

TOP 50 MOST-CITED ARTICLES IN CAFFEINE AND EXERCISE: CONTRIBUTIONS FOR PROFESSIONALS AND RESEARCHERS

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ABSTRACT

Objectives: To objectively identify the 50 most-cited articles on caffeine intake and physical exercise, as well as the characteristics that make these articles important for professionals and researchers in the field. **Materials and Methods:** Data were obtained from a Web of Science search with the keyword's "caffeine" and "exercise". No restrictions were applied based on abstract availability, study type, language and human versus non-human research subjects or any type of time limitation. **Results:** All articles were published in English and the number of citations ranged from 85 to 421 (median 124). Regarding the level of evidence, 32 of the articles were classified as level II, ten articles were level I, three articles were level III, and five articles were level V evidence. Among the 50 most-cited articles, 35 articles were original research and 15 were review articles. Most of the original studies (28) investigated caffeine intake on aerobic exercise, another four articles on strength training, and three articles on power training. Considering review studies, 14 investigated caffeine intakes on aerobic exercise and one on strength training. The 50 most cited articles were published in 17 journals, with 60% of the articles published by five journals, with the Journal of Applied Physiology having the highest number of publications. **Conclusions:** We present the 50 most cited articles on caffeine and exercise by number of citations. The studies presented in this article provide teachers, researchers, and students with a set of classic references about caffeine and exercise.

Key words: Caffeine. Exercise. Articles. Studies.

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RESUMO

Os 50 artigos mais citados em cafeína e exercício: contribuições para profissionais e pesquisadores

Objetivo: Identificar objetivamente os 50 artigos mais citados sobre ingestão de cafeína e exercício físico, bem como as características que tornam estes artigos importantes para profissionais e investigadores na área. **Materiais e Métodos:** Os dados foram obtidos a partir de uma pesquisa na Web of Science com a palavra-chave "cafeína" e "exercício". Não foram aplicadas restrições baseadas na disponibilidade do resumo, tipo de estudo, língua e temas de investigação humanos versus não humanos ou qualquer tipo de limitação de tempo. **Resultados:** Todos os artigos foram publicados em inglês e o número de citações variou entre 85 e 421 (mediana 124). Quanto ao nível de evidência, 32 dos artigos foram classificados como nível II, dez artigos foram de nível I, três artigos foram de nível III, e cinco artigos foram de nível V. Entre os 50 artigos mais citados, 35 eram artigos de investigação original e 15 eram artigos de revisão. A maioria dos estudos originais (28) investigou a ingestão de cafeína no exercício aeróbico, outros quatro artigos sobre treino de força, e três artigos sobre treino de potência. Considerando os estudos de revisão, 14 investigaram a ingestão de cafeína no exercício aeróbico e um sobre o treino de força. Os 50 artigos mais citados foram publicados em 17 revistas, com 60% dos artigos publicados por cinco revistas, sendo o Journal of Applied Physiology o que tem o maior número de publicações. **Conclusões:** Apresentamos os 50 artigos mais citados sobre cafeína e exercício físico por número de citações. Os estudos apresentados neste artigo fornecem a professores, investigadores e estudantes um conjunto de referências clássicas sobre a cafeína e o exercício físico.

Palavras-chave: Cafeína. Exercício. Artigos. Estudos.

INTRODUCTION

Caffeine (1, 3, 7-trimethylxanthine) is one of the most consumed psychoactive substances in the world (Cappelletti et al., 2015; Herman, Herman, 2013), being widely used by athletes and non-athletes (Del Coso; Muñoz; Muñoz-Guerra, 2011; Pickering; Grgic, 2019).

Caffeine intake have been known to increase performance for over 100 years, with the first study on the subject published in 1907 (Rivers, Webber, 1907).

Since then, caffeine efficacy has been well documented in endurance exercises (Jeukendrup, 2011), repeated high-intensity efforts (Baltazar-Martins et al., 2020; Grgic et al., 2020), and muscle endurance (Baltazar-Martins et al., 2020; Grgic et al., 2020), while its impact on maximum strength is less pronounced (Baltazar-Martins et al., 2020; Grgic et al., 2020).

Typically, the dosage of caffeine to increase performance varies between 3 and 6 mg·kg⁻¹, 45 to 60 minutes before exercise (Martins et al., 2020). Lower doses (ie, <3 mg·kg⁻¹) may also have ergogenic effects, although the magnitude is possibly lower, whereas higher doses of caffeine (ie, >6 mg·kg⁻¹) do not appear to result in additional improvement in physical performance (Martins et al., 2020).

