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REVIEW

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Effectiveness of high-intensity interval training on peripheral brain-derived neurotrophic factor in adults: A systematic review and network meta-analysis

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Abstract

Background: High-intensity interval training (HIIT) has emerged as an alternative training method to increase brain-derived neurotrophic factor (BDNF) levels, a crucial molecule involved in plastic brain changes. Its effect compared to moderate-intensity continuous training (MICT) is controversial. We aimed to estimate, and to comparatively evaluate, the acute and chronic effects on peripheral BDNF levels after a HIIT, MICT intervention or a control condition in adults.

Methods: The CINAHL, Cochrane, PubMed, PEDro, Scopus, SPORTDiscus, and Web of Science databases were searched for randomized controlled trials (RCTs) from inception to June 30, 2023. A network meta-analysis was performed to assess the acute and chronic effects of HIIT versus control condition, HIIT versus MICT and MICT versus control condition on BDNF levels. Pooled standardized mean differences (SMDs) and their 95% confidence intervals (95% CIs) were calculated for RCTs using a random-effects model.

Results: A total of 22 RCTs were selected for the systematic review, with 656 participants (aged 20.4–79 years, 34.0% females) and 20 were selected for the network meta-analysis. Network SMD estimates were significant for HIIT versus control condition (1.49, 95% CI: 0.61, 2.38) and MICT versus control condition (1.08, 95% CI: 0.04, 2.12) for acutely BDNF increase. However, pairwise comparisons only resulted in a significant effect for HIIT versus control condition.

Conclusions: HIIT is the best training modality for acutely increasing peripheral BDNF levels in adults. HIIT may effectively increase BDNF levels in the long term.

KEYWORDS

cognition, high-intensity exercise, neuroplasticity, neurotrophin, physical activity

1 | INTRODUCTION

Brain-derived neurotrophic factor (BDNF) is a protein of the neurotrophin family expressed mostly in the hippocampus, although it is synthesized by many cell types (lungs, bladder, skeletal and cardiac muscle, plasma, etc.).[1] It is the most widely distributed neurotrophic factor in the brain and is required for the growth, survival, and differentiation of many neurons.[2] Thus, it is known that higher levels of BDNF in brain tissue and blood have been associated with better cognitive function, as it is a crucial molecule involved in plastic changes related to learning and memory.[3] However, in aging-dependent cognitive impairment and aged brains,[4] psychiatric disorders,[5,6] and neurodegenerative pathologies,[7,8] people develop abnormalities in brain function and have lower levels of BDNF.

Evidence supports that exercise is an effective strategy in the treatment of neurological[9] and mental illnesses.[10] In addition, several studies suggest that physical activity may stimulate cognitive benefits through the action of BDNF in the brain that could mediate this effect.[11] Thus, the elevation of BDNF concentrations in the peripheral circulation observed after exercise may result in increased neuronal growth, survival, and synaptogenesis due to the ability of this neurotrophin to cross the blood–brain barrier.[12] However, the association of exercise and peripheral BDNF levels might be influenced by exercise parameters (frequency, intensity, duration, exercise type).[13]

Traditionally, the literature has focused on aerobic exercise as the most common and standard method of improving cognition.[14] However, high-intensity interval training (HIIT), which involves high-intensity short or long bouts interspersed with rest or active recovery periods,[15] has recently emerged as an alternative training method for improving cognition[16,17] and increasing serum BDNF levels due to increased BDNF synthesis in the brain.[18] Previous studies showed that there was no difference between HIIT and moderate-intensity continuous training (MICT)[19,20] to improve serum BDNF levels, while Saucedo Marquez et al.[21] suggested that HIIT is more effective than continuous training. In fact, the main advantage of HIIT is that people can obtain the same benefits as other exercise modalities with shorter session time.[15] In addition, evidence indicates that a training intensity at a higher percentage of maximal oxygen consumption (VO_2max) or maximum heart rate (HRmax) during a training period appears to be more effective for BDNF response.[13] Similarly, a meta-analysis found that both acute and chronic intervallic exercise achieved BDNF expression in blood circulation in young adults,[22] as well as for elderly adults, with controversial findings for their expression after continuous training.[23]

Although high-intensity exercise and low/moderate-intensity intervallic exercise may have positive effects on BDNF, the combined effect of HIIT and whether it is superior to MICT has not been quantified from young adults to elderly individuals. Thus, the aim of this systematic review and network meta-analysis was to estimate, and to comparatively evaluate, the acute and chronic effects on peripheral BDNF levels after a HIIT or a MICT intervention compared to a control condition and HIIT compared to MICT in adults.

2 | METHODS

This systematic review and network meta-analysis was conducted according to the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions[24] and the Preferred Reporting Items for Systematic Reviews incorporating Network Meta-Analyses (PRISMA-NMA; Table S1)[25] and the PRISMA-S extension for reporting literature searches in systematic reviews (Table S2).[26] This review was registered in the PROSPERO database (registration number: CRD42022335827).

