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REVIEW ARTICLE

Effect of caffeine on the cardiovascular system and performance: A systematic review

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Abstract

Caffeine is a compound found in the leaves, seeds and fruits of plants such as coffee and guarana. The aim of the systematic review was to determine the influence of caffeine on cardiorespiratory functions and physical performance. The method was the collection of relevant literature in the period from 2011-2022, and their analysis. The results clearly show the benefit and positive influence of caffeine on both investigated areas. The recommended consumption of caffeine should be higher than 75mg in order to expect positive changes and effects. Also, doses above 600mg should not be exceeded due to side effects, especially on the heart. It is necessary to consume caffeine for at least 45 minutes before the planned activity to ensure complete absorption. Caffeine is a very powerful supplement, it is only necessary to take care of the method and amount of dosage.

Keywords: Activity, blood pressure, caffeine, HR, training, VO_{2max}.

Introduction

Caffeine use is increasing worldwide. The main motives are mainly concentration and improvement of memory and improvement of physical performance. Caffeine affects the cardiovascular system, with its positive inotropic and chronotropic effects, and the central nervous system by stimulating locomotor activity and anxiogenic effects (Lavie et al., 2019). Caffeine abuse and dependence are becoming more common and can lead to caffeine intoxication, putting individuals at risk of premature and unnatural death. This review summarizes major findings regarding caffeine's mechanisms of action (focusing on adenosine antagonism, intracellular calcium mobilization, and phosphodiesterase inhibition), use, abuse, dependence, intoxication, and lethal effects. It also suggests that the concepts of toxic and lethal doses are relative, doses below the toxic and/or lethal range may play a causal role in intoxication or death (Cappelletti et al., 2015; Dos Santos et al., 2018).

Caffeine is one of the most widely used dietary supplements in the general population and is therefore one of the most researched dietary supplements. Research carried out in the form of a survey of the population of US citizens found that 85% of the population consumes at least one beverage a day that contains caffeine, i.e. an average daily value of caffeine of 165 mg, where coffee is the primary contributor to caffeine intake in all age groups (Mitchell et al., 2014).

Caffeine is both a nutrient and a supplement at the same time and can very easily be classified in the category of "highly effective supplements" (Guest et al., 2021) Considering the huge amount of different supplements both on the world market and on our

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market, the question is often asked which supplements or nutritional supplements are effective for their purpose. Vitamins and minerals are essential nutrients for our body and their deficit causes various health problems, so their effect is the prevention of various problems (Ford et al., 2019). The question of effectiveness is a frequent topic of various studies that deal with testing supplements and their effect on athletes. Those studies have long classified caffeine in the category of nutrients that have a positive, and easily measurable, effect on athletes and therefore sports results, and to the extent that caffeine was a prohibited substance by WADA (World Anti-Doping Agency) until 2004. Caffeine was then considered an illegal substance. A large number of supplements have no measurable positive effect on performance, further demonstrating how unique caffeine is (Deventer et al., 2011).

The action of caffeine has several functions: The most important one is the blocking of the binding of adenosine to receptors, which directly reduces our subjective feeling of fatigue because the binding of adenosine to its own receptors causes an increase in the feeling of fatigue (Bjelica et al., 2020). In this way, it has a direct effect on the central nervous system and that is why athletes use it to delay the feeling of fatigue and to be more concentrated; with more focus during a race, match or game (Aksović et al., 2020). The effect is noticeable in practically every individual and this is probably one of the main reasons why a large number of people consume coffee, black tea or products and supplements with added caffeine.

Diaz-Lara et al. (2016) prove the effectiveness of caffeine on sports performance in order to improve performance in elite Brazilian Jiu-jitsu athletes. In their experimental research, they used a dose of 3mg/kg of caffeine, which they compared with the performance when the participants consumed a placebo. With the aforementioned research, they proved the effectiveness of caffeine on the strength of the hand grip, on the height of the jump during the countermovement jump (CMJ), the result of the 1RM (one-repetition-maximum) performance, and on the mean strength value during the bench press exercise.

Grgic et al. (2019) investigated the difference and effects of three doses of caffeine (2, 4 and 6 mg/kg) on muscle strength and endurance. Strength was assessed through 1RM and endurance through the number of repetitions until immediate muscle failure with a load equal to 60% of 1RM. In their studies, they proved a correlation between the dose of caffeine and the effect on the strength of the upper limbs, that is, a significant improvement in performance with doses of 4 and 6mg/kg.