Given its ergogenic potential, caffeine has received substantial scientific attention worldwide (Martins et al., 2020; Grgic et al., 2020), but even the most assiduous readers may find it difficult to stay up to date with the large pool of publications.

Thus, bibliometric analyses (using the number of times the article has been cited) can be fundamental to quantify the quality of the studies and also identify the areas/topics that have received the most scientific attention so far.

This type of analysis is broadly used in medicine (Arshi et al., 2016; Azer, 2016) and more recently it has also attracted the attention of researchers in various sports (Bilgiç, Isin, 2022; Brito et al., 2018).

However, to the best of our knowledge, there is still no bibliometric analysis that has been on caffeine intake and physical exercise.

Therefore, this study aimed to objectively identify the 50 most-cited articles on caffeine intake and exercise along with the characteristics that make them important for professionals and researchers in the field.

With this in mind, we used data from Web of Science citation indexing service to conduct a comprehensive and systematic search for citations from all publications specific to exercise and caffeine intake, periodic by periodic.

MATERIALS AND METHODS

The data in this study were obtained through research on the electronic platform Web of Science (Clarivate Analytics, USA), with no restrictions applied based on availability of abstract, study type, language, and human versus non-human research objects or any kind of time limitation. Keywords “caffeine” and “exercise” were searched in terms of topic (including three sections: paper title, abstract and author keywords) based on the complete collection of December 28, 2021, and reviewed on January 30, 2022, producing a total of 2,136 articles in human and non-human organisms, published between 1960 and 2021. Subsequently, they were listed based on citation frequency from the highest to the lowest and in humans only. All articles related to caffeine and exercise were considered eligible for analysis, but if no independent data were presented for caffeine and exercise, the article was excluded.

The 50 most-cited articles were published between 1978 and 2016 and reviewed by two researchers (LPG and EMA) with the following information extracted: (1) year of publication, (2) title of the journal, (3) number of citations, (4) authorship and (5) level of evidence (I-V) from the Oxford Center for Evidence-Based Medicine (Brito et al., 2018).

The articles were further independently characterized by two investigators (LPG and EMA) and discussed in the case of discrepancies. Then, a third investigator (SSA) re-analyzed all the articles, and a discussion was employed until a consensus was achieved. Each article was characterized according to category (original or review article), regarding the use of caffeine, coffee and both, type of the exercise (aerobic, strength and power), sex (male, female and both), levels of training (trained and untrained) and age group (youth, adult and all), considering young people aged <18 years and adults aged >18 years. When the information was not evidently provided in the article, these categories were considered unclear.

Statistical analysis

The distribution of a parameter (e.g., number of citations) was characterized by the median. The χ^2 test was used to compare two categorical variables.

To test the hypothesis if three or more samples characterized by their medians originated from the same distribution, the Kruskal-Wallis test was conducted. The level of significance was set at $p < 0.05$.

Data analysis were performed using GraphPad Prism (v6.0) and Statistical Package for the Social Sciences (SPSS v21.0).

RESULTS

The top 50 most-cited articles with caffeine and exercise are shown in table 1. All articles were published in English.

The number of citations ranged from 85 to 421, with a median of 124.

Most articles ($n=32$) were classified as level II evidence, while ten articles were level I, three articles were level III, and five articles level V evidence ($\chi^2=42,640$; $p < 0,001$).

No significant differences ($\chi^2=7,283$; $p=0,063$) were found between the citation medians of the articles and the level of evidence.

Table 1 - List of the top 50 most-cited articles caffeine and exercise.

