Review

Nootropic supplements for esports

A scoping review

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Abstract: *Background:* esports, or organized video game competitions, have been expanding quickly. The use of dietary supplements by esports players appears vulgarized but lacks supporting evidence. *Objectives:* To outline studies that tested the effects of dietary supplements on video gaming, summarize their findings, highlight knowledge gaps, and recommend future research. *Eligibility criteria:* Clinical trials published in English between 1990 and 2023 that assessed the effects of dietary supplements on the cognitive performance of video gamers. *Sources of evidence:* The Web of Science, PubMed, Scopus, and Google Scholar databases. *Charting methods:* PRISMA's (2020) flow diagram was used to create the data chart. *Results:* Sixteen studies were outlined. Thirteen were randomized, thirteen applied acute interventions, ten applied a crossover design and only three weren't placebo-controlled. Of the 10 studies that included caffeine (40–200 mg), four reported significant positive effects on cognition (attention, processing speed, working memory), two on first-person shooter video gaming performance (reaction time, hit accuracy, time to hit 60 targets), and one on Tetris game score. All 3 studies that included arginine silicate (1500 mg) reported significant improvements in one or more aspects of cognition (reaction time, attention, visual representation, and spatial planning). Two studies that tested sucrose (21 and 26.8 g) didn't report significant improvements, while one study that tested 26.1 g of glucose registered significant positive effects on processing speed and sustained attention. *Conclusions:* The published literature has focused on the effects of caffeine, which may exert both positive and negative effects on esports players. Additional, high-quality research is needed.

Keywords: esports, video games, dietary supplements, nootropics, cognitive enhancement

Introduction

esports emerged in the early 1990s, powered by the birth of the world wide web (www) and the development of software and hardware with network and multiplayer playing capabilities [1]. Since then, esports, or video game competitions, have been gaining relevance and accumulating an audience and currently represent a market worth millions of dollars [2].

The use of cognitive performance-enhancing drugs seems ubiquitous in esports [3], mainly prescription stimulants such as pharmaceutical amphetamines, methylphenidate, and modafinil [4]. The Ip, Urbano et al. (2021) survey revealed that 6.1% of online video game players use prescription medications to enhance their video gaming performance [5]. The highly competitive environment, the desire to win no matter the cost, the monetary prizes, the typically short professional careers, the long duration of tournament matches, and the almost complete absence of anti-doping testing, may explain why esports competitors resort to illegitimate use of controlled substances in an attempt to enhance their performance [3, 6], which threatens esports fair play [7] and increases the risk of health complications [8, 9, 10].

Health professionals should be able to advise esports competitors on these issues based on the current level of evidence, namely on alternatives, such as nootropic supplements that are not forbidden and do not harm health. Nootropics are compounds that improve one or more aspects of cognitive performance, including reaction time, alertness, memory, attention, and mood [11]. These and other elements of cognition are especially relevant to esports players, including fluid intelligence, executive function, fine motor skills, and resistance to mental fatigue [2]. In the United States, about 32% of young adults use dietary supplements (DS) regularly [12]. Various companies have been formulating and launching supplements targeted at esports players and actively promoting them as aids to improve performance in training and competitions [13, 14, 15].

DS recommendations should be sport-specific and accordingly to the subject's characteristics [16], including sports expertise (untrained versus highly trained) [17]. Mastery of video games is associated with brain adaptations that may decrease DS efficacy, including a decrease in cerebral glucose expenditure, even when accompanied by a sevenfold increase in gaming performance [18]. Furthermore, Melentev et al. (2020) demonstrated that highly competitive esports players present distinct electroencephalogram (EEG) activity compared to casual video gamers [19].

This warrants the conduction of investigations that assesses the efficacy of DS on video gamers. This scoping

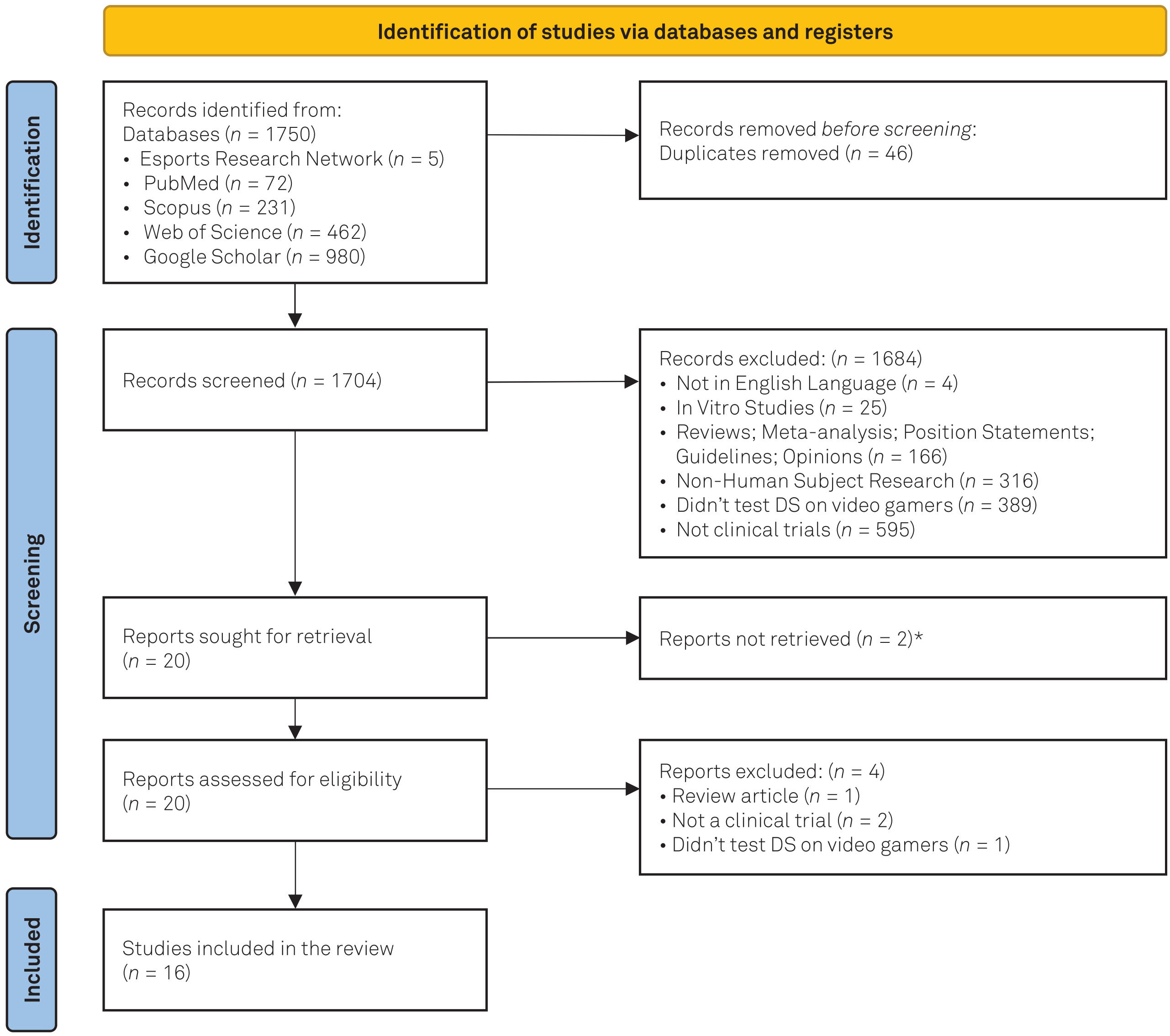

Figure 1. PRISMA 2020 flow diagram. *Although the full article of the studies authored by Emerson et al. (2022), and Kriter (2020) could not be retrieved because these authors only published an abstract, the authors of this scoping review chose to include these studies as their content fit the scope of this review.

review will outline the studies that tested the effects of DS on video gaming, summarize their findings, highlight potential knowledge gaps, and recommend a future research agenda.

Methods

This scoping review adopted the methodology described in the PRISMA Extension for Scoping Reviews [20]. A review protocol has been registered on the Open Science Framework website and can be found at https://osf.io/k32w4/.

The application of the methodology, the database searches, and the selection of articles to be assessed for inclusion in this review were carried out by the first author. All authors assessed the titles and abstracts independently and came to an agreement on the final articles to be included. The initial search strategy was devised, tested, and refined by the lead author (Fernando J. Ribeiro), who received academic training in researching bibliographic databases. To identify pertinent papers, the lead author searched the Web of Science, PubMed, Scopus, and Google Scholar databases applying keywords related to esports, nutrition, and DS. The entire Esports Research Network database was also manually screened for relevant articles by reading the items' titles.

The eligibility criteria included studies that tested the effects of DS on video gaming, published in English, between 1990 (the beginning of esports history) [1] and 2023. Studies that did not investigate the effects of DS on video gaming performance were excluded, as well as animal trials, recommendations, and letters to the editor.

On PubMed, on Advanced Search, the following keywords and boolean operators were inserted in the "Query Preview" field: ("esport*" OR "e-sport*" OR "e-gamer*" OR "egamer*" OR "video gamer*" OR "cognitive enhancement") AND ("nutrition" OR "nutrient*" OR "supplement*" OR "nootropic*" OR "caffeine"). The search was limited to clinical trials; Language: English; Species: Humans; Publication date – custom range: 1990-01-01 to 2023-05-25.

Following the search in each database, conducted in May 2023, the returned references were exported to Endnote X9. The duplicates were then removed, as well as the references written in other languages than English. The titles and abstracts of the remaining articles were screened and those that didn't fit the eligibility criteria were removed. The full text of the remaining articles was obtained and read for identification of potentially relevant publications. The final decision for the inclusion of the retrieved articles was made by consensus and discussion between the authors of this review. The authors divided the studies into groups based on the categories of DS tested and assessed their content to present their findings, identify potential gaps in knowledge, and recommend future research.

The lead author applied the PRISMA (2020) flow diagram as a basis for creating the data chart [21]. The database search strategy is available as electronic supplementary material (ESM) 1. In a continual procedure, the data has been plotted separately, then the findings were presented and discussed between the authors (Table 1). A form has been created and tested by the author's team to extract and present key information regarding the studies described in this review, including the reported year of publication, country of origin, aims/purpose, study population, subjects age, sample size, study design, methodology/methods, intervention type/duration, substances tested, comparator, outcome measures, and key findings (Table 1).

As clinical studies may be affected by methodological errors that can influence the outcomes of studies that tested the effects of a treatment, a critical appraisal of the included articles was conducted through the Jadad, Moore et al. (1996) scale (Table 2), which assesses the methodological quality of clinical trials, including randomization, double-blinding, and description of withdrawals and dropouts [22]. JADAD has high validity evidence, has been evaluated for reliability in various scenarios, and is one of the most referenced scales to assess the methodological quality of randomized controlled trials [23]. Its scale score ranges from 0 (very poor quality) to 5 (rigorous). Clinical trial articles with a score of 0–2 are considered poor quality, while those with a value of 3–5 points are deemed top quality [22, 24].

Results

Search results

The searches yielded a total of 1750 references, which were exported to EndNote X9. A total of 46 duplicates were removed. Of the remaining 1704 articles, 4 were written in another language than English, 166 were reviews, meta-analyses, position statements, guidelines or opinion articles, 133 were books, magazine articles, website articles, patents, supplementary material or multimedia content, 595 weren't clinical trials, 316 didn't involve human subjects, 25 were in vitro studies, and 445 didn't test the effects of DS on video gaming and thus were removed.