Therefore, the aim of the systematic review is to determine the effect of caffeine on cardiorespiratory functions and performance.

Methods

Research data for the purposes of this paper were collected through electronic databases, Google Scholar, PubMed, and ResearchGate. The search for papers was carried out for the period from December 2011 to January 2022. When researching databases, the following keywords were used: caffeine, activity, training, HR, and blood pressure. The found research titles, abstracts, and full texts were then read and analyzed.

In order for the research to be accepted for the final analysis, it had to meet three basic criteria: the first criterion refers to the issue of the influence of caffeine on physiological parameters, the second to the influence of caffeine on motor performance (abilities), and the third criterion is the implementation of the analysis of papers in the selected period.

Research that met the set criteria was then analyzed and presented based on the following parameters: reference (author's first letter and year of publication of the research), sample of participants, applied treatment and research results.

Results

Based on keywords, 164 studies were identified. The number of studies that were immediately excluded based on the title, duplicate papers, as well as papers that were excluded based on the period when they were published is 81, while 83 studies were included in the further analysis.

Through further analysis of 83 studies, 31 studies were excluded based on several criteria: abstracts, because they were systematic review studies, as well as inadequate information needed for our research. The remaining five studies met the set criteria, which are studies published in the period from 2011 to 2021 and focused on the influence of caffeine on the cardiovascular system, six studies in the period from 2015 to 2022 give an account of the influence of caffeine

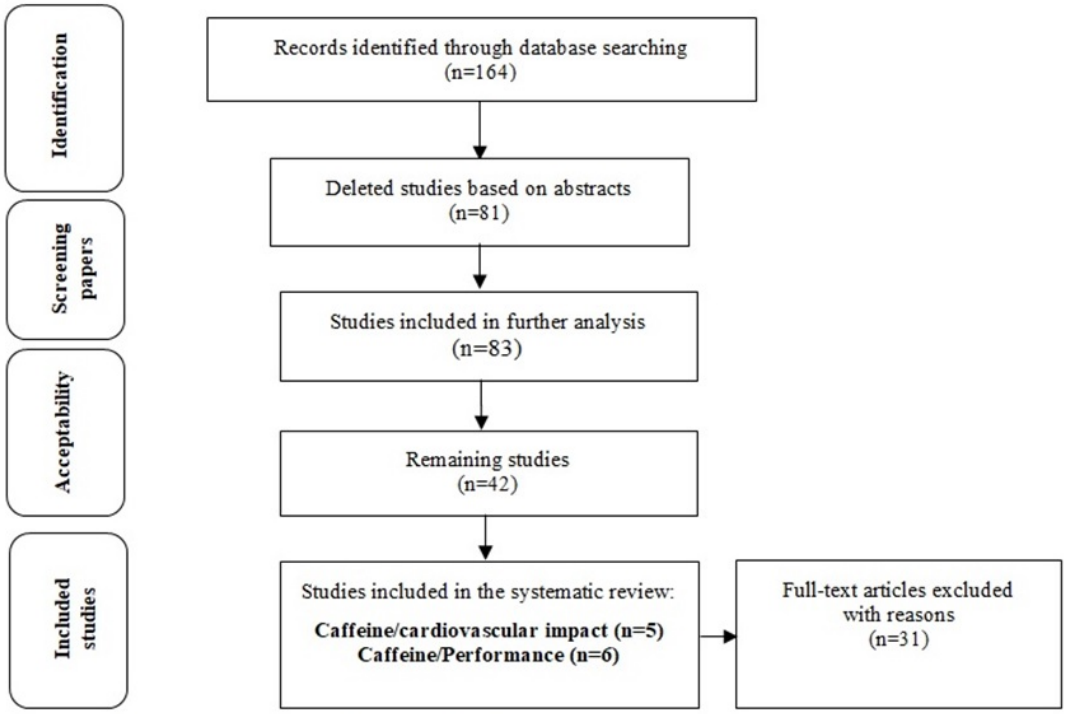

Figure 1. Flow chart diagram of the study selection.

on physical performance. The procedure of collection, analysis and elimination of found studies are shown in Figure 1.