Ranking	Authors	Year	Title	Journal	Citations (n)
30	McLellan et al.,	2016	A review of caffeine's effects on cognitive physical and occupational performance	Neuroscience Biobehavioral Reviews	114
42	Hodgson et al.,	2013	The Metabolic and Performance Effects of Caffeine Compared to Coffee during Endurance Exercise	Plos one	94
9	Goldstein et al.,	2010	International society of sports nutrition position stand: caffeine and performance	J Int Society Sports Nutrition	175
18	Astorino et al.,	2010	Efficacy of acute caffeine ingestion for short-term high-intensity exercise performance: a systematic review	J Strength and Conditioning Research	138
28	Warren et al.,	2010	Effect of Caffeine Ingestion on Muscular Strength and Endurance: A Meta-Analysis	Med Sci Sports Exerc	119
6	Davis et al.,	2009	Caffeine and Anaerobic Performance Ergogenic Value and Mechanisms of Action	Sports Med	200
19	Maki et al.,	2009	Green Tea Catechin Consumption Enhances Exercise-Induced Abdominal Fat Loss in Overweight and Obese Adults	J Nutrition	135
22	Ganio et al.,	2009	Effect of caffeine on sport-specific endurance performance: a systematic review	J Strength Conditioning Research	128
7	Burke et al.,	2008	Caffeine and sports performance	App Physiol Nutri Metabo-Physiol Appliquee Nutri Metabo	198
39	Astorino et al.,	2008	Effect of caffeine ingestion on one-repetition maximum muscular strength	European J Applied Physiol	96
40	Sokmen et al.,	2008	Caffeine use in sports: considerations for the athlete	J Strength Conditioning Research	95
45	Woolf et al.,	2008	The effect of caffeine as an ergogenic aid in anaerobic exercise	Int J Sport Nutrition Exerc Metabolism	88
46	Jenkins et al.,	2008	Ergogenic effects of low doses of caffeine on cycling performance	Int J Sport Nutrition Exerc Metabolism	88
48	Tarnopolsky et al.,	2008	Effect of caffeine on the neuromuscular system - potential as an ergogenic aid	App Physiol Nutri Metabo-Physiol Appliquee Nutri Metabo	86
50	Glaister et al.,	2008	Caffeine Supplementation and Multiple Sprint Running Performance	Med Sci Sports Exerc	85

15	Maughan et al.,	2007	The use of dietary supplements by athletes	J Sports Sci	140
27	Schneiker et al.,	2006	Effects of caffeine on prolonged intermittent-sprint ability in team-sport athletes	Med Sci Sports Exerc	120
36	Beck et al.,	2006	The acute effects of a caffeine-containing supplement on strength, muscular endurance, and anaerobic capabilities	J Strength Conditioning Research	102
49	Wiles et al.,	2006	The effects of caffeine ingestion on performance time speed and power during a laboratory-based 1 km cycling time-trial	J Sports Sci	86
4	Doherty et al.,	2005	Effects of caffeine ingestion on rating of perceived exertion during and after exercise: a meta-analysis	Scandinavian J Med Sci Sports	239
25	Stuart et al.,	2005	Multiple effects of caffeine on simulated high-intensity team-sport performance	Med Sci Sports Exerc	124
21	Doherty et al.,	2004	Effects of caffeine ingestion on exercise testing: A meta-analysis	Int J Sport Nutrition Exerc Metabolism	129
37	Doherty et al.,	2004	Caffeine lowers perceptual response and increases power output during high-intensity cycling	J Sports Sci	99
33	Motl et al.,	2003	Effect of caffeine on perceptions of leg muscle pain during moderate intensity cycling exercise	Journal of Pain	106
10	Cox et al.,	2002	Effect of different protocols of caffeine intake on metabolism and endurance performance	J Applied Physiol	172
17	Bell et al.,	2002	Exercise endurance 1, 3, and 6 h after caffeine ingestion in caffeine users and nonusers	J Applied Physiol	139
32	Thong et al.,	2002	Caffeine-induced impairment of insulin action but not insulin signaling in human skeletal muscle is reduced by exercise	Diabetes	110
1	Graham et al.,	2001	Caffeine and exercise - Metabolism endurance and performance	Sports Med	421
29	Bell et al.,	2001	Effect of caffeine and ephedrine ingestion on anaerobic exercise performance	Med Sci Sports Exerc	119
38	Jeukendrup et al.,	2001	Improving cycling performance - How should we spend our time and money	Sports Med	98
47	Baum et al.,	2001	The influence of a taurine containing drink on cardiac parameters before and after exercise measured by echocardiography	Amino Acids	88
20	Bruce et al.,	2000	Enhancement of 2000-m rowing performance after caffeine ingestion	Med Sci Sports Exerc	131
23	Graham et al.,	2000	Caffeine ingestion does not alter carbohydrate or fat metabolism in human skeletal muscle during exercise	J Physiology-London	128
43	Greer et al.,	2000	Comparison of caffeine and theophylline ingestion: exercise metabolism and endurance	J Applied Physiol	94
11	Graham et al.,	1998	Metabolic and exercise endurance effects of coffee and caffeine ingestion	J Applied Physiol	169
13	Kovacs et al.,	1998	Effect of caffeinated drinks on substrate metabolism, caffeine excretion, and performance	J Applied Physiol	158