The full articles of the remaining 20 references were sought for retrieval, and 18 were obtained. Although the full article of the studies authored by Emerson et al. (2022), and Kriter (2020) could not be retrieved because these authors only published an abstract, the authors of this scoping review chose to include these studies as their content fit the scope of this review.

The full articles of the 18 references were assessed for eligibility, and 4 reports of clinical trials were excluded as they didn't evaluate the effects of DS on video gaming. Finally, a total of 16 studies remained and were included in this review [13, 14, 15, 25, 26, 27, 28, 29, 30, 31, 32, 33].

Quality of evidence

The mean score of the sixteen trials included in this review on the JADAD scale was 2.2 (ranging from 0 to 5). According to this scale, the trials conducted by La Monica et al. (2021) [15], Rhoden et al. (2021) [27], Tartar et al. (2021) [29], Furukado et al. (2022) [34], Emerson et al. (2022) [35], Lange et al. (2014) [32], Kriter (2020) [31], and Molesworth et al. (2008) [36] are low-quality studies (0–2 points), while the remaining eight studies classify as high quality (3–5 points) [13, 14, 25, 26, 28, 30, 33, 37]. Of note, only the articles authored by Franke et al. (2017) [28], and Bloomer et al. (2022) [37] reported withdrawals and dropouts. To our knowledge, none of the included articles has been retracted.

Included studies

This subsection presents a brief description of the characteristics and findings of the sixteen studies included in this review, ordered according to the main active substance tested in each study.

Table 1. Data items

Authors (year)	Country of origin	Aims/ purpose	Study population	Age¹	Sample size	Study design	Methodology	Intervention type	Comparator	Outcome measures	Key findings
Sowinki et al. (2021)	USA	Examine the acute effects of a combination of arginine, silicate, and inositol on cognitive performance.	Experienced esports players	23 (5) y	*n*=26 (18♂, 8♀)	Randomized, double-blind, placebo-controlled, crossover, prospective.	In 2 trials, 7–14 days apart, after 8–12 hours of fasting, volunteers underwent cognitive tests before receiving a supplement or placebo. They repeated the tests 15 min after ingestion, then played a video game for 60 min before repeating the tests.	1500 mg (~21.1 mg/kg) arginine silicate+100 mg inositol; Acute ingestion.	Placebo	Berg-Wisconsin Card Sorting Task test; Go/No-Go test; Sternberg Task test; Psychomotor Vigilance Task test; Cambridge Brain Sciences Reasoning and Concentration tests; Light Tracking Reaction test; Video game performance.	Video game performance (n) Berg-Wisconsin Card Sorting Task test (n) Go/No-Go test (n) Psychomotor Vigilance Task Test (n) Cambridge Brain Sciences tests (n) Light Tracking Reaction Test (n) ↓ Reaction time (Sternberg Task Test) ☺
Tartar et al. (2019)	USA	Examine the effects of a combination of arginine, silicate, and inositol on cognitive performance.	Experienced esports players	28.6 (5.4) y	*n*=60 (50♂, 10♀)	Randomized, double-blind, placebo-controlled, parallel-group, prospective.	Volunteers ingested a supplement or placebo for 7 days. On days 1 and 7, before and 15 min after dosing, subjects completed a battery of cognitive tests, played a video game for 60 min, and repeated the cognitive tests.	1500 mg (~17.4 mg/kg) arginine silicate +100 mg inositol; Ingested daily for 7 days.	Placebo	Trail Making Test (TMT) A and B; Stroop Test; Video game performance.	Video game performance (n) Stroop test (n) TMT A completion time (n) TMT B completion time (n) ↓ TMT B errors ☺
Emerson et al. (2022)	USA	Examine the effects of a combination of arginine, silicate, and inositol on cognitive performance.	Experienced esports players	[18–32 y]	*n*=9 (♂,♀)²	Open-label, parallel-group, prospective.	Volunteers ingested a supplement daily for 7 days. On days 1 and 7, subjects completed a set of cognitive tests.	600 mg arginine +105 mg silicon +385 mg inositol +60 mg potassium; Ingested daily for 7 days.	Pre-suppl-ementation regime cognitive test scores	6 Cambridge Brain Sciences tasks: – Feature Match (Visual perception); – Double Trouble (Stroop test for attention); – Mental Rotations (Visual representation); – Polygons (Object relationship); – Odd One Out (Deductive reasoning); – Spatial Planning (Forethought/ sequencing).	↑ Attention/concentration ☺ ↑ Visual representation ☺ ↑ Spatial planning ☺ Visual perception (n) Visuospatial processing (n) Deductive reasoning (n)

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Table 1. Data items (Continued)

Authors (year)	Country of origin	Aims/ purpose	Study population	Age¹	Sample size	Study design	Methodology	Intervention type	Comparator	Outcome measures	Key findings
Lange et al. (2014)	Germany	Assess the influence of glucose on cognitive and gaming performance.	University students; Tetris players	21.8 (2.6) y	*n*=70 (62♀, 8♂)	Randomized, blinded, placebo-controlled, parallel-group.	Volunteers ingested either 250 mL of caffeine-free soda sweetened with sugar or an artificial sweetener ≥10-15 min before playing Tetris for 10 min.	26.8 g of sugar; Acute ingestion.	Placebo	Video game performance (Tetris): % of single-line clears; – % of four-line clears; – Total number of lines; – Number of restarts; – Total score.	n
Rhoden et al. (2021)	USA	Assess the link between blood glucose levels and performance in esports.	Experienced esports players	22 (3.0) y	*n*=10 (9♂, 1♀)	Randomized, crossover.	In 2 trials, 24 hours apart, 8-hour fasting volunteers had a nutritious bar and continued fasting before having their performance assessed during 1 hour of video gaming.	Cliff bar containing 44 g of carbohydrates (21 g sugar); Acute ingestion.	Fasting	Video game performance (osu!; Aim Hero).	n
Furukado et al. (2022)	Japan	Assess the influence of glucose on cognitive and gaming performance.	University students	20.3 (1.2) y	*n*=20 (♂)	Randomized, double-blind, placebo-controlled, crossover.	In 2 trials, 2 weeks apart, volunteers received a placebo or a candy containing glucose and completed cognitive tests and EEG assessments before and after playing a racing game.	Glucose (26.1 g); Acute ingestion.	Placebo	Trail-making tests (TMT-A and TMT-B); Racing game performance (Gran Turismo Sport); Electroencephalogram (EEG) power.	↑ Processing speed ☺ ↑ Sustained attention ☺ ↑ Alpha and sensorimotor rhythm waves (EEG) at 25 min ☺
Molesworth et al. (2008)	Australia	Determine the acute effects of caffeine on video game performance	Aircraft pilots	20.6 (2.2) y	*n*=42 (♂)	Randomized, placebo-controlled, single-blind, between-subjects.	Volunteers played a game (baseline) before ingesting a placebo (0 mg), 3 mg, or 5 mg/kg of caffeine. 30 min later they played another game (final test).	Caffeine (5 mg/kg); Acute ingestion.	Caffeine: 3 mg/kg; Placebo.	Video game Space Fortress total score (Control, Speed, and Accuracy).	n

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Table 1. Data items (Continued)

Authors (year)	Country of origin	Aims/ purpose	Study population	Age[1]	Sample size	Study design	Methodology	Intervention type	Comparator	Outcome measures	Key findings
Sainz et al. (2020)	Spain	Determine the acute effects of caffeine on reaction time and video game performance.	Professional esports players: 7 FN and 8 CS: GO players	22 (3) y	n=15 (♂)	Randomized double-blind, placebo-controlled, cross-over.	In 3 trials, 3 days apart, 8-hour fasting participants ingested a placebo or caffeine. 45 min later, they completed a reaction time test and played an FPS game.	Caffeine (3 mg/kg/ bodyweight); Acute ingestion.	Placebo	Simple Visual Reaction test; FPS video game performance (3D Aim Trainer).	↑ Hit accuracy ☺ ↓ Reaction time ☺ ↓ Time to hit 60 targets ☺
Franke et al. (2017)	Germany	Assess the acute effects of methyl-phenidate, modafinil, and caffeine on cognitive and chess performance.	Elite chess players	37.3 (12.5) y	n=39 (♂)	Randomized, double-blind, placebo-controlled, cross-over.	On 4 trials, 7 days apart, the volunteers took breakfast, completed a set of cognitive tests, ingested caffeine, methylphenidate, modafinil, or a placebo, then played 10 chess games against a computer program, followed by another round of tests. The procedure was repeated in the afternoon, after lunch.	Caffeine (200 mg, ~2.5 mg/kg); Ingested twice a day with a 4 h interval; Acute ingestion.	Placebo	Stroop task; Psycho-Motor-Vigilance-Test; Trail-Making-Test; Wisconsin-Card-Sorting-Test; Balloon Analogue Risk Task; Tower of Hanoi.	Interference inhibition (n) Selective attention (n) Alertness (n) Psychomotor speed (n) Risk-taking (n) Behavior control (n) Cognitive control (n) Planning capacity (n) Problem-solving capacity (n) Chess game score (n) ↑ Time of reflection per game ☹
La Monica et al. (2021)	USA	Assess the acute effects of a combination of caffeine, methylliberine, and theacrine, on video game performance.	Recreational video gamers	23.4 (5.7) y	n=9 (♂)	Repeated measures, double-blind, crossover, placebo-controlled.	In 3 trials, 8-hour fasting participants ingested either a placebo, caffeine, or a combination of caffeine, methylliberine, and theacrine and then completed four 20-min gaming sessions designed to assess performance at 0, 60, 120, and 180 min.	125 mg (~1.5 mg/ kg) caffeine+75 mg methylliberine +50 mg theacrine (CMT); Acute ingestion.	Caffeine (125 mg); Placebo	FPS video game performance (Aimlab).	CMT: ↑ Visuospatial working memory vs. PL and Caffeine ☺ CMT: ↓ Median kill time vs. PL ☺ Caffeine: ↑ Time on target tracking vs. PL and CMT ☺ Caffeine: ↓ Reaction time for false alarms vs. PL and CMT ☹

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Table 1. Data items (Continued)