2.1 | Search strategy and study selection

A systematic search was conducted in the CINAHL (via EBSCOhost), Cochrane CENTRAL, MEDLINE (via PubMed), Physiotherapy Evidence Database (PEDro), Scopus, SPORTDiscus (via EBSCOhost), and Web of Science databases from inception to June 30, 2023. Randomized controlled trials (RCTs) reporting the effect of HIIT versus control condition or versus MICT and MICT versus control condition on peripheral BDNF in adults were included. The search strategy combined the following terms with Boolean operators (in the databases allowed), following the PICO strategy (population, intervention, comparison and outcome): "young adult", "adult", "older", "senior", "elderly", "vigorous physical exercise", "high-intensity interval training", "high intensity intermittent training", "HIIT", "SIIT", "intermittent training", "interval running", "moderate intensity training", "moderate intensity continuous training", "MICT", "BDNF", "brain derived neurotrophic factor", "random", "randomized", "randomized controlled trial", "controlled trial", "RCT". The references of the included studies were also reviewed. The complete search strategy for each database is available in Table S3. Email alerts were used to update the search. Study authors were contacted in case of missing data.

The inclusion criteria for the systematic review and meta-analysis were as follows: (1) type of studies:

randomized controlled trials (RCTs); (2) type of participants: adults ≥18 years old; (3) type of intervention: physical exercise described as HIIT that reached >75% HRmax or VO_2max in aerobic or strength modalities[27] or MICT that reached ≤75% HRmax or VO_2max; (4) comparison: control condition (nonexercise or slow intensity exercise as stretching exercise) or MICT; and (5) outcome: concentration of BDNF in serum or plasma. Moreover, the studies were excluded when: (1) participants were animal models.

Two independent reviewers (E.R.G. and A.T.C.) conducted the literature search, screening, and trial selection. When there were disagreements, a third researcher made the final decision (V.M.V.).

2.2 | Data extraction

The included studies were reviewed in full text, and the main data were extracted and synthesized in an ad hoc table including: (1) study characteristics (author's name, year of publication, and country), (2) population characteristics (sample size, proportion of women, age, health status, body mass index, baseline VO_2max, baseline levels of BDNF and pre-post mean difference in BDNF levels after training), (3) intervention characteristics (type of intervention in each group, frequency, duration, intensity, and volume), and (4) outcome.

Primary data were extracted from each of the included studies (including pre-post mean BDNF values, standard deviation and sample size of the intervention and control groups). For crossover RCTs, measurements from the intervention (HIIT/MICT) and control condition periods were considered and analyzed as if the trial were a parallel-group trial of HIIT versus control condition, or MICT versus control condition.[24]

For statistical analysis, BDNF values were transformed to the same unit (ng/mL) (where 1 ng/mL = 1000 pg/mL). To evaluate the acute effect of exercise, the first BDNF measurement immediately after the first training session was considered for the analyses. For the chronic effect, the data obtained at the end of the training program were considered. Studies that included more than one group performing the same type of intervention (HIIT or MICT) were analyzed as different. The mature BDNF data were considered in the case of studies evaluating precursor BDNF and mature BDNF, since BDNF is initially synthesized as a precursor, which is proteolytically processed into mature BDNF.[28]

These data were independently extracted by two reviewers (E.R.G. and A.T.C.). A third reviewer (V.M.V.) was consulted to resolve disagreements between reviewers.

2.3 | Risk of bias assessment

Two reviewers (E.R.G. and A.T.C.) independently assessed the risk of bias of the included studies using the Cochrane Risk of Bias Tool for Randomized Clinical Trials (RoB 2.0).[24] Any discrepancies were resolved by a third reviewer (V.M.V.). The revised Cochrane Collaboration tool for assessing risk of bias covers bias in five domains: randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of reported outcome. Each of these domains can be categorized as "low risk of bias," "unclear risk of bias," and "high risk of bias." Therefore, the overall risk for each of the studies was classified as "low risk of bias" when a low risk of bias was determined for all domains; "unclear risk of bias" when at least one domain had unclear risk but no high risk of bias for any specific domain; and "high risk of bias" when at least one domain was assessed as high risk of bias or as unclear risk of bias in multiple domains.[29]

2.4 | Evidence quality assessment

The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) tool was used to assess the quality of evidence and make recommendations.[30] Based on study design, risk of bias, indirect evidence, inconsistency, publication bias and imprecision, each outcome was judged as high, moderate, low, or very low evidence value. Two reviewers (E.R.G. and A.T.C.) carried out the quality of evidence assessment. Any disagreement was solved by consensus, and, if it could not be reached, a third reviewer was consulted (V.M.V.).

