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ARTICLE

Effects of Caffeine on Healthy Adults' Cardiovascular and Neurological Systems

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Abstract

Caffeine is widely used by adults for its stimulating effects despite documented adverse health effects. The purpose of this systematic review was to highlight and document the cardiovascular and neurological effects of caffeine consumption in healthy and recreationally active adults. The most common adverse effects of caffeine on the cardiovascular system encountered during the search were elevated systolic blood pressure, followed by elevated diastolic blood pressure, and elevated heart rates. The most common adverse effect of caffeine on the neurological system encountered during the search was affected sleep patterns. Most of the significant findings ($p \leq 0.05$) of adverse effects resulted from synthetic sources of caffeine, such as in tablet, capsule, pre-workout supplement, or energy drink form.

1 | INTRODUCTION

Caffeine, as a supplement and as a psychoactive drug, is widely used for its positive effects on physical performance and cognitive function (National Library of Medicine, 2022; Kuakini Health System, 2022; Martins et al, 2020). Caffeine is a stimulant and increases brain activity (Better Health Channel, 2020). Caffeine is mostly used for its benefits in cognitive function (Bello et al, 2019; Guest et al, 2021; Kim et al, 2021). In a clinical trial, caffeine showed significantly improved reaction time and performance in elite soccer athletes during a match (Bello et al, 2019). Caffeine is used by athletes in all types of sports: endurance, resistance, elite, and recreationally active (Guest et al, 2021; Martins et al, 2020). However, despite such beneficial advantages, healthy adults can experience adverse effects from the overuse of caffeine (Murray, 2021; Mayo Clinic, 2022; Better Health Channel, 2020). Caffeine toxicity, specifically negative neurological or cardiovascular effects, has been observed and documented in healthy adults who regularly and abundantly consume caffeine (Murray, 2021). Further research and delving into the literature can uncover the severity of such negative outcomes. The purpose of this systematic review was to highlight and document the cardiovascular and neurological effects of caffeine consumption in healthy and recreationally active adults. The authors' hypotheses

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are as stated:

H_1: Caffeine will have negative adverse effects on both the cardiovascular system and the nervous system.

H_2: Caffeine will have negative adverse effects on only the cardiovascular system.

H_3: Caffeine will have negative adverse effects on only the nervous system.

H_4: Data collected from this systemic review will not provide enough information to affirm any definitive negative effects of caffeine on the cardiovascular or nervous system.

H_0: Caffeine will not have negative adverse effects on the cardiovascular and nervous systems.

Elaborating on the severity and gravity of caffeine toxicity in healthy adults could potentially instill responsible caffeine consumption habits in adults that use caffeine for its benefits. The objective of this review was to identify any adverse effects of caffeine use on a healthy human adult's cardiovascular or neurological systems.

2 | METHODS

Protocol and registration

The authors used the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA) to complete this review. As part of the PRISMA protocol, this systemized review was registered with PROSPERO (PROSPERO ID CRD42022313490).

Search strategy

The research articles for this systemized review were collected from three databases: PubMed, CINAHL, and Embase. The search was performed between February 13 and February 14, 2022. The search strategy utilized was: (Adult*) AND (Athlete* OR Sport* OR Exercise* OR workout*) AND (Preworkout supplement* OR Caffeine supplement* OR Pre-workout supplement* OR energy drink*) AND (cardiovascular OR neurological OR stroke* OR tachycardia OR bradycardia OR sleep OR heart OR blood). The results were limited to clinical trials published between 2017 and 2022, as well as clinical trials that were available as full text without subscription or purchase. The search results were further refined to articles published in the English language.

Eligibility criteria

The process in this systematic review required the authors first skimmed titles of the retrieved reports, followed by the abstract, and finally full text. Publications that matched one or more exclusionary criteria were removed. Table 1 describes the authors' inclusionary and exclusionary criteria.