Authors (year)	Country of origin	Aims/ purpose	Study population	Age¹	Sample size	Study design	Methodology	Intervention type	Comparator	Outcome measures	Key findings
Tartar et al. (2021)	USA	Assess the acute effects of caffeine, methylliberine, and theacrine on cognitive performance.	Experienced esports players (FPS)	20.5 (2.0) y	*n*=50 (♂)	Randomized, repeated measures, double-blind, crossover, placebo-controlled.	In 3 trials, 1 week apart, volunteers received either a placebo, caffeine, or a combination of caffeine, methylliberine, and theacrine and then completed a set of cognitive tests.	125 mg (~1.5 mg/kg) caffeine+75 mg methylliberine +50 mg theacrine (CDT); Acute ingestion.	Caffeine (125 mg); Placebo	Flanker Test of Inhibitory Control; Psychomotor Vigilance Task; Pattern Comparison Processing Speed Test; Dimensional Change Card Sort Test; Electroencephalogram (EEG) power.	CDT & Caffeine: ↑ Attention, inhibitory control (Flanker test) vs. PL ☺ CDT: ↓ Reaction time (Psychomotor vigilance test) pre to post ☺ Caffeine: ↓ Delta power (EEG) ☹ CDT: ↑ Delta & theta bands (EEG) ☺ Pattern Comparison Processing Speed Test (n) Dimensional Change Card Sort Test (executive function) (n)
Bloomer et al. (2022)	USA	Assess the acute effects of caffeine and polyphenols on cognitive and video game performance.	Experienced esports players (FN)	22 (3.0) y	*n*=49 (47♂, 2♀)	Randomized, double-blind, placebo-controlled, crossover.	In 3 trials, 7 days apart, on a 3-hour fast, volunteers received either a placebo, caffeine, or a combination of caffeine and polyphenol antioxidants, and then completed cognitive tests.	Combination of 270 mg (~3.3 mg/kg) caffeine and polyphenols; Acute ingestion.	Caffeine (270 mg); Placebo	Reaction Time (Go/No-Go); Digit Symbol Substitution Test; AX-Continuous Performance Test; Third-person shooter video game performance (FN).	n
Leonard et al. (2023)	USA	Assess the acute and 30-day effects of a combination of microalgae (Phaeodactylum tricornutum) and guarana on cognitive and video game performance.	Experienced esports players (FPS, LOL, Super Smash Bros, Rocket League)	21.7 (4.1) y	*n*=61 (51♂, 10♀)	Randomized, double-blind, placebo-controlled, parallel-group, prospective.	Volunteers ingested a supplement daily for 30 days. On days 1 and 30, subjects completed a set of cognitive tests and played video games for 60 min.	Low dose: 4.4 mg of fucoxanthin +40-44 mg (~0.5–0.6 mg/kg) of caffeine, OR; High dose: 8.8 mg of fucoxanthin +40–44 mg of caffeine.	Placebo	Berg-Wisconsin Card Sorting Task; Go/No-Go Task; Sternberg Task; Psychomotor Vigilance Task; Light Tracking Reaction Test; Video game performance (FPS, LOL, Super Smash Bros, Rocket League).	n
Thomas et al. (2019)	USA	Examine the acute effects of a sugar-free energy drink on cognition and video game performance.	Professional esports players (LOL)	21 (2) y	*n*=9 (♂)	Randomized, double-blind, placebo-controlled, cross-over.	Volunteers completed cognitive tests before consuming an energy drink or a placebo, then repeated the tests after playing each of the 3 competitive LOL games.	Sugar-free energy drink (Reload™) containing 150 mg (~1.9 mg/kg) caffeine; Acute ingestion.	Placebo	Eriksen Flanker test; Go/No-go test; N-back test; Hand grip strength.	Attention (n) Reaction time (n) Response inhibition (n) Fatigue (n) ↑ Working memory ☺

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Table 1. Data items (Continued)

Authors (year)	Country of origin	Aims/ purpose	Study population	Age¹	Sample size	Study design	Methodology	Intervention type	Comparator	Outcome measures	Key findings
Schwager et al. (2023)	USA	Examine the acute effects of a sugar-free energy drink on cognition and video game performance.	Video gamers	25.2 (5.8) y	*N*=45 (37♂, 8♀)	Randomized, double-blind, placebo-controlled, cross-over.	40 min after ingesting the supplement, the volunteers were subjected to a battery of cognitive tests and played 5 different video games.	Sugar-free energy drink (C4 Smart Energy) containing 200 mg caffeine and tyrosine; Acute ingestion.	Placebo	10 CNS Vital Signs tests: – Verbal Memory Test; – Visual Memory Test; – Finger Tapping Test; – Symbol Digit Coding; – Stroop Test; Shifting Attention Test; – Continuous Performance Test; – Perception of Emotions Test; – Non-Verbal Reasoning Test; – Four Parts Continuous Performance Test.Video game performance (Tetris, Four-in-a-Row, Rayman Legend, FIFA-14, Call of Duty: Advanced Warfare).	Visual memory (n) Verbal memory (n) Composite memory (n) Reaction time (n) Simple attention (n) Complex attention (n) Processing speed (n) Social acuity (n) Reasoning (n) ↑ Cognitive flexibility ☺ ↑ Executive function ☺ ↑ Sustained attention ☺ ↑ Motor speed ☺ ↑ Psychomotor speed ☺ ↑ Working memory ☺ ↑ Tetris game scores ☺ Four-in-a-Row (n) Rayman Legend (n) FIFA-14 (n) Call of Duty: Advanced Warfare (n)
Kriter (2020)	USA	Examine the acute effects of a sugar-containing energy drink on recognition and reaction.	Not reported	Not reported	*n*=5	Not reported	The volunteers played 5 rounds of Tetris before ingesting the supplement, then practiced for 15 min and played 5 additional rounds of Tetris.	Energy drink (Red Bull) containing 80 mg of caffeine, 21.5 g of sucrose, 5.3 g of glucose, and 1000 mg of taurine; Acute ingestion.	Tetris score before ingesting the energy drink.	Tetris game scores.	n

Abbreviations: FPS: First-person shooter; CS: GO: Counter-Strike: Global Offensive; FN: Fortnite; LOL: League of Legends; EEG: Electroencephalogram; TMT: Trail Making Test; CDT: Combination of 125 mg caffeine+75 mg methylliberine+50 mg theacrine; CMT: Combination of 125mg caffeine+75 mg methylliberine+50 mg theacrine; PL: Placebo; ↑: Increase; ↓: decrease; n: No statistically significant differences; ☺: improved cognitive/gaming performance; ☹: worsening cognitive/gaming performance; ¹Age: Mean (SD); [2]Did not report the sample size for each sex.

Table 2. JADAD evaluation scale

	Sowinski et al. (2021)	Tartar et al. (2019)	Tartar et al. (2021)	Thomas et al. (2019)	Sainz et al. (2020)	Franke et al. (2017)	La Monica et al. (2021)	Rhoden et al. (2021)	Bloomer et al. (2022)	Furukado et al. (2022)	Emerson et al. (2022)	Leonard et al (2023)	Schwager et al. (2023)	Lange et al. (2014)	Kriter (2020)	Molesworth et al. (2008)
Was the study described as randomized?	1	1	1	1	1	1	0	1	1	1	0	1	1	1	0	1
The method was described and appropriate? (+1)	–	–	–	–	1	–	–	–	–	–	–	1	–	–	–	–
The method was described and inappropriate? (−1)	–	–	–	–	–	–	–	−1	–	–	–	–	–	–	–	–
Was the study described as double-blind?	1	1	1	1	1	1	1	0	1	1	0	1	1	0	0	0
The method was described and appropriate? (+1)	1	1	–	1	1	1	1	–	1	–	–	1	1	–	–	–
The method was described and inappropriate? (−1)	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Was there a description of withdrawals and dropouts?	0	0	0	0	0	1	0	0	0	0	0	1	1	0	0	0
Total Score	**3**	**3**	**2**	**3**	**4**	**4**	**2**	**0**	**3**	**2**	**0**	**5**	4	**1**	**0**	**2**

Caffeine

In an experiment with a randomized, placebo-controlled, single-blind, between-subjects repeated measures design, Molesworth et al. (2008) [36] tested the effects of caffeine supplementation on video game performance (Space Fortress). Forty-two Australian pilots with a mean age of 20.6 (SD=2.2) and 135.7 (SD=76.8) hours of flight experience were recruited and randomly divided into three groups (0 mg, 3 mg, or 5 mg/kg of caffeine). After being briefed on the rules and mechanics of the video game Space Fortress, the volunteers played a game session to obtain baseline values. Then, they ingested a lemon-flavored drink containing either zero, three, or five mg of caffeine per kg of body weight, and 30 minutes later, they played one last game. Each game session lasted about 3 minutes. The Cognitive Psychophysiological Laboratory at the University of Illinois created Space Fortress, a freely accessible video game, to measure the ability to perform complicated interactive tasks. The authors registered the video game's total score, which comprised the sub-variables control, speed, and accuracy. Control assesses hand-eye coordination and dexterity while the player tries to maintain the ship's direction and position during the game. Speed assesses working memory capacity and reaction time as the player recognizes and responds to stimuli (enemy mines). Accuracy assesses psychomotor skill as the player successfully hits his target (fortress). The authors of this study did not detect any statistically significant differences between the three groups in any of the evaluated variables. No assessments or occurrences of side effects have been reported.

The effects of caffeine on the cognitive performance of professional esports players have been tested in a double-blind, placebo-controlled crossover study conducted by Sainz et al. (2020) in Spain [26]. The volunteers consisted of 7 Fortnite and 8 Counter-Strike: Global Offensive professional male players, with a mean age of 22 (SD=3) years, and which averaged 10 (SD=2) hours of esports training per day. On two occasions, separated by 3 days, they received 3 mg/kg of caffeine or a placebo, 45 to 60 min before performing 5 attempts in a simple visual reaction time and 3 attempts at a 2-min FPS game (3D Aim Trainer) in which each subject had to hit 60 fixed targets on each occasion and that included hit accuracy and average hit time variables. These investigators observed significant improvements of caffeine on the simple visual reaction time test [0.20 (SD=0.01) vs. 0.19 (SD=0.01) s, $p<0.01$], in the mean time entailed to hit 60 targets that showed in each try at the FPS computer game [0.92 (SD=0.07) vs. 0.88 (SD=0.07) s, $p<0.01$], and on the targets hit accuracy [98.8 (SD=0.92) vs. 99.8 (SD=0.35) of targets hit, $p<0.01$] compared to the placebo condition.

In a randomized placebo-controlled crossover study, Franke et al. (2017) [28] tested the effects of 200 mg

Table 3. Limitations of the included studies

	Molesworth et al. (2008)	Sainz et al. (2020)	Franke et al. (2017)	Thomas et al. (2019)	La Monica et al. (2021)	Bloomer et al. (2022)	Tartar et al. (2021)	Leonard et al. (2023)	Schwager et al. (2023)	Kriter (2020)	Tartar et al. (2019)	Sowinski et al. (2021)	Emerson et al. (2022)	Rhoden et al. (2021)	Furukado et al. (2022)	Lange et al. (2014)
Main DS tested	Caffeine											L-Arginine	Carbohydrates			
Excluded smokers	–	Yes	Yes	–	–	–	Yes	–	Yes	–	Yes	–	–	–	–	–
Excluded consumers of caffeine-containing beverages	–	Yes	Yes	–	Yes	–	Yes	Yes	–	–	–	Yes	–	–	–	–
Requested to stop caffeine intake before testing	Yes	Yes	–	Yes	Yes	Yes	–	Yes	Yes	–	Yes	–	–	–	–	–
Reported habitual caffeine consumption	–	–	–	–	–	Yes	–	–	Yes	–	–	–	–	Yes	–	–
Requested to stop alcohol intake before testing	No	Yes	–	–	No	Yes	–	–	Yes	–	Yes	–	–	–	–	–
Excluded DS users	No	Yes	–	–	Yes	–	–	Yes	–	–	–	Yes	–	–	–	–
Requested to cease DS intake before testing	–	–	–	–	Yes	–	–	Yes	–	–	Yes	Yes	–	–	–	–
Excluded medicine users	–	Yes	Yes	–	Yes	–	Yes	–	–	–	–	Yes	–	–	Yes	–
Assessed sleepiness or sleep duration/quality	Yes	Yes	–	–	–	–	–	Yes	Yes	–	–	–	–	–	–	–
Assessed physical exercise before testing	–	Yes	–	–	–	Yes	–	Yes	Yes	–	–	–	–	–	–	–
Requested to refrain from or moderate physical exercise	–	Yes	–	–	Yes	–	–	–	Yes	–	–	–	–	–	–	–
Assessed the volunteer's typical diet (e.g. food diary)	–	–	–	–	Yes	Yes	–	Yes	Yes	–	–	Yes	–	–	–	–
The DS was tested for purity and potency by a third-party laboratory	–	–	–	–	Yes	–	–	–	Yes	–	No	Yes	–	–	–	–
The DS manufacturer/source was stated	–	Yes	–	Yes	Yes	–	–	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
The DS dosage was adjusted to the volunteer's body weight (kg)	Yes	Yes	–	No	No	–	–	No	No	–	–	–	–	–	–	–
Reported if the DS was consumed in a fasted or fed state	Yes	–	Yes	–	Yes	Yes	–	Yes	Yes	–	–	Yes	–	Yes	–	Yes
Reported the specific hours of the day for DS and tests administration	Yes	Yes	Yes	Yes	–	Yes	–	–	–	–	–	–	–	–	–	–
Reported the number of hours of videogame play per day/week	Yes	Yes	–	Yes	–	Yes	–	–	–	–	–	–	Yes	Yes	–	–
Reported esports players expertise level (e.g. professional)	–	Yes	Yes	Yes	Yes	–	–	–	–	–	–	–	–	–	–	–