Discussion

Effect of Caffeine on Cardiovascular Changes

Table 1 shows five studies. All research was of an experimental nature, i.e. they had a control and an experimental group. In three studies (Rezaimanesh et al., 2011; Norian et al., 2014; Sampiao-Jorge et al., 2021) the sample consisted of athletes, and in the remaining two studies recreational exercisers and students (Gonzaga et al., 2017; Malhas, 2018). The total number of participants included in the review was 136, of which 15 were female in the research (Malhas, 2018). Caffeine consumption most often ranged from 5-6mg/kg or in total from 300-498mg.

Analyzing all research in detail, it can be seen that in most research there was an increase in heart rate, systolic and diastolic pressure. If we analyze the study (Malhas, 2018) in more detail, we can see that the author believes that a higher caffeine intake of 400mg could cause side effects, while this is not the case in the study (Norian et al., 2014).

CAF intake is associated with a series of reversible and transient physiological effects in general, and cardiovascular effects in particular. This report attempts to understand where demarcations exist in caffeine intake and corresponding cardiovascular effects among different subpopulations. The available literature suggests that the cardiovascular effects experienced by caffeine consumers at levels up to 600mg/day are in most cases mild, transient, and reversible, with no lasting adverse effects. The point at which caffeine intake can cause damage to the cardiovascular system has not been partially identified, as data on the effects of daily intakes greater than 600mg are limited. However, the evidence reviewed in this review suggests that typical moderate caffeine intake is not associated with increased risks of overall cardiovascular disease; arrhythmia; heart failure; changes in blood pressure in regular coffee drinkers; or hypertension in baseline populations (Turnbull et al., 2017).

Energy drinks and other energy products have exploded in popularity in recent years; however, their use is not without risk. Caffeine is the main active ingredient in energy drinks, and excessive consumption can cause acute caffeine poisoning, resulting in tachycardia, vomiting, cardiac arrhythmias, seizures and death. The effects of chronic intake of high doses of caffeine in children and adolescents are unknown. Caffeine can raise blood pressure, disrupt adolescent sleep patterns, worsen psychiatric illness, cause physiological dependence, and increase the risk of subsequent dependence (Wolk et al., 2012). Caffeine is the most popular 'drug' in the world, and tea and coffee are a part of daily life. As a psychoactive stimulant,

there is potential concern about adverse cardiovascular creaking. Cardiovascular conditions, including hypertension, coronary artery disease, arrhythmias, and heart failure, affect billions of patients worldwide. Tea and coffee intake, especially in moderate doses, does not appear to be harmful and may even be beneficial in a number of cardiovascular conditions, including coronary artery disease, heart failure, and arrhythmias (Voskoboinik et al., 2019). The main objective of this review was to collect, present and analyze the available information, including the latest findings on the effects of caffeine on human health and the functioning of human body systems. In short, we can conclude, however, that caffeine has a multidirectional effect on various organs of the human body, and due to its antioxidant properties, it was, and still is, an interesting topic for research, including those aimed at developing new therapeutic strategies (Rodak et al., 2021).

Although the effects of excess caffeine have been widely studied, little information is available on potential interactions between other active ingredients in energy drinks and caffeine. One of the active ingredients that often mentioned as a candidate for caffeine interaction is beta-amino acid, taurine. Although taurine is considered a conditionally essential nutrient for humans and is thought to play a key role in several human diseases, clinical studies evaluating the effects of taurine are limited. However, based on this review of possible interactions between caffeine and taurine, we conclude that taurine should counteract several of the side effects of excess caffeine. In accordance with this conclusion, in March 2003, the European Union's Scientific Committee for Food published a report summarizing their research on the potential interactions of energy drink ingredients. At the cardiovascular level, they concluded that "if there are any interactions between caffeine and taurine, taurine could reduce the cardiovascular effects of caffeine." Although these interactions have yet to be further investigated in humans, the physiological functions of taurine appear to be inconsistent with adverse cardiovascular symptoms associated with excessive consumption of caffeine-taurine-containing beverages (Schaffer et al., 2014).

Table 1
Effect of caffeine on the cardiovascular system.