Table 1: *Inclusionary and exclusionary criteria.*

Criteria	Inclusion	Exclusion
Demographic information of participants	Healthy adults (age 18 years old and older) of any gender. No restriction on the country of origin, nationality, or ethnicity.	Studies involving minors.
Health Status / problem / condition	N/A	Study participants with pre-existing conditions*
Intervention / exposure	Caffeine or pre-workout supplementation	N/A
Outcome	Outcomes measured must include either cardiovascular or neurological health effects	Outcomes that had no mention of cardiovascular or neurological effects
Study design preferences	Clinical trials and interventions	Reviews or case studies
Size of study groups	Study groups of two or more individuals	Sample sizes of one participant
Publication language	Studies had to be published or translated into the English language	Studies not translated to English
Publication year range	Five years	Studies published prior to the year 2017
Other	Full-text availability only	N/A

Note: *Pre-Existing conditions that were considered exclusionary to the authors conducting the search were: pregnancy, high body mass index (BMI), hypertension (HTN), cardiovascular disease (CVD), diabetes, or cancer.

Data extraction and quality assurance

The Cochrane data extraction template (Ryan et al, 2016) was utilized by the authors for the data extraction and synthesis process. The data extracted from the articles included: Title of publication, year published, journal, DOI, details of the study

(number of participants and gender breakdown, age range, intervention, outcomes measured), the purpose of the study, and relevant outcomes and results, including p values for significance. Quality assurance of the literature was conducted using the Quality Criteria Checklist for primary research published by the Academy of Nutrition and Dietetics Evidence Analysis Library (Academy of Nutrition and Dietetics, 2016).

Studies that passed the initial screening process were reviewed in full text. All forms of caffeine supplementation and sources were included in this review. Figure 1: PRISMA flow chart demonstrates the literature search process and the removal of reports that did not meet the inclusionary criteria for this review.

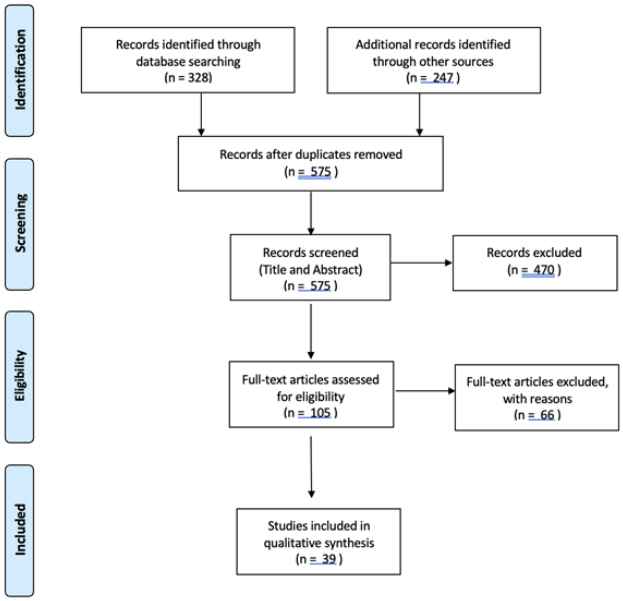

Figure1: *PRISMA flow diagram*

3 | RESULTS

Of the 575 reports retrieved from the initial searches, thirty-nine studies were used in this systematized review. The following subsections describe the cardiovascular and neurological effects documented in studies that used caffeine as part of their intervention. Due to the varying sources of caffeine used in the interventions, a subsection on the types of caffeine is included. A subsection on exercise performance benefits is also included as it was a common outcome in many studies. A final quality assurance and bias assessment subsection analyzed the quality of the article content and intervention protocols.

Sources of caffeine

The studies had varying sources of caffeine used in the interventions and clinical trials. Most of the studies (n=13) used caffeine in tablet or capsule form due to the ease of use and measurement. Energy drinks were the second common source of caffeine found in intervention protocols (n=10), followed by coffee (n=7) and pre-workout powder drinks (n=7). Five studies relied on a self-reported questionnaire to document caffeine intake by participants. Three studies used a form of tea, either green or black, as a caffeine source in their trial. Finally, two studies used a miscellaneous caffeinated juice or beverage in their protocol that did not fit into any of the aforementioned categories of caffeine sources. Due to the varying sources of caffeine used in these trials, it is important to note which sources had profound or significant effects on healthy adults' cardiovascular or neurological systems.