(Continued on next page)

Table 3. Limitations of the included studies (Continued)

	Molesworth et al. (2008)	Sainz et al. (2020)	Franke et al. (2017)	Thomas et al. (2019)	La Monica et al. (2021)	Bloomer et al. (2022)	Tartar et al. (2021)	Leonard et al. (2023)	Schwager et al. (2023)	Kriter (2020)	Tartar et al. (2019)	Sowinski et al. (2021)	Emerson et al. (2022)	Rhoden et al. (2021)	Furukado et al. (2022)	Lange et al. (2014)
Reported the specific video game genre the volunteers typically played	–	Yes	Yes	Yes	–	Yes	Yes	Yes	–	–	–	–	–	–	–	Yes
Assessed DS side effects	–	–	Yes	–	Yes	Yes	Yes	Yes	Yes	–	Yes	Yes	–	–	–	–
Performed sample size calculations	–	–	Yes	–	–	–	–	Yes	–	–	–	–	–	–	–	–
Enrolled a sufficient number of volunteers to detect effect sizes (n≥15)	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes
The study was funded by a food or DS company	–	–	No	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	Yes	Yes	–	Yes	–

Abbreviations: DS: dietary supplement.

(~2.5 mg/kg) of caffeine on 39 German male chess players [mean age: 37.3 (SD=12.5) y, body weight: 81.0 kg (SD=13.9), height: 179.7 (SD=6.9) cm, BMI 25.0 (SD=3.7) kg/m^2] in a battery of cognitive tests and a series of rapid chess games. These were highly skilled tournament players, with a mean ELO score of 1670.4 (SD=340.0) and an intelligence quotient (IQ) of 127.7 (SD=11.3). The set of cognitive tests included the Stroop task, Psycho-Motor-Vigilance-Test, Trail-Making-Test, Wisconsin-Card-Sorting-Test, Balloon Analogue Risk Task, and Tower of Hanoi. Each chess game had a time limit of 15 min, in which the participants played against a computer program. Although these investigators detected trends for an improved score in all games [from 0.510 (SD=0.028) to 0.543 (SD=0.023); p=0.164], caffeine significantly increased the average time of decisive reflection per chess game (from 436.8 (SD not stated) to 530.1 (SD not stated) s; p<0.001), which increased timeout game losses in comparison with the placebo condition (from 30 (SD not stated) to 70 (SD not stated) games; p=0.023). Short-term adverse effects were reported by 6 volunteers (8 events) treated with caffeine. The most common were headaches (3 subjects).

Thomas et al. (2019) [13] conducted a randomized, double-blind, placebo-controlled, crossover study in which they tested the effects of an energy drink (Reload^{TM}) containing 150 mg (~1.9 mg/kg) of caffeine on attention, reaction time, working memory, and fatigue on players of League of Legends, an action real-time strategy game. The 9 participants were members of a professional male team that trained in esports for an average of 10.3 (SD=2.1) hours a day and had a mean age of 21 (SD=2) y, body weight: 80.1 kg (SD=13.9), height: 177.0 (SD=7.0) cm, BMI 25.6 (SD=3.4) kg/m^2]). The cognitive tests applied included measures of attention (Erikson Flanker Test), reaction time and response inhibition (Go/No-Go visual test), working memory (n-back test), and fatigue (hand grip strength and finger tap speed). The mean reaction time significantly improved in the n-back test for the energy drink [−171 ms (95% CI, −327.91 to −14.09), p<0.004] versus the placebo condition [−92 ms (95% CI, −213.63 to 29.63)], indicating enhanced working memory. These investigators didn't observe any statistically significant effects in the remaining cognitive tests. Of note, the energy drink included 12 g of glycerol, 150 µg of cobalamin, 70 mg of magnesium, 40 mg of sodium, and a non-disclosed quantity of theanine, NADH, choline, phosphatidylserine, alpha-glycerylphosphorylcholine, and L-Carnitine. No health side effects were assessed nor described in this study.

In a repeated-measures, double-blind, crossover, placebo-controlled trial, La Monica et al. (2021) [15] tested the acute effects of 125 mg (~1.5 mg/kg) of caffeine, or a combination of 125 mg of caffeine with 50 mg of theacrine and 75 mg of methylliberine (CMT) on nine male amateur esports players [mean age: 23.4 (SD=5.7) y, body weight: 86.0 kg (SD=17.1), height: 178.9 (SD=5.8) cm, BMI: 26.7 (SD=4.0) kg/m^2], on a first-person shooter game (Aim Lab). Aim Lab included 4 tasks: 1) the Spidershot, in which the participant must shoot an orb three times to "kill" the target, which is presented on the screen at pseudo-random intervals. It assesses motor control, precision, accuracy, and reaction time; 2) the TriggerControl, a go/no-go style test, evaluates visual processing speed and accurateness, as well as the cognitive capacity to prevent premature responses, false alarms, and reaction time; 3) the Spheretrack, in which one must maintain the crosshair of a virtual weapon on a moving orb as long as possible, tests motor control and visuospatial processing of motion 4) the Capacity, in which the participant is required to recognize and shoot targets that have changed color, assesses visuospatial working memory. On the Spidershot task, CMT lowered reaction time from starting point compared with placebo (Effect Size as ξ=0.35; p=0.017), while the decrease with the caffeine alone wasn't statistical significance in comparison with the placebo condition (ξ=0.35; p=0.061). On the Spheretrack task, caffeine increased the proportion of time on target compared to CMT (ξ=0.50; p=0.047) and placebo (ξ=0.50; p=0.008). CMT improved the visual capacity threshold in the Capacity task compared with caffeine (ξ=0.48; p=0.007) and a placebo (ξ=0.48; p=0.030). However, caffeine provided a significant reduction in the time to kill in comparison with the placebo (ξ=0.37; p=0.018), while the reduction in the CMT condition didn't reach statistical significance compared to the placebo (ξ=0.37; p=0.065). Additionally, in TriggerControl, caffeine significantly decreased reaction time for false alarms (trigger happy) compared to both CMT (ξ=0.61; p=0.001) and placebo (ξ=0.61; p=0.002). Despite the authors stating an absence of adverse effects, the caffeine condition caused a significantly substantial rise in jitteriness compared to the placebo (ξ=0.27; p=0.043) and they registered a significantly greater increase from baseline in systolic blood pressure for CMT (ξ=0.37; p=0.020) and caffeine (ξ=0.37; p=0.025) compared to placebo.

More recently, Tartar et al. (2021) [29] also trialed caffeine (125 mg, or ~1.5 mg/kg), and a combination of 75 mg of Theacrine, 50 mg of Methylliberine, and 125 mg of caffeine (CDT) in a randomized, placebo-controlled, double-blinded, crossover study. The group of volunteers consisted of 50 amateur players [age: 18–40 years, mean body weight: 81.7 kg (SD=17.2), height: 177.6 (SD=9.1) cm], who accumulated at least 10 hours of practice in first-person shooter video games. These researchers tested the effects of each treatment on the Flanker Test of Inhibitory Control, which measures attention and inhibitory control; the Psychomotor Vigilance Task, which measures sustained attention through simple reaction time assessment; the Pattern Comparison Processing Speed Test, which assesses processing speed; the Dimensional Change Card Sort Test, which measures executive function. Additional tests included EEG alpha, beta, delta, and theta frequency bands while the volunteers performed the cognitive tests. These authors reported statistically significant increases in the Flanker test (attention and inhibitory control) score, from pre- to post-ingestion, for the CDT [from mean=60.6 (SD=9.9) to mean=63.0 (SD=8.1); p=0.004] and caffeine condition [from mean=60.0 (SD=10.4) to mean=63.1 (SD=8.7); p=0.002]. Significant declines (enhancement) were registered on the Psychomotor Vigilance Test reaction time, in the CDT condition from pre- to post-dose [from mean=283.4 (SD=90.0) ms to mean=267.5 (SD=63.2) ms; p=0.044]. They also observed significant decreases in delta power in the caffeine group from pre- to post-dose [from mean=31.5 (SD=20.1) to mean=25.9 (SD=14.9); p=0.035], but significant increases in the delta band (which may represent enhanced attention to internal cognitive processes) in the CDT group from pre to post-dose [from mean=25.8 (SD=13.7) to mean=29.6 to (SD=14.9); p=0.050] and theta bands (associated with higher greater cognitive control) [from mean=15.8 (SD=7.3) to mean=18.5 (SD=11.0); p=0.041]. No statistically significant differences were registered on the Pattern Comparison Processing Speed Test and Dimensional Change Card Sort Test. Regarding side effects, despite reporting jitteriness, heart rate, and blood pressure assessments, these authors provide no data or results regarding these variables.

Bloomer et al. (2022) [37] assessed the effects of a blend of caffeine and antioxidant polyphenols (AmaTea® Max) on experienced players of Fortnite, a third-person shooter video game. This placebo-controlled, double-blind, randomized study involved 49 healthy individuals [mean age: 22 (SD=3) y, body weight: 82 kg (SD=19), height: 178 (SD=8) cm), BMI 26 (SD=5) kg/m^2] which played video games a minimum of 4 h/day, 4 days a week. On three occasions, separated by a week, the volunteers ingested either a placebo, 270 mg (~3.3 mg/kg) of caffeine, or a blend of 270 mg of caffeine and polyphenol antioxidants (AmaTea®). The volunteers arrived at each laboratory visit in a 3-hour fasted state and played Fortnite during 4 periods of 1 hour each. Their cognitive performance was assessed through Fortnite videogame statistics, namely the number of "kills" per match and the overall placement (ranking) of their team. Additionally, they were subjected to the Digit Symbol Substitution test and the Reaction Time test, performed at baseline and repeated at 1, 2, 3, and after 4 hours of gameplay.

The AX-Continuous Performance Test was also applied at baseline and after 4 hours of Fortnite gaming. These authors didn't register statistically significant differences regarding any cognitive tests or any aspect of gaming performance. Regarding side effects, caffeine, and AmaTea® significantly raised systolic blood pressure (SBP) compared to the placebo (p<0.05). It increased from 123 (SD=13) at hour 0 to 131 (SD=13) mmHg at hour 3 for caffeine, and from 122 (SD=11) at hour 0 to 131 (SD=13) mmHg at hour 3 in the AmaTea® condition. Additionally, the caffeine condition, but not AmaTea®, was associated with significantly higher jitteriness compared to the placebo condition (p=0.02), increasing from 26 (SD=27) at hour 0 to 35 (SD=28) at hour 1.