16	Greer et al.,	1998	Caffeine, performance, and metabolism during repeated Wingate exercise tests	J Applied Physiol	140
34	Van Soeren et al.,	1998	Effect of caffeine on metabolism, exercise endurance, and catecholamine responses after withdrawal	J Applied Physiol	106
44	Bell et al.,	1998	Effects of caffeine ephedrine and their combination on time to exhaustion during high-intensity exercise	European J Applied Physiol Occupational Physiol	89
14	Vandenbergh et al.,	1996	Caffeine counteracts the ergogenic action of muscle creatine loading	J Applied Physiol	148
24	Jackman et al.,	1996	Metabolic, catecholamine, and endurance responses to caffeine during intense exercise	J Applied Physiol	127
3	Graham et al.,	1995	Metabolic, catecholamine, and exercise performance responses to various doses of caffeine	J Applied Physiology	292
12	Pasman et al.,	1995	The effect of different dosages of caffeine on endurance performance time	Int J Sports Med	161
41	Tarnopolsky et al.,	1994	Caffeine and endurance performance	Sports Med	95
8	Spriet et al.,	1992	Caffeine ingestion and muscle metabolism during prolonged exercise in humans	American J Physiol	183
26	Collomp et al.,	1992	Benefits of caffeine ingestion on sprint performance in trained and untrained swimmers	European J Applied Physiol Occupational Physiol	124
35	Anselme et al.,	1992	Caffeine increases maximal anaerobic power and blood lactate concentration	Euro J Applied Physiol Occupational Physiol	105
5	Graham et al.,	1991	Performance and metabolic responses to a high caffeine dose during prolonged exercise	J Applied Physiol	209
31	Collomp et al.,	1991	Effects of caffeine ingestion on performance and anaerobic metabolism during the wingate test	Int J Sports Med	114
2	Costill et al.,	1978	Effects of caffeine ingestion on metabolism and exercise performance	Med Sci in Sports Exerc	406

Of the top 50 most-cited articles, 35 [2, 3, 5, 8, 10, 11, 12, 13, 14, 16, 17, 19, 20, 23, 24, 25, 26, 27, 29, 31, 32, 33, 34, 35, 36, 37, 39, 42, 43, 44, 45, 46, 47, 49, 50] were original research and 15 [1, 4, 6, 7, 9, 15, 18, 21, 22, 28, 30, 40,

41, 48] were review articles ($\chi^2=8,000$; $p=0,005$).

No significant differences were detected for the number of citations according to the type of article ($\chi^2=1,213$; $p=0.271$; figure 1).

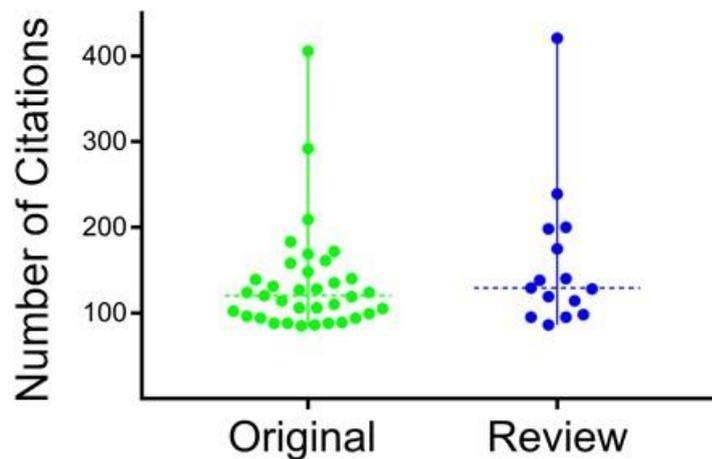


Figure 1 - Distribution of top 50 most-cited articles with caffeine and exercise per type of study.