Caffeine and cardiovascular effects

The most common adverse effects of caffeine on the cardiovascular system were elevated systolic blood pressure, followed by elevated diastolic blood pressure, and elevated heart rates. The studies that published significantly elevated systolic blood pressure as a result of caffeine ingestion are listed in Table 3 with their publication year, p-values, and caffeine intervention. The caffeine source for each intervention is reported along with the most often recurring significant findings due to their similarities. It is important to note the amounts of caffeine (measured in milligrams [mg]), and whether the source is naturally occurring (coffee, tea, or chocolate) or synthetic (capsule, tablet, energy drink, pre-workout supplement, or soft drink). In Table 3, all interventions that resulted in a significantly elevated systolic blood pressure featured one or more synthetic sources of caffeine.

Table 3: *Studies identifying elevated systolic blood pressure as an outcome of their interventions.*

Study citation and *p*-value	Caffeine source
Chtourou et al 2019 ($p<0.05$)	Red Bull energy drink 80mg of caffeine
Ioakeimidis et al, 2018 (p <0.01)	240mg caffeine tablet OR coffee espresso 80mg
Köksal et al, 2017 (p=0.44)	150.0 ± 122.06 mg per day of varying sources*
Nowak et al, 2019 (p=0.206)	Unnamed energy drink containing 192mg caffeine
Melik et al, 2019 (p<0.05)	One serving of a 200mg caffeine powder dissolved in water
Peveler et al, 2017 (p=0.001)	Three energy drinks were used in this intervention: Red Bull energy drink with 80mg caffeine, Monster energy drink with 163mg caffeine, and a 5-hour energy shot with 207mg caffeine
Salicio et al, 2016)	Tablet containing a caffeine dose of 6mg per kilogram (kg) of body weight
Shah et al, 2019 (p<0.001)	Two unnamed energy drinks containing 304-320mg of caffeine in each serving

** Self-reported by participants.*

Conversely, elevated diastolic blood pressure was also often reported in caffeine trials, though not as frequently as elevated systolic blood pressure. Table 4 lists the studies that published elevated diastolic blood pressure, along with their publication year, p-values, and caffeine intervention. Once again, the caffeine amount and source are listed due to the comparison of naturally occurring sources versus synthetic sources. In Table 4, all interventions that ultimately resulted in a significantly elevated diastolic blood pressure featured one or more synthetic sources of caffeine.

Table 4: *Studies identifying elevated diastolic blood pressure as an outcome of their interventions*

Study citation and *p*-value	Caffeine source
Cameron et al, 2018 ($p=0.011$)	Pre-workout supplement containing caffeine (no amount listed)
Chtourou et al 2019 ($p<0.05$)	Red Bull energy drink containing 80mg caffeine
Ioakeimidis et al, 2018 ($p<0.05$)	240mg caffeine tablet OR coffee espresso 80mg
Melik et al, 2019 ($p<0.05$)	One serving of a 200mg caffeine powder dissolved in water
Nowak et al, 2019 ($p<0.001$)	Unnamed energy drink containing 192mg caffeine
Shah et al, 2019 ($p<0.001$)	Two unnamed energy drinks containing 304-320 mg of caffeine in each serving
Verma et al, 2021 ($p=0.033$)	Three unnamed energy drinks containing 150-180mg caffeine per serving

The third most common significant finding amongst publications was elevated heart rate. The six articles that documented significantly elevated heart rates as a result of a caffeine intervention are listed in Table 5 along with their p-values and caffeine source. As with the interventions that significantly elevated systolic and diastolic blood pressure, the caffeine source used in the interventions reported in Table 5 come from a synthetic source.