In a crossover design study that hasn't been randomized, double-blinded, or controlled for placebo, Kriter (2020) [31] aimed to investigate if supplementation with caffeine, provided through an energy drink (Red Bull), improves recognition capacity and reaction time, as assessed through Tetris game scores. For this experiment, the author recruited 5 volunteers, which played a session of 5 rounds of Tetris, then drank the energy drink before playing an additional session of 5 rounds of the Tetris video game. Each session was preceded by 15 minutes of Tetris "warm-up". Assuming that the volunteers have received the "classic" Red Bull energy drink, one serving (250 mL) would have provided 80 mg of caffeine per serving, 21.5 g of sucrose, 5.3 g of glucose, 1,000 mg of taurine, 60 mg of glucuronolactone, 50 mg of inositol and vitamins (niacin, panthenol, B6, B12) [38]. Although the author reported gradual trends for improvements in Tetris score in the Red Bull condition, he didn't observe statistically significant differences between the two sessions of Tetris video gaming. No additional information was provided by the author regarding the participant characteristics or side-effect assessment [31].

In a randomized, double-blind, placebo-controlled, crossover trial, Schwager et al. (2023) [33] tested the acute effects of an energy drink (C4 Smart Energy) on the cognitive function and gaming performance of 45 healthy young adults [37 males, 8 females; mean age=25.2 (SD=5.8) y; height=173.2 (SD=8.9) cm; weight=76.7 (SD=15.4) kg; BMI=25.5 (SD=4.4) kg/m^2] who played video games at least 1 h per week.

On two occasions, separated by a one-week washout period, the participants ingested either a placebo beverage or a sugar-free energy drink containing 200 mg of caffeine, potassium, niacin, vitamin B12, citicoline, and tyrosine. Fourteen minutes after ingesting the drink, the volunteers were subjected to a battery of 10 cognitive tests (CNS Vital Signs) which included the Verbal Memory Test, Visual Memory Test, Finger Tapping Test, Symbol Digit Coding, Stroop Test, Shifting Attention Test, Continuous Performance Test, Perception of Emotions Test, Non-Verbal Reasoning Test, and the Four Parts Continuous Performance Test. These tests assessed 15 cognitive domains: verbal memory, visual memory, composite memory, psychomotor speed, reaction time, complex attention, cognitive flexibility, processing speed, motor speed, executive function, simple attention, social acuity, reasoning, sustained attention, and working memory. Afterward, the participants' gaming performance was assessed in five different video games: Tetris, Four-in-a-Row, Rayman Legend, FIFA-14, and Call of Duty: Advanced Warfare. Adverse events were also assessed, including blood pressure, oxygen saturation, heart rate, cardiac electrical activity, heart palpitations, nausea, vomiting, bloating, diarrhea, constipation, itching, headache, fatigue and sleep duration, sleep disruptions, and sleep quality. The energy drink condition outperformed the placebo condition in terms of cognitive flexibility (absolute mean or median difference [95% CI]=+4.3 [2.2; 6.4]; p<0.001; d=0.63), executive function (+4.3 [2.3; 6.3]; p<0.001; d=0.63), sustained attention (+2.1 [0.6; 3.6]; p=0.01; d=0.44), motor speed (+2.9 [0.8; 4.9]; p<0.001; d=0.44), psychomotor speed (+3.9 [0.1; 7.7]; p=0.04; d=0.32) working memory (+1.0 [0.1; 1.9]; p=0.02; d=0.35), and in Tetris gaming scores (+463 [−419; 2,065] points; p=0.049; d=0.30). There were no statistically significant differences in complex attention, composite memory, visual memory, verbal memory, reaction time, reasoning, processing speed, social acuity, or simple attention, nor the scores in the video games Four-in-a-Row, Rainbow Legends, FIFA-14, and Call of Duty: Advanced Warfare. Except for blood pressure, there were no significant differences regarding side effects. The energy drink condition raised systolic and diastolic blood pressure by 2.9–5.0 mmHg and 3.7–5.4 mmHg, respectively.

In a double-blind, placebo-controlled, parallel trial, Leonard et al. (2023) [30] tested the acute and 30-day effects of a combination of microalgae (Phaeodactylum tricornutum) and guarana extract on the cognitive function and video-game performance of experienced esports players. The 61 volunteers (51 males, 10 females) averaged 21.7 (SD=4.1) y, 173.4 (SD=8.2) cm, 73 (SD=13) kg, and 24.2 (SD=3.6) kg/m2. 35 subjects played a first-person shooter game (Call of Duty: n=18, Overwatch: n=7, Valorant: n=10), 13 played Super Smash Bros., 11 played League of Legends, and 2 played Rocket League. The volunteers were randomly distributed into three groups. One placebo group; one low-dose group that ingested 440 mg of Phaeodactylum tricornutum extract, including 4.4 mg of fucoxanthin and 500 mg of guarana, containing 40–44 mg (or ~0.5–0.6 mg/kg) of caffeine; and one high dose group that ingested 880 mg of Phaeodactylum tricornutum extract (8.8 mg of fucoxanthin) and 500 mg of guarana. A battery of cognitive tests was administered at baseline, 15 minutes after taking the DS, and after 60 minutes of competitive gameplay using the participants' favorite video game. Subjects took the DS for 30 days before repeating pre- and post-gaming cognitive function assessments. The cognitive tests included the Berg-Wisconsin Card Sorting Task, the Go/No-Go Task, the Sternberg Task, the Psychomotor Vigilance Task, and the Light Tracking Reaction Test. The video game's performance was assessed through in-game scores. Questionnaires were used to assess potential side effects, namely sleep quality and duration, dizziness, rapid heart rate, heart palpitations, shortness of breath, fuzzy vision, and anxiousness. No statistically significant differences were registered between the 3 groups regarding cognitive performance, in-game performance, or side effects. However, some statistically significant (p<0.05) positive effects on cognitive performance (reaction times, reasoning, learning, executive control, attention shifting, and impulsiveness) were observed after acute supplementation, but mainly after 30-day supplementation.

L-Arginine

In a parallel-group, placebo-controlled trial, Tartar et al. (2019) [14] tested the effects of a supplement (nooLVL®) containing 1500 mg (~17.4 mg/kg) of arginine silicate and 100 mg of inositol, administered for seven days, on the cognitive performance of 50 males and 10 female amateur esports players [mean age: 28.6 (SD=5.4) y, body weight: 86.0 kg (SD=17.3), height: 178.6 (SD=6.7) cm], BMI 26.9 (SD=4.7) kg/m^2), who played video games for ≥5 hours per week. On two visits (7 days apart), the volunteers completed the Trail Making Test (TMT Parts A and B), and the Stroop Tests before, and 15 min after dosing. The TMT-A, B, and Stroop Test were again applied after 60 min of video game playing. Additionally, the subject's performance was also assessed through in-game scores. No significant differences were detected regarding video game performance and cognitive tests except for the TMT – Part B test, conducted on the first visit, in which the treatment group made significantly fewer errors in comparison with the placebo group fifteen minutes after supplement ingestion (p=0.04). Additionally, these investigators reported minimal and similar frequency of adverse effects (blood pressure and heart rate) in both groups, but without describing them in detail.

In a later study, Sowinski et al. (2021) [25] trialed the same supplement [1500 mg of arginine silicate, or ~21.1 mg/kg) +100 mg of inositol] on 26 healthy individuals with a mean age of 23 (SD=5) y, 71.1 kg (SD=13.8) of body weight, 171 (SD=11) cm of height, and a BMI of 20.7 (SD=3.5) kg/m^2, on a set of cognitive tests and gaming performance. The volunteers were experienced esports players who played video games at least 5 hours a week in the past 6 months. In this double-blind, randomized, placebo-controlled, and crossover trial, they acutely administered nooLVL®, or a placebo on two different occasions, separated by a 7 to 14-day interval. On each occasion, the volunteers fasted for 8 hours and then ingested the supplement or placebo (maltodextrin), before initiating a battery of cognitive tests, which included the Berg-Wisconsin Card Sorting Task test, Go/No-Go test, Sternberg Task Test, Psychomotor Vigilance Task Test, Cambridge Brain Sciences Reasoning and Concentration test, and a Visual Reaction Test. The subjects ingested the treatment, and 15 min later repeated the battery of cognitive tests. Hereafter, participants played their preferred eGame for one hour before repeating the battery of tests. No significant improvements in gaming performance were observed. In comparison with the placebo, supplementation with arginine+inositol only provided statistically significant improvements in the Sternberg Mean Present Reaction Time, namely in post-game 4 Letter Absent Reaction time (ES, as η_p^2=0.31; p=0.05), 6 Letter Present Reaction Time (η_p^2=0.41; p<0.01), 6 Letter Absent Reaction Time (η_p^2= 0.36; p=0.01), Mean Present Reaction Time (η_p^2=0.21; p=0.02), and Mean Absent Reaction Time (η_p^2=0.24; p=0.03). These investigators assessed side effects through a questionnaire. Reported adverse effects were sporadic and of mild severity, and there were no significant differences across regimens.

In a randomized, double-blind, placebo-controlled, parallel-group, prospective study, Emerson et al. (2022) [35] assessed the effects of nooLVL® on the cognitive performance of nine experienced esports players (18–32 y) who played video games at least 3–5 hours/week in the previous 6 months. The volunteers ingested 1600 mg of nooLVL® (600 mg of arginine, 105 mg of silicon, 385 mg inositol, and 60 mg potassium) per day for seven days, and were subjected to a battery of computerized cognitive tests at baseline, on day 1, and again 7 days after ingesting the supplement. These investigators detected statistically significant differences in the Stroop test (attention/concentration) when comparing baseline versus day 1 (p=0.0019), baseline versus day 7 (p=0.0005), and day 1 compared to day 7 (p=0.0369). Significance was also observed in the Mental rotations test (visual representation) when contrasting the baseline to day 1 (p=0.0506) and baseline to day 7 (p=0.0192). Outcomes of the Spatial Planning test (forethought and sequencing) also significantly improved when comparing day 7 to the baseline (p=0.0266). However, results from the Feature Match (visual perception), Polygons (object relationship), and Odd One Out (deductive reasoning) tests did not demonstrate significance (p values not reported).

Carbohydrates

In 2014, Lange et al. [32] conducted a randomized, placebo-controlled, parallel-group trial. Their purpose was to verify if the consumption of a sugar-containing drink after an initial self-control task (a go/no-go task) improved self-control performance in another self-control task (a Tetris video game). These authors recruited 70 university students

(62 female), who averaged 21.8 (SD=2.6) years, 21.5 (SD=2.8) kg/m^2, and 2.4 (SD=1.0) years of Tetris experience. The participants were randomly distributed into two groups. An experimental group consumed 250 mL of soda (7 Up®) containing 26.8 g of sugar [39], while a control group consumed 250 mL of sugar-free, artificially sweetened soda (7 Up Light®). All participants were asked to arrive at the laboratory in a fasted state (≥1.5 hours). After an initial blood glucose assessment, they completed a battery of behavioral tasks and psychometric questionnaires for about an hour and then performed the go/no-go task (75 initial training trials plus 450 subsequent test trials). Then, they consumed the drink (classic 7 Up® or 7 Up Light®). 10 to 15 minutes later, and after a second blood glucose assessment, the volunteers played Tetris for 10 minutes, commencing from level one, having been instructed to reach the highest total score possible. The investigators assessed various Tetris gaming performance parameters, namely the percentage of single-line clears, the percentage of four-line clears, the total number of lines, the number of restarts, and the total score. Although the authors registered a significant increase in blood glucose in the group that ingested the drink with sugar ($t(34)=10.04$, $p<0.001$, $d=3.44$), and a significant decrease in blood glucose in the control group ($t(34)=4.74$, $p<0.001$, $d=1.63$), they did not detect statistically significant differences between the two conditions, in terms of performance, on any of the variables related to performance in Tetris. No side effects were assessed or reported.