References	Population	Grouping	Treatment	Protocol	Results
Rezaimanesh et al., 2011	2 EG+CG M, - yo	Athletes n=45	EG1+EG2 5 mg/kg	60 min. before the activity 180 min. before the activity Monarch bike + Alstead	HR↑ SIS+DIA pressure ↑ Glucose ↑
Norian et al., 2014	EG+CG M, 23.6 yo	Soccer players n=30	Caffeine 6 mg/kg Approximately 498 mg	60 min. before the activity Different forms of sprints	$V0_2max$ ↑ HR ↑
Gonzaga et al., 2017	EG+CG M, 23.5 yo	Recreational people n=32	Caffeine 300 mg	Treadmill/Bruce protocol Activity duration 30 min.	DIA pressure ↓ SpO2~ HR~
Malhas, 2018	EG+CG F, 25.5 yo	Students n=15	Caffeine 400 mg	Bicycle ergometer Activity duration 15/30/60/90/120 min.	Pressure~ HR~ More caffeine= Nus appearance +
Sampaio-Jorge et al., 2021	EG+CG M, 34.1 yo	Cyclists n=14	Caffeine 6mg/kg x 4 days 474 mg/1896 mg	Caffeine 60 min. before the activity Time trial 16km	Cardio effect ↑ Vagus tone ↑

M: Males; F: Females; n: Number of participants; EG: Experimental group; CG: Control group; ↑: Statistically significant increase p<0.05, p<0.01; ↓: Statistically significant decrease p<0.05, p<0.01; SIS: Systolic pressure; DIA: Diastolic pressure; HR: Heart rate.

Effect of Caffeine on Sports Performance

Table 2 shows six studies. All research was of an experimental nature, ie. they had a control and an experimental group. In three studies (Lara et al., 2015; Abian et al., 2015; Del Coso et al., 2016) the sample consisted of athletes, and in the remaining three studies recreational exercisers, athletes and swimmers (Prins et al., 2016; Peveler, 2017; Yuet al., 2022). The total number of participants included in the review was 112 and all persons are male. Caffeine consumption most often ranged from 3-6mg/kg or in total from 163-240mg.

Analyzing all researches in detail, it can be seen that in most researches there was an increase in performance in the form of jumpiness, speed as well as an increase in intensity during the activity.

Regarding sports performance, caffeine improves general and muscular endurance, increases the mobilization of fat from adipose tissue and muscle cells and increased the number of engaged muscle fibers were noted. Also, it reduces the perception of fatigue and increases motor activity. In small doses (1-2mg/kg) it improves attention, visual information, reaction time and alertness. However, these positive effects are caused by caffeine only if applied up to a certain dose. Beyond that limit, there is no improvement, and negative ones can also occur, i.e. harmful consequences. When evaluating the ergogenic effect of caffeine on athletes, it is very important to determine the right experimental design. Namely, large inter-individual differences in the effect of caffeine in athletes are even more pronounced, and the habit of drinking coffee causes tolerance to the effect of caffeine. Thereby, there are several mechanisms of action of caffeine, some of which have not been fully or not investigated at all. If we add to this that there are different physical, psychomotor and psychological demands in sports, the problem becomes more complicated. Because of the above, the examination of the ergogenic effect of caffeine on athletes must take into account all these factors.

Table 2
Effect of caffeine on the sport performance.

References	Population	Grouping	Treatment	Protocol	Results
Lara et al., 2015	EG+CG M, 20.2 yo	Swimmers n=14	Caffeine 3 mg/kg Approximately 221 mg	60 min. before the activity Activity duration 45 s.	Performance ↑ Side Effects -
Abian et al., 2015	EG+CG M, 25.4 yo	Badminton n=16	Caffeine 3 mg/kg Approximately 215 mg	60 min. before the activity Activity duration 45 min.	Performance ↑ Jumps + Movement +
Del Coso et al., 2016	EG+CG M, 23.2 yo	Hockey players n=13	Caffeine 3 mg/kg Approximately 228 mg	60 min. before the activity Activity duration 50 min.	Performance ↑ Sprint + Intensity + Speed +
Prins et al., 2016	EG+CG M, 20.4 yo	Athletes recreationists n=18	Caffeine Approximately 160 mg	60 min. before the activity Activity duration 20 min.	Performance ↑ Running 5km +
Peveler et al., 2017	EG+CG M, 22.9 yo	Swimmers recreationists n=15	Caffeine x 2 80 mg 163 mg	60 min. before the activity Activity duration 15 min.	Performance~ Blood pressure +
Yu et al., 2022	EG x 3+CG M, 24.7 yo	Recreational people random selection n=36	Caffeine x 2 240 mg 237 mg	60 min. before the activity Activity duration 5, 10, 15 min. and after activities	Performance ↑ Heart recovery ↓ HR ↑ Blood pressure~

M: Males; F: Females; n: Number of participants; EG: Experimental group; CG: Control group; ↑: Statistically significant increase p<0.05, p<0.01; ↓: Statistically significant decrease p<0.05, p<0.01; SIS: Systolic pressure; DIA: Diastolic pressure; HR: Heart rate.