Table 5: *Studies identifying elevated heart rate as an outcome of their interventions.*

Study citation and *p*-value	Caffeine source
Cameron et al, 2018 ($p=0.002$)	Pre-workout supplement containing caffeine (no amount listed)
Clark et al, 2020 ($p<0.05$)	Unnamed energy drink containing 140mg per serving
Kliszczewicz et al, 2018 ($p<0.05$)	Tablet of 100mg of caffeine in addition to 100mg citrus aurantium
Salicio et al, 2016)	Tablet containing a caffeine dose of 6mg per kg of body weight
Suvi et al, 2017 ($p<0.05$)	Two doses of a capsule containing a caffeine dose of 6mg per kg of body weight
Verma et al, 2021 ($p=0.04$)	Three unnamed energy drinks containing 150-180mg of caffeine per serving

In some trials that led to elevated blood pressure and heart rates following caffeine intake, studies also observed a delayed return to baseline levels (Gonzaga et al, 2017; Gonzaga et al, 2019; Yu et al, 2022). Gonzaga et al (2017) observed a significantly ($p<0.05$) longer wait time for both diastolic and systolic blood pressure to return to baseline levels. Furthermore, heart rate recovery to baseline was significantly ($p<0.05$) faster in placebo trials (Gonzaga et al, 2017). Yu et al (2022) recorded significantly ($p<0.05$) slower cardiovascular recovery for heart rate, systolic blood pressure, and diastolic blood pressure. These findings are consistent with what would be expected from a stimulant such as caffeine (Mayo Clinic, 2022). Caffeine's stimulant properties also significantly ($p<0.05$) contributed to the delays in autonomic system response to exercise and its return to baseline levels (Gonzaga et al, 2017; Gonzaga et al, 2019). Findings such as these demonstrated

caffeine's ability to not only act as a stimulant and increase cardiovascular activity, but also its effect on the cardiovascular system's ability to maintain that level of elevated activity and delay the return to baseline levels.

Circulation is also affected by caffeine intake in clinical trials. Blood flow activity was hyperactive and elevated in caffeine trials (Melik et al, 2018; Martin et al, 2017). Vascular activity increased significantly ($p=0.00422$) following caffeine ingestion and exercise (Melik et al, 2018). Additionally, caffeine significantly ($p<0.01$) increased the post-occlusive reactive hyperemia response in the same protocol (Melik et al, 2018). Femoral artery blood flow increased significantly ($p=0.006$) in a caffeine trial that used a leg press exercise protocol to compare the stimulant's effect on exercise compared to a placebo (Martin et al, 2017). The documented effects reveal caffeine's effect on blood flow-adding another component of the cardiovascular system that is impacted by caffeine.

Heart function and rhythm were also impacted by caffeine ingestion. Upon taking caffeine supplementation, further significant ($p\leq0.05$) effects such as increased pulse pressure (Ioakeimidis et al, 2018), increased QT interval (Shah et al, 2019), and heart palpitations (Verma et al, 2021; Kliszczewicz et al, 2018) were observed in participants. The significant findings, combined with the aforementioned significant elevation in heart rate (Suvi et al, 2017; Verma et al, 2021; Cameron et al, 2018; Clark et al, 2020; Salicio et al, 2016; & Kliszczewicz et al, 2018) revealed practically all aspects of heartbeat function and rhythm are affected by caffeine supplementation.