In a randomized, cross-over trial conducted in 2021, Rhoden et al. [27] tested the effects of an energy bar (Cliff bar) containing 21 g (∼0.23 g/kg) of sucrose on the cognitive ability of eight males and one female amateur esports players who were members of a university esports club and played esports on average 18.9 (SD=14.3) hours per week [mean age: 20.3 (SD=1.2) y, body weight: 92.5 kg (SD=23.7), height: 179.3 (SD=4.5) cm), BMI 28.8 (SD=7.6) kg/m^2]. On one occasion, after at least an 8-hour night fast, they ingested the energy bar one hour before completing 60 minutes of gaming using two esports training platforms (Aim Hero and Osu!). The same procedure has been repeated on another occasion but in a fasted state. Osu! is a video game in which the user must use the mouse cursor to click and/or drag spherical objects and "sliders". Performance statistics comprised: targets missed, largest combo, accuracy (%), error pre (ms), error post (ms), unstable rate, and score. Aim Hero is a first-person shooter (FPS) style aim-training program used by FPS players to improve their aim. Recorded variables included: total shots, number of targets hit, accuracy (% of shots that hit the targets), time per hit(s), time to complete, and score. Despite significant increases in blood glucose levels in the fed versus fasted trial, no statistically significant differences were detected in gaming performance when comparing fed to fasted sessions ($p > 0.05$). No adverse effects were assessed or reported in this study.

Furukado et al. (2022) [34] led a randomized, crossover, double-blind, placebo-controlled study that investigated the effects of glucose ingestion on the cognitive performance of 20 male university students [mean age: 19.9 (SD=1.0) y, body weight: 63.9 kg (SD=6.0), height: 171.4 (SD=4.8) cm)] who typically did not play video games, during up to about 28 minutes of gameplay on the esport racing game "Gran Turismo Sport". On two occasions, separated by two weeks, they ingested either a 29 g weight candy containing 26.1 g (∼0.41 g/kg) of glucose, or a placebo containing erythritol. The TMT-A and B tests were applied at baseline and the end of the game. EEG measurements of the alpha, beta, and sensorimotor rhythm waves were also performed before, 5, 10, and 25 min after the game started. Although no statistically significant differences were detected on the TMT-B tests, the glucose condition showed a significant decrease in the time required to complete the TMT-A test compared with the placebo condition (ES as $d=0.41$, $p=0.08$). There were no significant differences in EEG measurements except for increases in the glucose versus placebo condition at 25 minutes after starting the race game, in the alpha ($d=0.45$, $p=0.06$) waves, indicating greater relaxation, and SMR ($d=0.70$, $p=0.005$) wavebands, which refer to both relaxed and concentrated states. These authors didn't report the methodology for side effects assessment nor their occurrence.

Discussion

Summary of evidence

From the total of sixteen studies included in this review, ten included caffeine in the tested substances [13, 15, 26, 28, 29, 30, 31, 33, 36, 37]. Six studies trialed isolated caffeine [15, 26, 28, 29, 36, 37]. Three studies trialed energy drinks containing caffeine [13, 31, 33]. Two studies tested the effects of a combination of 125 mg caffeine, 75 mg methylliberine, and 50 mg theacrine [15, 29], one study trialed the effects of a mix of 270 mg of caffeine with polyphenols [37] and another assessed the effects of a combination of caffeine and fucoxanthin. Three investigations assessed the effects of a combination of 1500 mg arginine+100 mg inositol [14, 25, 35]. Two studies examined the effects of sucrose [27, 32], and another tested the effects of glucose [34].

All 16 studies involved acute interventions except for the investigations conducted by Tartar et al. (2019) [14] and Emerson et al. (2022) [35], in which the volunteers ingested an arginine-based supplement or a placebo for seven consecutive days, and the study authored by Leonard et al.

(2023) [30], which tested the effects of a combination of a microalgae extract with guarana ingested daily for 30 days. Most studies (n=10) included a crossover design [13, 15, 25, 26, 27, 28, 29, 33, 34, 37]. The investigations authored by Emerson et al. (2020) [35], Rhoden et al. (2021) [27], and Kriter (2020) [31] were the only ones that didn't include a placebo group. Excluding the study by Kriter (2020) [31] which didn't detail volunteers, and the Franke et al. (2017) [28] research, where the subjects averaged 37.3 (SD=12.5) years, all studies involved young adult volunteers.

The 16 studies included a total of 519 participants. Eight studies included females as subjects [14, 25, 27, 30, 32, 33, 35, 37]. Excluding the nine participants of the Emerson et al. (2020) [35] study, and the five participants of the Kriter (2020) trial [31], which didn't detail the sex of the participants, males comprised the majority (90.7%) of the remaining total volunteer sample (n=505) of the remaining 14 studies.

The majority (10) of the studies included in this review included experienced esports players as subjects [13, 14, 25, 26, 27, 28, 29, 30, 35, 37], while the remaining studies enrolled recreational gamers [15], inexperienced players [34], or did not describe subjects gaming expertise level [31, 33, 36].

Only five studies reported on the video game name that the volunteers regularly played. Thomas et al. (2019) [13] enlisted League of Legends players. Bloomer et al. (2022) enrolled third-person shooter (Fortnite) gamers. Sainz et al. (2020) [26] incorporated Fortnite and first-person shooter (Counter-Strike: Global Offensive) players. Leonard et al. (2023) [30] included Call of Duty, Overwatch, Valorant, Super Smash Bros., League of Legends, and Rocket League players. While Tartar et al. (2021) [29] also recruited first-person shooter (FPS) players, they didn't specify the game title. The study by Frank et al. (2017) [28] is notable for involving skilled and highly competitive chess players. Online chess is regarded as an esport genre and has also seen a surge in popularity [40].

Although not based on studies performed on esports players, there is ample scientific literature that supports the nootropic effects of caffeine. In their systematic review, Torres and Kim (2019) concluded that caffeine consistently lowers marksman reaction time and that doses of 100–200 mg every 2 hours might mitigate performance decrements in marksman accuracy caused by stress and fatigue [41]. It has also been shown to significantly improve alertness, executive control, and performance on complex and simple attention tasks, including reaction time, and accuracy on simple tasks. Attention seems to be the most consistently enhanced domain [42]. Another review concluded that a dosage of ~0.5–4 mg/kg of caffeine improves reaction time, alertness, and vigilance. Additionally, caffeine helps to prevent the cognitive performance degradation associated with mental fatigue or sleep deprivation [43]. However, caffeine may cause undesirable effects, such as elevated blood pressure, anxiety, tremors, and decreased sleep quality [44]. Detrimental health problems, especially cardiovascular and psychological, have been documented in adolescents, mainly when ingesting high doses of caffeine [45]. According to EFSA, single doses of 3 mg/kg bodyweight do not raise health concerns for both adolescents and adults [44].

Caffeine may have a double-edged sword role in esports. The included studies reported significant improvements in a set of cognitive domains, including inhibitory control, cognitive flexibility, working memory, attention, time on target tracking, hit accuracy, and reaction speed [15, 26, 29, 33], which may be especially relevant for FPS players, in which accurate aim and speedier actions are considered two of the most crucial requirements for achieving victories [46], and caffeine may allow them to at least move up one level in the ranking system [47].

However, caffeine administration should be carefully considered as it may significantly impair gaming performance by increasing anxiety [29], impulsivity, and jitteriness [15], which may be limited by its co-ingestion with MTL and THC [15, 29]. Moreover, the influence of caffeine on decision-making and complex judgment is still unclear [43] and its supplementation implies potential negative effects, including increased sleep latency, decrease sleep efficiency, and reduced total sleep time [44], all of which could harm esports competitors' sleep hygiene, which already shows a tendency to disrupted sleep patterns [48]. Higher cortisol levels and anxiety before a competitive event have been reported in highly-skilled esports players [49], and caffeine consumption by a non-fatigued and highly aroused individual may produce an excessive arousal state and degrade cognitive performance [43].

Regarding supplementation with arginine, Sowinski et al. (2021) [25] registered significantly improved reaction times in some cognitive tests, and Emerson et al. (2020) [35] reported significantly improved attention, visual processing, and spatial planning. These results contrast with those of Tartar et al. (2019) [14] who, except for a lower number of errors committed in the TMT – Part B test on one of two occasions, didn't observe statistically significant improvements in cognitive tests compared to a placebo. Moreover, both Sowinski et al. (2021) [25] and Tartar et al. (2019) [14] failed to detect significant improvements in video gaming performance.

Concerning carbohydrates, Rhoden et al. (2021) [27] and Lange et al. (2014) [32] didn't observe significant improvements in video game performance with the administration of 21 and 26.8 g of sucrose, respectively. On the other hand, Furukado et al. (2022) [34] noted significant improvements in attention and processing speed with 26.1 g of glucose, which has metabolic effects distinct from sucrose and has more solid scientific support as a nootropic in healthy adult subjects [50].

Limitations

As we restricted our search to four databases and papers published in the English language, we may have missed relevant articles and grey literature published in other databases and written in other languages. Because esports has a higher presence in Southeast Asia [51], relevant papers could be outlined in those countries' bibliographic databases. For the Emerson et al. (2022) [35], and Kriter (2020) [31] studies, only an abstract was available, which limited the amount of information we were able to analyze, extract and summarize. Of note, despite having been published, the study conducted by Rhoden et al. (2021) [27] has not been peer-reviewed.

The studies included in this review were affected by several limitations:

a) Some lifestyle and dietary-related variables may affect cognitive performance, act as confounders in controlled studies, and should be assessed. These include medicines [52], nicotine [53], alcohol intake [54], sleep perturbations [55], physical exercise [56], diet style (e.g. ketogenic diet) [57], breakfast intake/omission [58], caffeine [43], and DS (e.g. *Bacopa monnieri*) [59] intake. However, only five studies excluded medicine users [15, 25, 26, 28, 29, 34], while merely four studies excluded smokers [14, 26, 28, 29], two requested participants to abstain from alcohol [14, 37], four requested to stop DS intake [14, 15, 25, 30], two excluded DS users [15, 25, 26, 30], three assessed sleepiness or sleep duration/quality [26, 30, 36], two requested volunteers to refrain or moderate from physical exercise 24 h before testing [15, 26], four assessed the volunteer's typical diet (e.g. food diary) [15, 25, 30, 37], and only eight reported if volunteers ingested the DS in a fasted or fed state [15, 25, 27, 28, 30, 32, 36, 37].
b) Methodologies varied greatly among the studies that tested caffeine. Seven studies requested volunteers to abstain from caffeine intake [13, 14, 15, 26, 30, 36, 37], and six studies excluded consumers of caffeine-containing beverages [15, 25, 26, 28, 29, 30]. The maximum dose of caffeine allowed for inclusion in the five studies that enforced a daily limit also differed. Sainz et al. (2020) [26] applied a limit of 80 mg, Sowinski et al. (2021) [25] imposed a value of 200 mg, Franke et al. (2017) [28] excluded those who ingested five or more daily cups of coffee, while Tartar et al. (2021) [29] and La Monica et al. (2021) [15] set a limit of 400 mg of caffeine per day.
c) Although the circadian rhythm can modulate the effect of nutrients in the human body [60], only five studies reported the specific hours of the day when the DS were administered and the tests were performed [13, 26, 28, 36, 37].
d) Ideally, the dosage of DS to be administered should be adjusted to each individual's weight, which only happened in the studies conducted by Molesworth et al. (2008) [36] and Sainz et al. (2020) [26].
e) The cognitive tests and video games used in these studies have not been validated as tools to assess cognitive performance in esports players [13], and some have not been properly tested in any specific population, with no existing data on their reliability, validity, and sensitivity to pharmacological or dietary interventions [61]. Indeed, Toth et al. (2019) [47] found that the Stroop Task did not distinguish cognitive inhibition capacity among Counter-Strike: Global Offensive competitors of various levels of skill.
f) Cognitive performance may peak around young adults age [62] and some of the cognitive tests applied may not have been cognitively challenging enough for experienced esports players (ceiling effect) [14].
g) Experienced esports players tend to have a different brain structure, with thickening in several areas, and greater cognitive capacities than non-gamers, including higher attention, visual, and memory capacities [2, 19]. Moreover, different esports genres have specific mechanics and may require distinct sets of cognitive abilities [63]. Thus, the results of studies conducted on players of a genre and expertise level may not be applicable or undesirable in others. Nonetheless, only four studies reported esports player's expertise level [13, 15, 26, 28], while six stated the number of hours of video game play per day or week [13, 26, 27, 35, 36, 37], and seven disclosed on the specific video game genre the volunteers typically played [13, 26, 28, 29, 30, 32, 37].
h) Because they comprised mostly male volunteers (90.7%), the included investigations failed to account for potential sex inequalities. Sex differences may have operated as a confounder, and the results may not apply to female egamers. For example, caffeine has shown greater arousing effects in males [64, 65].
i) Only two studies performed sample size calculations [28, 30] and some trials lacked statistical power to identify statistically significant effects due to the small sample size; Five studies included $\leq$10 individuals [13, 15, 27, 31, 35], and Sainz et al. (2020) [26] only included 15 volunteers.
j) Ten out of the 16 studies included in this review received funds from companies that commercialize the studied supplement or had authors that reported

conflicts of interest [13, 14, 15, 25, 29, 30, 33, 34, 35, 37], which are more likely to present positive results to industry sponsors [66, 67].