Regarding the sex of participants, the majority (n=22) of the 35 [3, 10, 12, 13, 14, 16, 20, 23, 25, 27, 29, 32, 33, 34, 36, 37, 39, 43, 44, 45, 46, 50] original research articles investigated male subjects, while no article was dedicated to the female group and only nine studies [2, 5, 11, 17, 19, 24, 26, 31, 35] were dedicated to both sexes (male and female). Another 12 studies [1, 4, 6, 7, 9, 18, 21, 22, 28, 40, 41, 48] were review articles and evaluated individuals of both sexes.

Overall, in seven studies [8, 15, 30, 38, 42, 47, 49], sex was unclear. Significant differences were detected for the number of citations according to the sex of the studied population, with articles that investigated man being more cited than articles that investigated woman ($\chi^2=4,217$; $p=0,040$).

Concerning the age group of participants, 34 [2, 3, 5, 8, 10, 11, 12, 13, 14, 16, 17, 19, 20, 23, 24, 25, 27, 29, 31, 32, 33, 34, 35, 36, 37, 39, 42, 43, 44, 45, 46, 47, 49, 50] original research articles investigated adult individuals, while one article [26] was dedicated to young individuals. No original article included both adult and youth individuals in their samples.

Considering the review studies, only one [4] of them evaluated adult individuals while five other studies investigated both adults and young individuals. Overall, in seven studies [1, 15, 22, 28, 30, 40, 41] the age group was unclear.

No significant differences were detected for the number of citations according

to the age group of the studied population ($\chi^2=0,093$; $p=0,955$).

With regard to the type of exercise investigated, most of the original studies (n = 28) analyzed aerobic exercise [2, 3, 5, 8, 10, 11, 12, 13, 17, 19, 20, 23, 24, 25, 26, 27, 32, 33, 34, 35, 37, 42, 43, 44, 46, 47, 49, 50], while three articles [14, 36, 39] were dedicated to strength training and only three [16, 29, 31] to power training.

Of the 15 review studies, 14 studies [1, 4, 6, 7, 9, 15, 18, 21, 22, 30, 40, 41, 48] evaluated aerobic exercise, and only one studied strength exercise [28].

No significant differences were detected for the number of citations according to the type of exercise investigated ($\chi^2=1,356$; $p=0,508$).

Regarding the participants' training status, 14 out of the 35 original articles classified individuals as active [8, 14, 16, 17, 24, 25, 26, 31, 32, 34, 35, 43, 44, 50] and one [19] studied non-active individuals.

Of the review articles, two included active individuals [1, 6], and three [9, 18, 48] evaluated active and non-active individuals. All other studies (n=30) did not classify individuals as active or non-active.

No significant differences were found between the number of citations and active and non-active individuals ($\chi^2=0,074$; $p=0,964$).

In addition, 18 of the original articles evaluated trained individuals [2, 3, 5, 10, 11, 12, 13, 20, 25, 27, 36, 37, 39, 42, 45, 46, 47, 49], while two evaluated untrained individuals [19,

29], and one article evaluated both trained and untrained individuals [26].

Of the review articles, five studied trained individuals [1, 7, 15, 28, 48], and seven evaluated trained and untrained individuals [4, 6, 9, 18, 21, 38, 40].

In 17 studies, it was not possible to classify participants as trained or untrained. No significant differences were detected for the number of citations according to trained and untrained individuals ($\chi^2=0,489$; $p=0,783$).

Concerning the ingestion of coffee or caffeine, within the original articles, 31 evaluated caffeine ingestion [3, 5, 8, 10, 12, 13,

14, 16, 17, 19, 20, 23, 24, 25, 26, 27, 29, 31, 32, 33, 34, 35, 36, 37, 39, 44, 45, 46, 47, 49, 50], whereas one study evaluated coffee ingestion [2], and three studies evaluated both coffee and caffeine [11, 42, 43].

Of the 15 review articles, seven evaluated caffeine [4, 15, 18, 21, 30, 38, 41], one evaluated coffee [6], and five studied both caffeine and coffee [1, 7, 9, 28, 40].

However, no significant differences were detected for the number of citations according to the ingestion of coffee or caffeine ($\chi^2=0,483$; $p=0,786$; figure 2).