Other dimensions of cardiovascular health were also affected by caffeine intake. The composition and makeup of the blood in participants were observed to have been affected by caffeine supplementation in clinical trials (Chtourou et al, 2019; Fye et al, 2021; Potgieter et al, 2018; Suvi et al, 2017; Verma et al, 2021). Studies reported significantly ($p\leq0.05$) elevated blood lactate and a decreased time to return to baseline lactate levels in participants who used caffeine (Fye et al, 2021; Potgieter et al, 2018; Suvi et al, 2017). Blood glucose also significantly ($p\leq0.05$) increased in participants who consumed energy drinks (Chtourou et al, 2019; Verma et al, 2021). Salicio et al (2017) documented effects on the cardiovascular system and its interaction with the muscular system. In its trial, Salicio et al (2017) reported significantly decreased oxidative stress ($p<0.05$) and further documented caffeine's ability to mimic muscular hypertrophy ($p<0.05$). In a retrospective study, caffeine was significantly ($p<0.05$) associated with increased incidences of cardiovascular disease and hypertension (Gaeini et al, 2019). The documented effects highlighted caffeine's ability to alter the circulatory function and cardiovascular health.

Though there were adverse effects to the cardiovascular system documented in most of the studies identified in this review, beneficial effects of caffeine were also reported following exercise trials. In D'Alessandro et al (2020) the beneficial effect on the participants' red blood cells' antioxidant capacity and xanthine metabolites was highlighted. Concurrently, Melik et al, 2019 reported decreased heart rate in caffeine trials ($p<0.05$). Furthermore, several studies observed the cardiovascular effects of caffeine intake after exercise reported nonsignificant results (Anderson et al, 2020; Brothers et al, 2017; Collins et al, 2017; Gaeini et al, 2019; Garcia et al, 2017; Jung et al, 2017; Karayigit et al, 2020; Marques et al, 2018; Nowa et al, 2019; Puente et al, 2017; VanDusseldorp et al, 2021). Table 6 lists each of the studies with nonsignificant findings along with their caffeine source. Unlike the studies identified in Table 3, Table 4, and Table 5, a few of the studies noted in table 6 utilized some naturally occurring sources of caffeine in their interventions (Gaeini et al, 2019; Anderson et al, 2020; Brothers et al, 2017; Karayigit et al, 2020; & Marques et al, 2018).

Table 6: *Studies that reported nonsignificant cardiovascular effects.*

Study citation	Caffeine source
Anderson et al, 2020	Instant coffee with 280mg of caffeine
Brothers et al, 2017	Unnamed energy drinks of a high caffeine dose (3mg per kg of body weight) and a low caffeine dose (2mg per kg of body weight) and coffee containing a caffeine dose of 2mg per kg of body weight
Collins et al, 2017	A pre-workout supplement containing 200mg of caffeine
Gaeini et al, 2019	Tea, coffee, chocolates, and soft drinks*
García et al, 2017	Three unnamed energy drinks were used in this intervention: energy drink A contained 149.5mg caffeine, energy drink B contained 147.2mg caffeine, and energy drink C contained 155mg caffeine
Jung et al, 2017	A pre-workout supplement containing 284mg of caffeine
Karayigit et al, 2020	Coffee containing a high or low dose of caffeine (3mg per kg of body weight or 6mg per kg of bodyweight)
Marques et al, 2018	Coffee containing a caffeine dose of 5.5mg per kg of bodyweight
Nowak et al, 2019	Unnamed energy drink containing 192mg caffeine
Puente et al, 2017	A single capsule containing a caffeine dose of 3mg per kg of bodyweight
VanDusseldorp et al, 2021	A pre-workout supplement containing 150mg of caffeine

* *Self-reported by participants.*

Caffeine and neurological effects

The most common adverse effect of caffeine on the neurological system was affected sleep patterns (Chang et al, 2021; Faris et al, 2017; Puente et al, 2017; Toblin et al, 2018; Unno et al, 2017; Verma et al, 2021). Table 7 identifies the studies that published any negative effects the caffeine regimen used in the intervention had on the participants' sleep patterns, along with their publication year, p-values, and caffeine intervention. The caffeine amount and source are listed due to the comparison of naturally occurring sources versus synthetic sources.