Caffeine is known to have a negative effect on particularly fine motor skills by causing tremors (in sports such as archery), in ball control and passing accuracy in soccer (which are skills that also require fine motor skills) caffeine did not have a negative effect on performance, on the contrary. And for sports on which caffeine has an ergogenic effect, it is important to know the following. It is considered that the dependence of the achieved effects on the consumed dose of caffeine has the form of an inverted U-shaped curve; lower doses have positive effects on performance, while doses higher than 500 mg decrease performance. Participants in the studies subjectively assessed how they felt after consuming caffeine; lower doses were associated with positive feelings of a burst of energy, while higher doses were associated with anxiety and tension. As with many other food supplements and medicines, the following pattern is visible in this case; the ergogenic, positive effects of caffeine increase with the dose, until at some point the side effects do not overpower them (Foskett et al., 2009).

A large number of studies have proven the ergogenic effect of caffeine in activities of longer duration, and that is why Davis & Green (2009) direct their study towards activities of strength and power, that is, activities of shorter duration and very high intensity. They emphasize that the existing hypothesis about the action of the caffeine mechanism, where the increased oxidation of free fatty acids by adrenaline leads to the saving of glycogen, cannot be valid for anaerobic activities. The authors attach importance to a new hypothesis that explains the effect of caffeine on the central nervous system, that is, its antagonistic effect on adenosine receptors and the arousal and perception of effort and pain.

The mentioned problem of the mechanism of action of caffeine is nicely explained by the authors in their study (Grgic et al., 2018), where they indicate the perception of effort and the perception of pain as key mechanisms of the positive effect of caffeine on performance in training with external load. In addition to the above, they add that these are the conclusions of current research and indicate the importance of future studies.

Duncan & Oxford (2011) examined the effect of 5mg/kg caffeine versus placebo on the bench press exercise. Testing was performed with the condition of 60% 1RM with the aim of achieving the maximum number of repetitions, that is, until immediate muscle failure. In addition, they monitor the mood state reaction before and after the test. Subjects achieved a significantly higher number of repetitions in the caffeine condition compared to the placebo condition. Furthermore, in the caffeine condition, their mood was better while the level of fatigue rating was lower.

Grgic et al. (2018) meta-analysis determined that caffeine has significant ergogenic effects on muscle strength and power. The meta-analysis covered research that had as a method of measuring 1RM for the manifestation of maximum muscle strength and vertical jump for the manifestation of strength. The authors of the study conclude that caffeine has a significant impact on the strength of the muscles of the upper versus lower part of the body and a significant impact on strength, and that further research is needed to determine the optimal dose and form of caffeine intake due to its individuality and variability among research participants.

Conclusion

Caffeine can cause sleep disturbances, especially if it is consumed in quantities greater than 100 mg immediately before going to bed. It is believed that caffeine increases alertness and attention, improves performance and endurance during training if it is consumed in a dose higher than 75mg. Caffeine stimulates the central nervous system and small doses (1.5 - 3 mg/kg) improve sports performance, especially in endurance sports, such as running, swimming, cycling and the like. Side effects with a total consumption of ~200-250mg/kg are minimal or absent. Recommended consumption is 30-60 min. before the activity, so that the effects are complete. Caffeine is a permitted substance in sports, which makes it a very popular supplement around the world. People suffering from hypertension, cardiovascular patients and people whose families have recorded cases of acute myocardial infarction should be especially careful. A large number of studies have proven the acute effect of caffeine on performance in tests and improvement of physical performance, and a further step would be to investigate the effects of caffeine on long-term adaptations of certain physical abilities.

Authors' Contribution

Study Design: BB; Data Collection: NA; Manuscript Preparation: MZ; Funds Collection: RP, OR.

Ethical Approval
No ethical approval is required.

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Conflict of Interest
The authors hereby declare that there was no conflict of interest in conducting this study.

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