k) Rhoden et al. (2021) [27] and Lange et al. (2014) [32] investigations tested sucrose, which has a distinct metabolism and may not provide the same cognitive effects as pure glucose or fructose [50].

l) It is common for DS to be misbranded [68, 69], and commercial energy drinks may be mislabeled and not contain the amount of caffeine described on the label [70], which may act as a confounder. When assessing the effects of a DS, validated analytical methods should be used for accurate quantification and purity assessment of its ingredients [71]. However, only two studies, La Monica et al. (2021) [15] and Sowinski et al. (2021) [25] had their DS tested by an independent third-party laboratory for purity and potency.

m) No study disclosed capsule composition (i.e., gelatin vs. cellulosic), which may have distinct disintegration and dissolution properties and consequently influence the ingredient's bioavailability and pharmacokinetics [72].

n) The methodology, study design, and cognitive tests used in the included studies vary greatly, making comparisons difficult.

o) The volunteers were assessed in a peaceful, low-stress testing environment that did not reproduce real competitive gaming conditions.

p) Only seven studies assessed side effects [14, 15, 25, 28, 29, 30, 37], limiting our ability to extract and provide information about adverse events associated with the DS investigated in the 16 studies included in this review.

Future directions

Although a limited number of DS have been trialed in esports players, an ample variety of dietary compounds have demonstrated cognitive-enhancing effects in healthy young individuals [73], which could also be useful for esports players and merit further study in this population. Tyrosine [74] and *Bacopa monnieri* [59] may be the most promising ones. As esports contests can suffer significant delays, or extend for several hours or even days at a time [46], supplementation with slow-release caffeine (300 mg/day) could be a preferable choice to support enhanced neural metabolism, improve cognition, offset possible sleep deprivation, minimize fatigue, and risk of adverse effects, including caffeine "crash" [75]. Thus, we propose that slow-release caffeine [75], varying doses of caffeine, and the co-ingestion of caffeine with other ingredients, such as glucose, tyrosine, green tea, vitamins, minerals, and other nutrients [76] should also be investigated in esports competitors, which will contribute to establishing optimal recommendations.

Glucose and carbohydrate sources of low, medium, and high glycaemic index (GI) values should be of special interest for future investigation on esports as the brain has a rapid metabolism and requires a minimum of 130 gr of glucose per day [77], its primary energy substrate in normal conditions. As its reserves are limited, this organ depends on a continued blood glucose supply, delivered by the liver [78]. Playing video games increases brain glucose consumption [79] and decreases glycemia [32]. In this context, glucose consumption may increase its availability, support brain areas under high cognitive load, and improve cognitive function [80]. Future studies that evaluate the effects of carbohydrates should involve amateur volunteers with less gaming time, in addition to professional esports players, as the ongoing practice of video games may decrease the brain's use of glucose over time [18].

Compared to arginine, supplementation with dietary nitrates, which are further reduced to nitrite, a NO reserve, may represent a more viable pathway to raise NO levels and increase blood-brain perfusion [81].

Future studies should account for and report on the esports genre, expertise level (e.g., amateur, semi-professional, or professional), and mean daily hours of gaming practice of the volunteers. They should also investigate which cognitive function parameters are independently associated with esports player performance, and then focus on assessing the acute and long-term effects of nootropics consumption on such variables. Quantifiable and validated performance metrics should be developed to measure the effects of DS on the cognitive and gaming performance of esports players. Additionally, we recommend that further investigations report the specific times of day when DS was administered and tests were performed. We also advise the recruitment of sample sizes that provide sufficient statistical power to detect effect sizes. Ideally, future research should also attempt to recreate the environmental characteristics typically observed in esports competitions.

Conclusion

This scoping review unveiled sixteen clinical trials. Ten assessed the effects of caffeine, two of which tested a combination of caffeine, methylliberine, and theacrine, one trialed the effects of a mix of caffeine and polyphenols, and another a combination of caffeine and fucoxanthin. Three studies assessed the effects of arginine, and three others studied the effects of carbohydrates on esports players.

The literature published to date suggests that caffeine may improve time on target tracking, hit accuracy, reaction speed, and the time required to strike a target, but may also impair gaming performance by increasing jitteriness, decisive reflection time, and losses on time-limited games. We advocate that scientific research into DS for esports is lacking and that additional high-quality research is required. The assessment of the nootropic potential of various nutritional supplements not yet tested in esports practitioners, including slow-release caffeine, nitrates, tyrosine, and others, could be considered for further research. Since research in this area has focused on the effects of caffeine on the performance of video gamers, and anticipating that more studies will be published soon, we do consider that this topic deserves to be addressed by a systematic review and meta-analysis.

Electronic supplementary material

The electronic supplementary material (ESM) is available with the online version of the article at https://doi.org/10.1024/0300-9831/a000790

ESM 1. Bibliographic databases search scheme (PDF).

References

1. Jonasson K, Thiborg J. Electronic sport and its impact on future sport. Sport Soc. 2010;13(2):287–99.
2. Campbell MJ, Toth AJ, Moran AP, Kowal M, Exton C. eSports: a new window on neurocognitive expertise? Prog Brain Res. 2018;240:161–74.
3. Jasny M. Doping in e-sports. An empirical exploration and search for sociological interpretations. Acta Univ Lodz, Folia Psychol. 2020;75:85–99.
4. Hamstead C. "Nobody talks about it because everyone is on it": Adderall presents esports with an enigma [Internet]. The Washington Post; 2020 [cited 2003 Mar 16]. Available from: https://www.washingtonpost.com/video-games/esports/2020/02/13/esports-adderall-drugs/
5. Ip EJ, Urbano EPT, Caballero J, Lau WB, Clauson KA, Torn RA, et al. The video gamer 500: performance-enhancing drug use and internet gaming disorder among adult video gamers. Comput Hum Behav. 2021;123;106890.
6. Rosenthal R. A tough pill to swallow: making the case for why eSports leagues must adopt strict banned substance policies to prevent disability discrimination. Va Sports & Ent. 2020.
7. Holden JT, Kaburakis A, Wall Tweedie J. Virtue(al) games – real drugs. Sport Ethics Philos. 2019;13(1):19–32.
8. Lakhan SE, Kirchgessner A. Prescription stimulants in individuals with and without attention deficit hyperactivity disorder: misuse, cognitive impact, and adverse effects. Brain Behav. 2012;2(5):661–77.
9. Schelleman H, Bilker WB, Kimmel SE, Daniel GW, Newcomb C, Guevara JP, et al. Amphetamines, atomoxetine and the risk of serious cardiovascular events in adults. PLoS One. 2013;8(1): e52991.
10. Kroutil LA, Van Brunt DL, Herman-Stahl MA, Heller DC, Bray RM, Penne MA. Nonmedical use of prescription stimulants in the United States. Drug Alcohol Depend. 2006;84(2):135–43.
11. Suliman NA, Mat Taib CN, Mohd Moklas MA, Adenan MI, Hidayat Baharuldin MT, Basir R. Establishing natural nootropics: recent molecular enhancement influenced by natural nootropic. Evid Based Complement Alternat Med. 2016;2016:4391375.
12. Cowan AE, Jun S, Gahche JJ, Tooze JA, Dwyer JT, Eicher-Miller HA, et al. Dietary supplement use differs by socioeconomic and health-related characteristics among US adults, NHANES 2011–2014. Nutrients. 2018;10(8):1114.
13. Thomas CJ, Rothschild J, Earnest CP, Blaisdell A. The effects of energy drink consumption on cognitive and physical performance in elite League of Legends players. Sports (Basel, Switzerland). 2019;7(9):196.
14. Tartar JL, Kalman D, Hewlings S. A prospective study evaluating the effects of a nutritional supplement intervention on cognition, mood states, and mental performance in video gamers. Nutrients. 2019;11(10):2326.
15. La Monica MB, Listman JB, Donovan I, Johnson TE, Heeger DJ, Mackey WE. Effects of TeaCrine® (theacrine), Dynamine™ (methylliberine), and caffeine on gamer psychomotor performance in a first-person shooter video game scenario. bioRxiv. 2021.
16. Maughan RJ, Burke LM, Dvorak J, Larson-Meyer DE, Peeling P, Phillips SM, et al. IOC consensus statement: dietary supplements and the high-performance athlete. Br J Sports Med. 2018;52(7):439–55.
17. Senefeld JW, Wiggins CC, Regimbal RJ, Dominelli PB, Baker SE, Joyner MJ. Ergogenic effect of nitrate supplementation: a systematic review and meta-analysis. Med Sci Sports Exerc. 2020;52(10).
18. Haier RJ, Siegel BV Jr., MacLachlan A, Soderling E, Lottenberg S, Buchsbaum MS. Regional glucose metabolic changes after learning a complex visuospatial/motor task: a positron emission tomographic study. Brain Res. 1992;570(1–2): 134–43.
19. Melentev N, Somov A, Burnaev E, Strelnikova I, Strelnikova G, Melenteva E, et al. editors. eSports players professional level and tiredness prediction using EEG and machine learning. 2020 IEEE SENSORS; 2020 25–28 Oct. 2020.
20. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med. 2018;169(7):467–73.
21. Kahale L, Elkhoury R, El Mikati I, Pardo-Hernandez H, Khamis A, Schünemann H, et al. Tailored PRISMA 2020 flow diagrams for living systematic reviews: a methodological survey and a proposal. F1000Res. 2021;10:192.
22. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJM, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control ClinTrials. 1996;17(1):1–12.
23. Olivo SA, Macedo LG, Gadotti IC, Fuentes J, Stanton T, Magee DJ. Scales to assess the quality of randomized controlled trials: a systematic review. Phys Ther. 2008;88(2):156–75.
24. Kim K, Jo J, Chung J, Kim J, Choi H, Lee S. Quality analysis of randomized controlled trials in the International Journal of Impotence Research: quality assessment and relevant clinical impact. Int J Impot Res. 2017;29(2):65–9.
25. Sowinski R, Gonzalez D, Xing D, Yoo C, Jenkins V, Nottingham K, et al. Effects of inositol-enhanced bonded arginine silicate

