 and ADORA2A (Southward et al., 2018). Guest et al. (2018) reported that caffeine improved endurance performance at a dose of 2 and 4 mg·kg$^{-1}$ body mass for fast metabolizers of caffeine who have the CYP1A2 AA genotype. In contrast, among the slow metabolizers, there was either no effect (AC genotype) or impaired performance (CC genotype) under the same caffeine conditions. Furthermore, the ADORA2A genotype has also been implicated in sleep quality and increases in sleep disturbance and individuals with the CC and TC genotypes appeared to confer greater sensitivity towards caffeine-induced sleep disturbance compared to the TT genotype (Rétey et al., 2007). The impact of these observations, alongside the performance benefits require further research.

There has been a long-standing paradigm that habitual caffeine intake may influence the ergogenicity of caffeine supplementation (Sökmen et al., 2008). Pickering and Kiely (2019) concluded that short-term pre-competition caffeine withdrawal appears to offer little benefit, and given the potential negative side effects, withdrawal strategies are not recommended. In addition, Irwin et al. (2011) concluded that acute caffeine supplementation positively effects exercise performance and provides an ergogenic benefit in regular caffeine users regardless of any withdrawal period. However, Clarke and Richardson (2021) demonstrated that the level of habitual caffeine ingestion was not associated with the magnitude of improvement in 5 km performance following the ingestion of coffee providing 3 mg·kg$^{-1}$ body mass of caffeine, a value below the habitual intake of the high-users. Similar findings have been reported by Grgic and Mikulic (2020) in that the acute effects of caffeine supplementation on resistance exercise, jumping, and Wingate performance were not affected by habitual caffeine intake and high users of caffeine do not appear to need more caffeine compared to low users to maintain performance (Dark et al., 2015). Therefore, the ingestion of caffeine at doses of 3 to 6 mg·kg$^{-1}$ body mass would appear to be beneficial for those with high and low habitual caffeine consumption.

## Side Effects

The side effects of caffeine ingestion can include gastrointestinal distress, increased ratings of nervousness and insomnia (Pallarés et al., 2013), all of which might limit its efficacy to enhance performance. The severity of side-effects associated with caffeine ingestion is dose dependent. Side-effects with caffeine seem to increase linearly with the dose ingested (Pallarés et al., 2013), so can be reduced by using smaller doses (Spriet, 2014). Caffeine definitely follows the saying “more is not always better”. Furthermore, regular caffeine users can suffer withdrawal symptoms, which can be associated with headaches, fatigue (Van Soeren and Graham, 1998), irritability, muscle pain, sleep disturbances, and nausea (Juliano and Griffiths, 2004), although tend to be temporary (Graham, 2001) and reversed with caffeine ingestion (James and Rogers, 2005). Nevertheless, such acute withdrawal symptoms, close to key competitions, may negatively affect athlete subjective confidence and well-being. In conclusion, due to the potential for side effects, it is important to practice with caffeine during a training session or friendly fixture, before using it for an important event.

## Conclusion

There are a number of considerations that need to be taken into account when deciding to use caffeine as an ergogenic aid (Figure 6). The ingestion of caffeine at doses of 3 to 6 $mg \cdot kg^{-1}$ body mass has been shown to enhance many aspects of exercise, including endurance, high-intensity exercise and team sports. Lower caffeine doses (≤3 $mg \cdot kg^{-1}$ body mass, ~200 mg) taken before exercise can also increase athletic performance, although these results can be more variable between individuals. Higher doses can result in additional side effects and do not confer additional performance benefits. Alternative sources of caffeine, such as coffee, caffeinated chewing gum, mouth rinses, and energy gels, have also been shown to improve performance. Studies report individual variation in the effectives of caffeine in improving performance. These differences may be associated with genetic variations and supplementation protocols, although training status and habitual caffeine ingestion appear less likely to be responsible. Finally, individuals should also be aware of the side-effects associated with caffeine ingestion, such as sleep disturbance and anxiety, and should practice using caffeine in training before ingesting prior to competition.

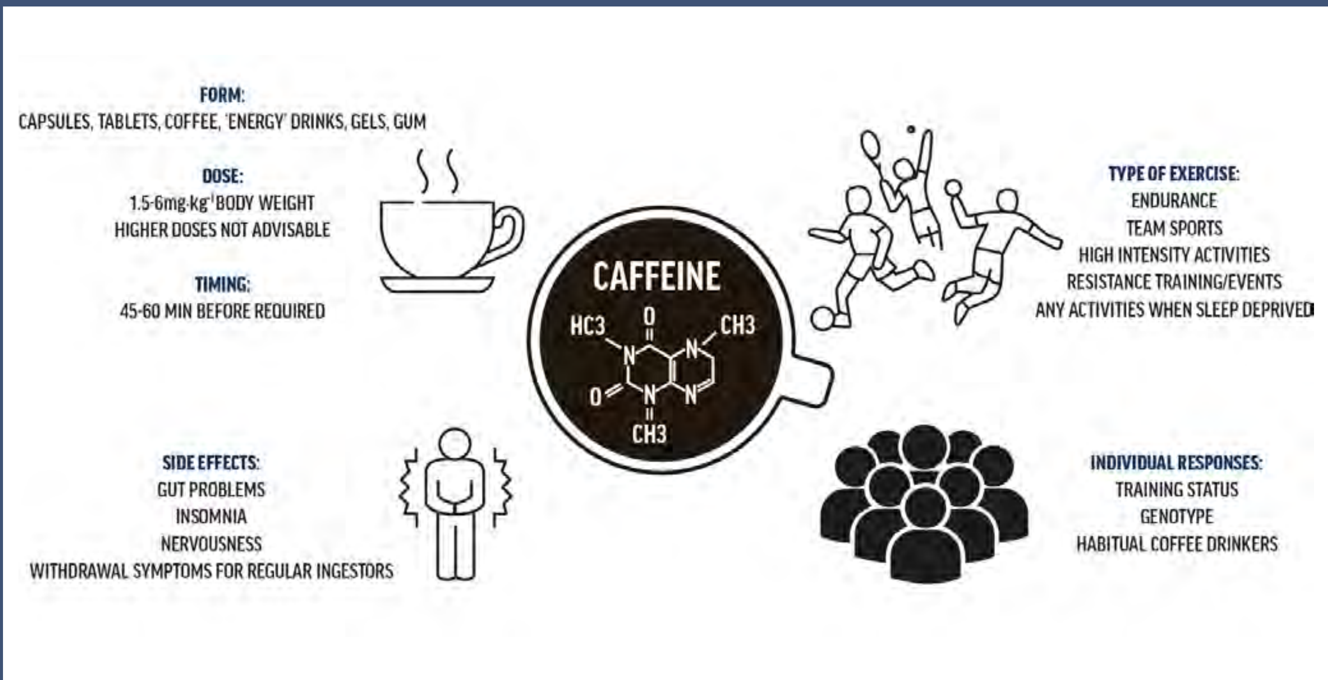


**Figure 6. Considerations when deciding to use caffeine as an ergogenic aid.**

# Author bio

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Neil is currently employed at Coventry University, where he is the MSc. Sports and Exercise Nutrition course director. Neil is also an accredited Fellow of the British Association of Sport and Exercise Sciences and holds Chartered Scientist status with the Science Council. He has 20 years' experience working with elite and recreational athletes, as well as commercial companies. His primary area of expertise and research is nutritional interventions and has co-authored over 50 peer-reviewed journal articles.

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