Table 7: *Studies identifying negative effects on participants' sleep patterns.*

Significant finding	Study citation and *p*-value	Caffeine source
Poor sleep quality	Faris et al (2017) ($p<0.05$)	Unnamed energy drinks*
	Unno et al (2017) ($p<0.05$)	Green tea with a high dose of caffeine (50-100mg) or a low dose of caffeine (10-40mg)
	Verma et al (2021) ($p<0.05$)	Three unnamed energy drinks containing 150-180mg of caffeine per serving
Shorter sleep time	Chang et al (2021) ($p<0.05$)	Daily caffeine intake reported via questionnaire*
Significant overall changes in sleep pattern	Faris et al (2017) ($p<0.05$)	Unnamed energy drinks*
Insomnia and trouble sleeping	Puente et al, 2017 ($p=0.041$)	A single capsule containing a caffeine dose of 3mg per kg of bodyweight
	Toblin et al, 2018 ($p<0.05$)	Unnamed energy drinks*

* Self-reported by participants.

Further developments in participants' sleep patterns were impacts on fatigue levels as a result of caffeine intake. An increase in fatigue was reported in Toblin et al, 2018 ($p<0.001$), but at the same time, fatigue decreased in Unno et al, 2017 and Fye et al, 2021. Connell et al (2017) reported caffeine can significantly protect eye motor function when experiencing fatigue ($p<0.05$). Due to caffeine's role as a stimulant, it is understandable that fatigue would decrease after consumption, and motor function would improve under fatigue as well.

Along with motor function, cognitive function was impacted by caffeine supplementation in clinical trials. Cameron et al (2018) ($p=0.046$), Jung et al (2017) ($p<0.001$), and Karayigit et al (2020) ($p=0.035$) demonstrated improved cognition in their clinical trials. Additionally, caffeine intake reduced reaction time in sports performance (Chtourou et al, 2019 ($p<0.0005$)). Findings such as these demonstrated positive effects on the neurological system in caffeine trials, conflicting with the negative significant outcomes listed in Table 7.

Caffeine's effects on the neurological system went beyond sleep, cognition, and motor function – it also impacted mood. Toblin et al (2018) documented a significant increase in aggression in its protocol participants ($p<0.05$). Participants also reported a nonsignificant increase in jitters and tingly sensations (Cameron et al, 2018). However, there were positive effects reported in trials as well. Jung et al (2017) published an improvement in participants' self-reported optimism, vigor, and energy ($p=0.004$). Significantly lower stress was observed in Unno et al, 2017 ($p<0.05$) among participants that consumed a low dose of caffeinated green tea. The documented positive and negative effects of caffeine ingestion on mood revealed the versatility on behalf of the supplement and could prove to be advantageous for healthy adults.

Ultimately, only one study reported no significant impacts on the nervous system from caffeine use (Weibel et al, 2021). In Weibel et al (2021), participants completed a questionnaire to report any adverse effects on their sleep patterns. There were no significant results that acknowledged or signaled any altered sleep quality because of caffeine consumption (Weibel et al, 2021).

Caffeine and performance benefits

Despite the documented adverse cardiovascular and neurological effects of caffeine, many studies reported performance benefits in exercise when caffeine was used as a stimulating supplement before a workout or exercise regimen (Anderson et al, 2018; Cameron et al, 2018; Chtourou et al, 2019; Karayigit et al, 2020; & Potgieter et al, 2018). Table 8 lists the studies that reported significant improvement to exercise performance with their citation, p-value, exercise protocol, and caffeine source.

Table 8: *Studies identifying significantly improved exercise performance as an outcome of their intervention.*

Study citation	Exercise protocol and significant finding	Caffeine source
Cameron et al, 2018	Significantly improved upper body endurance in bench press repetition until exhaustion trial (p=0.037) Significantly improved anaerobic spring capabilities (p=0.039).	Pre-workout supplement containing caffeine (no amount listed)
Chtourou et al, 2019	Significant improvements in peak cycling power (p=0.0250) Significant improvements in average cycling power (p=0.0093) Significant improvements in handgrip force (p=0.0027)	Red Bull energy drink containing 80mg of caffeine
Karayigit et al, 2020	Significantly improved muscular endurance in the lower body (p=0.025)	Coffee containing a high or low dose of caffeine (3mg per kg of body weight or 6mg per kg of body weight)
Potgieter et al, 2018	Significantly improved triathlon performance in swim time (p<0.05) and overall completion (p<0.05)	A capsule containing a caffeine dose of 6mg per kg of body weight