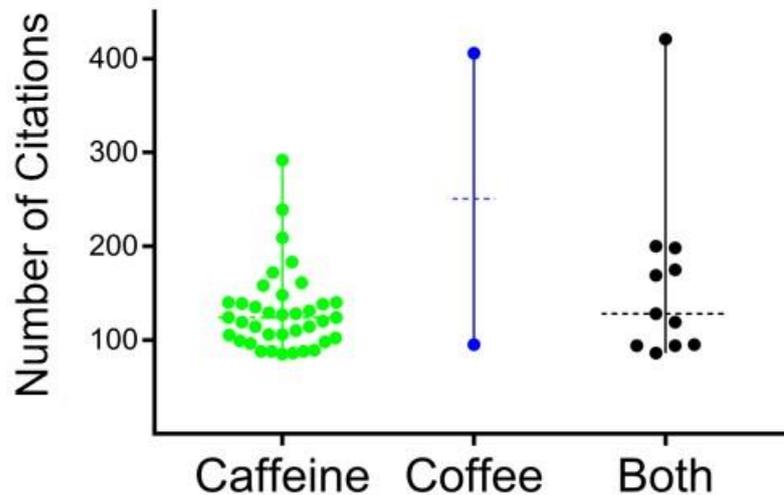


Figure 2 - Distribution of top 50 most-cited articles that studied coffee, caffeine, or both.

The top 50 most frequently cited articles were published in 17 journals (table 1), with 60% of the articles published by five journals: Journal of Applied Physiology (n=11), Medicine and Science in Sports and Exercise (n=7), European Journal of Applied Physiology and Occupational Physiology (n=4), Journal of

Strength and Conditioning Research (n=4), and Sports Medicine (n=4).

The articles were published from 1978 to 2016 (figure 3). The oldest article was published in 1978 in Medicine and Science in Sports and Exercise, and the most recent in 2016 in Neuroscience and Biobehavioral Reviews.

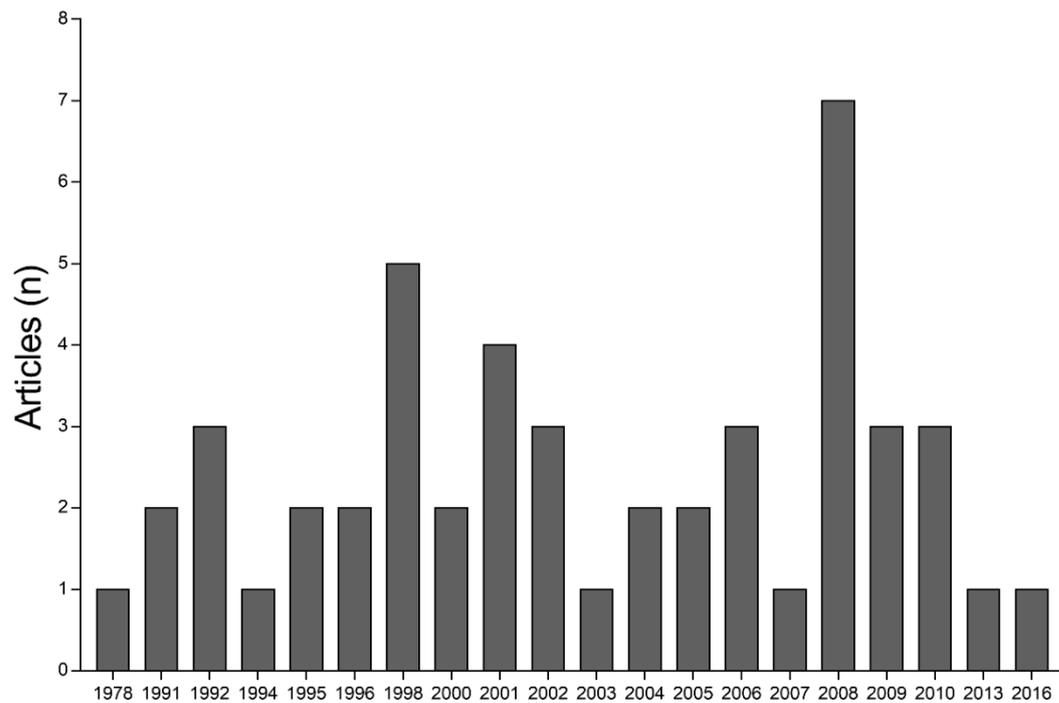


Figure 3 - Chronological distribution according to year of publication of the top 50 most-cited articles with caffeine and exercise.

Overall, the top 50 most-cited articles encompassed 203 authors in total, with an average number of 4,06 authors per article.

There were four single-author articles. The maximum number of coauthors in an article was 13.

The list of authors with two or more articles in the top 50 is presented in table 2.