ingestion on cognitive and executive function in gamers. Nutrients. 2021;13(11):3758.
26. Sainz I, Collado-Mateo D, Coso JD. Effect of acute caffeine intake on hit accuracy and reaction time in professional e-sports players. Physiol Behav. 2020;224:113031.
27. Rhoden G, Nelson H, Valladao S, Andre T. Blood glucose levels in response to 1 hour of esports training: a pilot study. IJESPORTS. 2021;1(1).
28. Franke AG, Gransmark P, Agricola A, Schuhle K, Rommel T, Sebastian A, et al. Methylphenidate, modafinil, and caffeine for cognitive enhancement in chess: A double-blind, randomised controlled trial. Eur Neuropsychopharmacol. 2017;27(3):248–60.
29. Tartar JL, Banks JB, Marang M, Pizzo F, Antonio J. A combination of caffeine, TeaCrine® (theacrine), and Dynamine® (methylliberine) increases cognitive performance and reaction time without interfering with mood in adult male egamers. Cureus. 2021;13(12):e20534.
30. Leonard M, Maury J, Dickerson B, Gonzalez DE, Kendra J, Jenkins V, et al. Effects of dietary supplementation of a microalgae extract containing fucoxanthin combined with guarana on cognitive function and gaming performance. Nutrients. 2023;15(8):1918.
31. Kriter A. A study to determine if caffeine has a positive effect on recognition and reaction. SC Acad Sci. 2020.
32. Lange F, Seer C, Rapior M, Rose J, Eggert F. Turn it all you want: still no effect of sugar consumption on ego depletion. J Eur Psychol Stud. 2014;5(3):1–8.
33. Schwager LE, Helwig NJ, Rogers EM, Banks NF, Alpers JP, Schulte SL, et al. Novel energy drink improves cognitive function and mood, without influencing myocardial oxygen demand or ventricular repolarization in adult gamers: a randomized, double-blind, placebo-controlled, crossover trial. J Am Coll Nutr. 2023;1–15.
34. Furukado R, Hagiwara G, Inagaki H. Effects of glucose Ramune candy ingestion on concentration during esports play and cognitive function. J Digit Life. 2022;2.
35. Emerson K, Perez Ojalvo S, Greenberg D. Effects of a bonded arginine silicate inositol combination (nooLVL®) on cognitive function in esports gamers. FASEB J. 2022;36(S1).
36. Molesworth BR, Young R, editors. Caffeine: mitigating the effects of fatigue on the flight deck? Proc Hum Factors Ergon; 2008: SAGE Publications Sage CA: Los Angeles, CA.
37. Bloomer RJ, Martin KR, Pence JC. Impact of AmaTea® Max on physiological measures and gaming performance in active gamers: a placebo-controlled, double-blind, randomized study. J Clin Transl Res. 2022;8(2):93–102.
38. Alford C, Cox H, Wescott R. The effects of red bull energy drink on human performance and mood. Amino Acids. 2001;21(2):139–50.
39. Original 7UP – nutritional facts [internet]. Dr Pepper/Seven Up, Inc; [cited 2023 May 28]. Available from: https://www.7up.com/en/products/7up
40. Taylor-Hill G. Exploring the surprising rise of chess esports [internet]. ESPORTS.NET; 2022 [cited 2023 Mar 6]. Available from: https://www.esports.net/news/chess-esports-growth/
41. Torres C, Kim Y. The effects of caffeine on marksmanship accuracy and reaction time: a systematic review. Ergonomics. 2019;62(8):1023–32.
42. Einöther SJ, Giesbrecht T. Caffeine as an attention enhancer: reviewing existing assumptions. Psychopharmacology (Berl). 2013;225(2):251–74.
43. McLellan TM, Caldwell JA, Lieberman HR. A review of caffeine's effects on cognitive, physical and occupational performance. Neurosci Biobehav Rev. 2016;71:294–312.
44. EFSA Panel on Dietetic Products N, Allergies. Scientific opinion on the safety of caffeine. EFSA Journal. 2015;13(5):4102.
45. Alsunni AA. Energy drink consumption: beneficial and adverse health effects. Int J Health Sci. 2015;9(4):468–74.
46. Nagorsky E, Wiemeyer J. The structure of performance and training in esports. PLoS One. 2020;15(8):e0237584-e.
47. Toth AJ, Kowal M, Campbell MJ. The color-word stroop task does not differentiate cognitive inhibition ability among esports gamers of varying expertise. Front Psychol. 2019;10:2852.
48. Lee S, Bonnar D, Roane B, Gradisar M, Jang E, Suh S, Sleep characteristics and mood of professional esports athletes: a multi-national study. Sleep. 2020;43(Issue 2):A75–A6.
49. Mendoza G, Clemente-Suárez VJ, Alvero-Cruz JR, Rivilla I, García-Romero J, Fernández-Navas M, et al. The role of experience, perceived match importance, and anxiety on cortisol response in an official esports competition. Int J Environ Res Public Health. 2021;18(6):2893.
50. García CR, Piernas C, Martínez-Rodríguez A, Hernández-Morante JJ. Effect of glucose and sucrose on cognition in healthy humans: a systematic review and meta-analysis of interventional studies. Nutr Rev. 2021;79(2):171–87.
51. Yue Y, Rui W, Chiang Siu Ling S. Development of E-sports industry in China: current situation, trend and research hotspot. IJESPORTS. 2020;1(1).
52. Nevado-Holgado AJ, Kim CH, Winchester L, Gallacher J, Lovestone S. Commonly prescribed drugs associate with cognitive function: a cross-sectional study in UK Biobank. BMJ Open. 2016;6(11):e012177.
53. Heishman SJ, Kleykamp BA, Singleton EG. Meta-analysis of the acute effects of nicotine and smoking on human performance. Psychopharmacology (Berl). 2010;210(4):453–69.
54. Van Skike CE, Goodlett C, Matthews DB. Acute alcohol and cognition: remembering what it causes us to forget. Alcohol. 2019;79:105–25.
55. Wardle-Pinkston S, Slavish DC, Taylor DJ. Insomnia and cognitive performance: a systematic review and meta-analysis. Sleep Med Rev. 2019;48:101205.
56. Chang H, Kim K, Jung YJ, Kato M. Effects of acute high-Intensity resistance exercise on cognitive function and oxygenation in prefrontal cortex. J Exerc Nutrition Biochem. 2017;21(2):1–8.
57. D'Anci KE, Watts KL, Kanarek RB, Taylor HA. Low-carbohydrate weight-loss diets. Effects on cognition and mood. Appetite. 2009;52(1):96–103.
58. Adolphus K, Lawton CL, Champ CL, Dye L. The effects of breakfast and breakfast composition on cognition in children and adolescents: a systematic review. Adv Nutr. 2016;7(3):590s–612s.
59. Kongkeaw C, Dilokthornsakul P, Thanarangsarit P, Limpeanchob N, Norman Scholfield C. Meta-analysis of randomized controlled trials on cognitive effects of *Bacopa monnieri* extract. J Ethnopharmacol. 2014;151(1):528–35.
60. Flanagan A, Bechtold DA, Pot GK, Johnston JD. Chrono-nutrition: from molecular and neuronal mechanisms to human epidemiology and timed feeding patterns. J Neurochem. 2021;157(1):53–72.
61. de Jager CA, Dye L, de Bruin EA, Butler L, Fletcher J, Lamport DJ, et al. Criteria for validation and selection of cognitive tests for investigating the effects of foods and nutrients. Nutr Rev. 2014;72(3):162–79.
62. Thompson JJ, Blair MR, Henrey AJ. Over the hill at 24: persistent age-related cognitive-motor decline in reaction times in an ecologically valid video game task begins in early adulthood. PLoS One. 2014;9(4):e94215.

63. Ray NR, O'Connell MA, Nashiro K, Smith ET, Qin S, Basak C. Evaluating the relationship between white matter integrity, cognition, and varieties of video game learning. Restor Neurol Neurosci. 2017;35(5):437–56.
64. Adan A, Prat G, Fabbri M, Sànchez-Turet M. Early effects of caffeinated and decaffeinated coffee on subjective state and gender differences. Prog Neuropsychopharmacol Biol Psychiatry. 2008;32(7):1698–703.
65. Temple JL, Dewey AM, Briatico LN. Effects of acute caffeine administration on adolescents. Exp Clin Psychopharmacol. 2010;18(6):510–20.
66. Friedman LS, Richter ED. Relationship between conflicts of interest and research results. J Gen Intern Med. 2004;19(1): 51–6.
67. Cherla DV, Viso CP, Holihan JL, Bernardi K, Moses ML, Mueck KM, et al. The effect of financial conflict of interest, disclosure status, and relevance on medical research from the United States. J Gen Intern Med. 2019;34(3):429–34.
68. Navarro V, Avula B, Khan I, Verma M, Seeff L, Serrano J, et al. The contents of herbal and dietary supplements implicated in liver injury in the United States are frequently mislabeled. Hepatol Commun. 2019;3(6):792–4.
69. Martínez-Sanz JM, Sospedra I, Ortiz CM, Baladía E, Gil-Izquierdo A, Ortiz-Moncada R. Intended or unintended doping? A review of the presence of doping substances in dietary supplements used in sports. Nutrients. 2017;9(10):1093.
70. Attipoe S, Leggit J, Deuster PA. Caffeine content in popular energy drinks and energy shots. Mil Med. 2016;181(9):1016–20.
71. Hosbas Coskun S, Wise SA, Kuszak AJ. The importance of reference materials and method validation for advancing research on the health effects of dietary supplements and other natural products. Front Nutr. 2021;8;786261.
72. Gusev PA, Andrews KW, Savarala S, Tey PT, Han F, Oh L, et al. Disintegration and dissolution testing of green tea dietary supplements: application and evaluation of United States pharmacopeial standards. J Pharm Sci. 2020;109(6):1933–42.
73. Meeusen R, Decroix L. Nutritional supplements and the brain. Int J Sport Nutr Exerc Metab. 2018;28(2):200–11.
74. Jongkees BJ, Hommel B, Kühn S, Colzato LS. Effect of tyrosine supplementation on clinical and healthy populations under stress or cognitive demands – a review. J Psychiatr Res. 2015;70:50–7.
75. Gonzalez AM, Hoffman JR, Wells AJ, Mangine GT, Townsend JR, Jajtner AR, et al. Pharmacokinetics of caffeine administered in a time-release versus regular tablet form. J Int Soc Sports Nutr. 2014;11(Suppl 1):P23.
76. Childs E. Influence of energy drink ingredients on mood and cognitive performance. Nutr Rev. 2014;72(S1):48–59.
77. EFSA Panel on Dietetic Products N, Allergies. Scientific opinion on the substantiation of a health claim related to glycaemic carbohydrates and contribution to normal cognitive function pursuant to article 13 (5) of regulation (EC) No 1924/ 2006. EFSA Journal. 2015;13(2):4027.
78. Murray B, Rosenbloom C. Fundamentals of glycogen metabolism for coaches and athletes. Nutr Rev. 2018;76(4):243–59.
79. Haier RJ, Siegel B, Tang C, Abel L, Buchsbaum MS. Intelligence and changes in regional cerebral glucose metabolic rate following learning. Intelligence. 1992;16(3):415–26.
80. Smith MA, Riby LM, Eekelen JA, Foster JK. Glucose enhancement of human memory: a comprehensive research review of the glucose memory facilitation effect. Neurosci Biobehav Rev. 2011;35(3):770–83.
81. Bryan NS. Nitrite in nitric oxide biology: cause or consequence? A systems-based review. Free Radic Biol Med. 2006;41(5):691–701.

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