Following the protocol in Anderson et al (2018), participants were asked to guess if each consumed caffeine or the placebo. Participants who guessed they had consumed caffeine, either correctly or incorrectly, had improved performance (Anderson et al., 2020). This suggests the performance boost documented in the caffeine trial may also be psychological (Anderson et al., 2020). As reported in other categories, some studies also published interventions in which caffeine had no significant impact on performance (Jodra et al, 2020; Marques et al, 2018; & Peveler et al, 2017).

Quality assurance results

Quality assurance of the literature was conducted using the Quality Criteria Checklist for primary research published by the Academy of Nutrition and Dietetics Evidence Analysis Library (Academy of Nutrition and Dietetics, 2016). In total, 37 studies were used for this systemized review. Twenty-nine of those studies were given a "+" rating, which, according to the Quality Criteria Checklist conveys a strong quality primary research report (Academy of Nutrition and Dietetics, 2016). Four studies received a rating of "∅", signaling a neutral quality publication. The remaining four studies received a "-" rating, indicating a study that did not meet the standards of a strong quality primary research report (Academy of Nutrition and Dietetics, 2016). Overall, the quality of the studies used in this systemized review was good and strong; further analysis of the quality assessment is in the **Quality** assessment section of this review.

4 | DISCUSSION

The results of our synthesized review were conflicting and inconclusive. Cardiovascular effects were non-significant ($p > 0.05$) in numerous publications – in fact, there were more publications that identified nonsignificant cardiovascular effects (n=11) than publications that published significant impacts on systolic blood pressure (n=8), diastolic blood pressure (n=7), or heart rate (n=6). These hyperactive effects were already well-known and published in numerous journals and government health agency websites and therefore do not constitute any new recommendations (Better Health Channel, 2020; Guest et al, 2021; Office of the Commissioner; 2018). However, when referring to Table 3, Table 4, and Table 5 in the Caffeine and cardiovascular effects section, it is important to note how many significant findings of adverse effects resulted from synthetic sources of caffeine, such as in tablet, capsule, pre-workout supplement, or energy drink form. In Table 6, naturally occurring sources of caffeine – such as coffee, tea, or chocolates – were identified as some of the caffeine

interventions used in trials that led to nonsignificant findings regarding cardiovascular measures. As a result of this difference in adverse health effects because of using synthetic versus naturally occurring sources of caffeine, it is reasonable to assume healthy adults should prioritize using naturally occurring sources of caffeine over synthetic, lab-made sources (energy drinks, sodas, pre-workout supplements, tablets, or capsules) to avoid the potential adverse cardiovascular effects.

Neurological side effects of caffeine predominantly surrounded sleep. This was anticipated, considering the stimulating effects of caffeine (Better Health Channel, 2020). The impact of caffeine on the psychology of the participants was mixed, and therefore not used to influence the authors' recommendations.

Ultimately, the evidence found in our systemized review is not enough to confidently arrive at a conclusion on the potential negative effects of caffeine on a healthy adult's neurological and cardiovascular systems. It is important to note participants of the studies were healthy adults who were able to participate in an exercise protocol or regimen. Adults with pre-existing conditions who have other health considerations or adverse effects were not documented in the studies used in this review. Therefore, the conclusions and recommendations reported in our systemized review do not apply to adults with pre-existing conditions. Based on the nature of the performance benefits, as well as the mixed results regarding adverse effects, it is recommended to continue following the International Society of Sport Nutrition's position regarding caffeine consumption for healthy adults:

- 3-6 milligrams per kilogram of body weight, though a dose of as little as 2 milligrams per kilogram of body weight should be enough to feel a difference during exercise (Guest et al, 2021).
- The utmost maximum dose a healthy adult can consume in a single day is 400mg, according to the Food and Drug Administration (Office of the Commissioner, 2018).