Table 2 List of authors with two or more articles in the top 50 most-cited articles in caffeine and exercise:

Authors	articles (n)
Graham TE	5
Doherty M	3
Bell DG	3
Collomp K	2
Tarnopolsky MA	2
Greer F	2
Astorino TA	2

DISCUSSION

The present study aimed to determine the 50 most-cited articles (based on Web of Science citation indexing) on caffeine intake and exercise.

Our findings revealed that there is a poor relationship between the evidence levels of the Oxford Centre for Evidence-Based Medicine and the number of citations of the

articles published between 1978 to 2016, which is similar to others research done previously (Brito et al., 2018).

Among the articles with the highest number of citations, there seems to exist a prevalence of original research articles, however the total citations analysis indicated that there are no major differences between the types of articles.

When the sex of participants was analyzed, it was possible to observe that none of the 35 original research articles analyzed investigated exclusively female individuals, demonstrating the low number of studies related to pre-workout supplementation for the female audience (Lane et al., 2019).

The same occurred in reviews, which indicates the need for studies on pre-workout supplementation for female individuals (Rayagonzález et al., 2020).

In fact, the present study showed, by the results of the analysis of the number of citations, a significant difference between men compared to women.

When the age range was analyzed, little is reported on caffeine and exercise for individuals under 18 years of age. In addition, in some articles it was not possible to identify the age range of the participants, which may lead to doubts in prescribing this supplementation for youth training.

The articles related to aerobic exercise predominated among the publications analyzed, but no significant differences were observed between citations on articles that investigated aerobic, strength and power exercises.

Regarding active or non-active individuals, only fifteen of the original articles presented this classification, while in the review publications, 66% of the studies did not allow this identification. This is somehow troublesome because this identification may be important when interpreting the prescription and results of caffeine use in exercise.

The Journal of Applied Physiology was the one with the largest number of articles on this theme, giving space for the publication of studies on this aspect. As for the authors, Terry E. Graham was the most cited one, being an important reference for future studies.

Original publications and reviews followed the trend of few publications related to caffeine intake through coffee ingestion, which indicates that more research on this type of ingestion may be necessary. The difference between coffee and caffeine intake is due to the concentration factor of caffeine in capsules and caffeine in the usual coffee we drink (Grgic et al., 2020).

In the last few decades, the available scientific literature on caffeine and exercise has increased drastically in terms of quantity and quality.

However, to our knowledge, this is the first bibliometric analysis conducted on caffeine and exercise. In medical literature, the number of times an article is cited by other authors can be used as a measurement of influence within an environment for authors, journals, and study topics (Arshi et al., 2016; Azer, 2016).

This list of the 50 most-cited articles in caffeine and exercise provides seminal articles in the field for historical purposes, indicating authors and topics that have had profound influence on knowledge production in recent years.

The articles within this list provide a historical analysis of the evolution on caffeine and exercise research, practice, and the controversies over the use of this substance as a guide for future research studies and clinical practice (Seriwala et al., 2015).

We have some limitations in this study, such as the fact that it is not possible to observe all the articles in relation to aspects that may alter the percentage of the final information, due to unclear or missing information in some of the articles.

Another limitation is the only one electronic research platform, the Web of Science (Clarivate Analytics, USA), which narrows the citation analyses, since data may not reflect the total number of citations when observing other platforms as well (Brito et al., 2018).

The implications of this study are multifold. First, implications for readers: although the selection of articles is somehow unique, the number of citations collected provides a useful perspective on these articles. Researchers may also benefit from our results, as this study may assist them in writing a possibly influential article.

The articles analyzed in this study are good examples for academic writing, since most influential articles are based on innovative ideas that are carefully researched, well written, and that advance knowledge in the area of study. Finally, the selection of articles provides practical implications for caffeine or derivatives' prescription for exercise.

CONCLUSIONS

In conclusion, we present the 50 most cited caffeine and exercise articles by total number of citations, using data from the Web of Science citation indexing service.

Our analysis found that the largest number of these articles were original articles classified as level 2 evidence (Oxford Center for Evidence-Based Medicine), although no significant difference between average citations and level of evidence was reported.

All articles were in English, with a predominance of studies that investigated caffeine ingestion by male active/trained participants and on aerobic exercise.

The studies presented in this article provide teachers, researchers, and students with a group of classic citations on caffeine and exercise.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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