The authors agree with the above-mentioned recommendations and guidelines from the Food and Drug Administration and the International Journals of Sports Nutrition (Guest et al, 2021` Office of the Commissioner, 2018), and would like to add healthy adults purposely seek naturally occurring sources of caffeine as opposed to synthetic, lab-made sources.

Quality assessment

The Academy of Nutrition and Dietetics Evidence Analysis Library has published a conclusion grading table to use once all studies in a review have received a rating based on the Quality Criteria Checklist for primary research (Academy of Nutrition and Dietetics, 2016). Based on the quality of the studies, consistency of findings, and quantity of both the studies in this review and the average sample size of the protocols, the authors identify the evidence and conclusion of this systemized review as a II - Fair quality. The studies were overall "+", strong quality publications, though many of the trials featured small sample sizes (n=25, small sample sizes according to the authors were those that included ≤35 participants). The consistency of whether effects were significantly negative or nonsignificant was divided as well, with many studies identifying nonsignificant results (n=11 for cardiovascular effects, n=1 for neurological effects). Two major strengths of the studies included the low p-values and high levels of significance in the authors' results. This, combined with the number of strong quality publications, bolstered the conclusion rating of this review.

Strengths and limitations

In this systemized review, the authors were limited by the scope of the search strategy and by the limited availability of full-text articles accessible via their institution. Not all articles published on the subject matter were available to review. Additionally, the authors missed out on relevant studies and publications not published in the English language due to not meeting the inclusionary language criteria.

Regarding the impact on participants' mood under neurological effects of caffeine supplementation, is important to note the unreliability in the self-reported nature of these results. All articles published with self-reported caffeine intake amounts were limited by participant integrity and ability to correctly measure or estimate caffeine consumption.

Furthermore, studies were limited by their study samples, particularly whether the participants were habitual caffeine consumers. The integrity and lifestyle of the participants played a major role in the limitations and quality assessments of the studies.

Application for practitioner

Until a more definitive conclusion is reached on the adverse neurological and cardiovascular effects of caffeine intake on healthy adults, it is recommended to follow published recommended dosage amounts in peer-reviewed journals and government health organizations. Any doubt or concerns regarding the risks of adverse health effects stemming from caffeine use should be addressed with a primary care physician (Mayo Clinic, 2022).

As previously mentioned in the Discussion section, healthy adults should use naturally occurring caffeine sources over synthetic or lab-made sources. While the authors cannot confidently declare synthetic sources of caffeine as dangerous for heart health, the evidence collected in this systematic review revealed a vast majority of studies published significant adverse effects on the cardiovascular system used synthetic sources of caffeine, with the exception of Ioakeimidis et al (2018) that used both a 240mg tablet of caffeine and 240mg triple coffee espresso in their trial. Therefore, the authors recommend using natural sources of caffeine such as coffees, teas, or chocolates for their performance-enhancing and cognitive benefits.

5 | CONCLUSION

One of the authors' original hypotheses stated caffeine would have negative adverse effects on both the cardiovascular system and the nervous system. Ultimately, the effects on the cardiovascular system were mixed. The effects on the nervous system were as anticipated, due to the natural stimulant properties of caffeine (Better Health Channel, 2020). The literature explored in our systemized review summarized the acute effects of caffeine consumption on the cardiovascular and neurological systems of healthy adults, mostly young adults. Further research is needed to determine the long-term effects of caffeine consumption on healthy and recreationally active adults' cardiovascular and neurological systems. Short-term acute impacts were conflicting and inconclusive; the authors were not able to make a recommendation based on the literature collected for the systemic review. Recommendations and guidelines for caffeine dosing should follow the International Society of Sports Nutrition and the Food and Beverage Administration (Guest et al, 2021; Office of the Commissioner, 2018).

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