2.5 | Data analysis and network meta-analysis

The included studies were summarized qualitatively in an ad hoc table describing the types of direct and indirect comparisons. Our systematic review and network meta-analysis were carried out in accordance with the PRISMA-NMA statement under a frequentist perspective.[25]

A network geometry plot was used to display the overall evidence for chronic and acute effect. The size of the nodes was considered proportional to the number of patients randomized to the intervention, while the thickness of the edges indicated the frequency with which each comparison occurred in the network (number of studies). Different colors were used for the edges and nodes to show the distribution of different trial characteristics and comparisons.

The consistency assessment tested whether the intervention effect calculated from direct comparisons was robust with those calculated by indirect comparisons. For this purpose, we used the Wald test, and we evaluated local inconsistency using the side-splitting method, because of its low statistical power.[31]

The estimated pooled standardized mean differences (SMDs) of the mean differences for BDNF, their 95% confidence intervals (95% CIs) and their corresponding 95% prediction intervals (which represents an estimate of a range in which the results of future studies are expected to be found) were calculated using Hedge's g to reduce the possibility of overestimating the effect size in very small samples.[32] We conduct a standard pairwise meta-analysis using a random-effects model with the DerSimonian and Laird method[33] for direct and indirect comparisons among HIIT, MICT, and control condition to estimate the chronic and acute effects. Heterogeneity was evaluated using the I^2 statistic, which is classified as unimportant (0%–30%), moderate (30%–50%), substantial (50%–75%), or considerable (75%–100%). The corresponding *p* values and 95% CIs were also considered for the assessment of I^2 heterogeneity.[24] Furthermore, we calculated the τ^2 statistic to determine the size and clinical relevance of heterogeneity. We classified the degree of clinical relevance based on the following thresholds: values below 0.04 were considered as indicating low relevance, values ranging from 0.14 to 0.40 indicated moderate relevance, and values exceeding 0.40 denoted substantial relevance. To depict these results, we created forest plot and a league table, where all relative effects estimates and their corresponding 95% CI are shown on the lower diagonal, while the upper diagonal including all direct (pairwise) estimates.

When data on standard deviation were missing, they were estimated using the standard error, Cis, or statistical tests (*t*-test, *F*-test, or a *p*-value) following the recommendations of the Cochrane Handbook.[24] When no numerical data were displayed, the web-based tool WebPlotDigitizer 4.6. was used to estimate through graphs.

The pooled effect of each intervention was performed using a frequentist approach of the network meta-analysis. The transitivity requirement was assessed to check that the synthesis of direct comparisons of two interventions had been conducted in similar populations for the most important clinical and methodological characteristics. Therefore, it was assumed that the populations included in these studies were similar in the baseline distribution of the effect modifier. For this purpose, all participants in the studies included in the network meta-analysis were checked for the same baseline characteristics (on average) that could modify the treatment effect.[34]

The probability that HIIT, MICT, or control condition was the most effective was presented using rankograms.[35] In addition, the surface under cumulative ranking (SUCRA) was estimated for each intervention. SUCRA consists of assigning a numerical value between 0 and 1 to simplify the ranking of each intervention in the rankogram. A SUCRA value of approximately 1 is the best intervention, and a SUCRA value of approximately 0 is the worst intervention.[36]

A sensitivity analysis was performed to determine the robustness of the estimates by removing each study from the analysis one by one. For comparisons with a significant effect on BDNF after the intervention, subgroup analyses were conducted according to the characteristic of the training intervention sessions time (≤30 and >30 min), duration program (≤6 weeks and >6 weeks) and also for the HIIT intervention characteristics in terms of number of bouts (<5 and ≥5), bouts duration (≤2 and >2 min) and resting time (≤2 and >2 min), and the health status of the subjects (healthy and diseased). Meta-regression models were used to determine the potential influence of baseline mean age, VO_2max, body mass index (BMI), percentage of females and baseline levels of BDNF on effect estimates. Finally, publication bias was evaluated using Egger's regression asymmetry test, with p values less than 0.10 considered statistically significant. STATA Statistical software, version 16 (StataCorp LLC) was used to perform the statistical analyses.

3 | RESULTS

3.1 | Study selection

From the 274 studies identified in the literature search, 22 RCTs[19,20,37–55] (Figure 1) were included in the systematic review after a full-text review of the potentially eligible articles (excluded studies with reasons for exclusion are available in Table S4). All were included in the network meta-analysis except Slusher et al.[50] and Schmolesky et al.[53] because the data were not available, and no reply was received from the authors.

3.2 | Characteristics of studies and participants

Studies were conducted on three continents: 12 in America,[19,37–39,42,43,46–50,53] four in Europe[44,51,52,54–56] and three in Asia[20,41,45] (one study did not report the country[40]) and published between 2013 and 2022. Among the 22 RCTs included in the present systematic review,

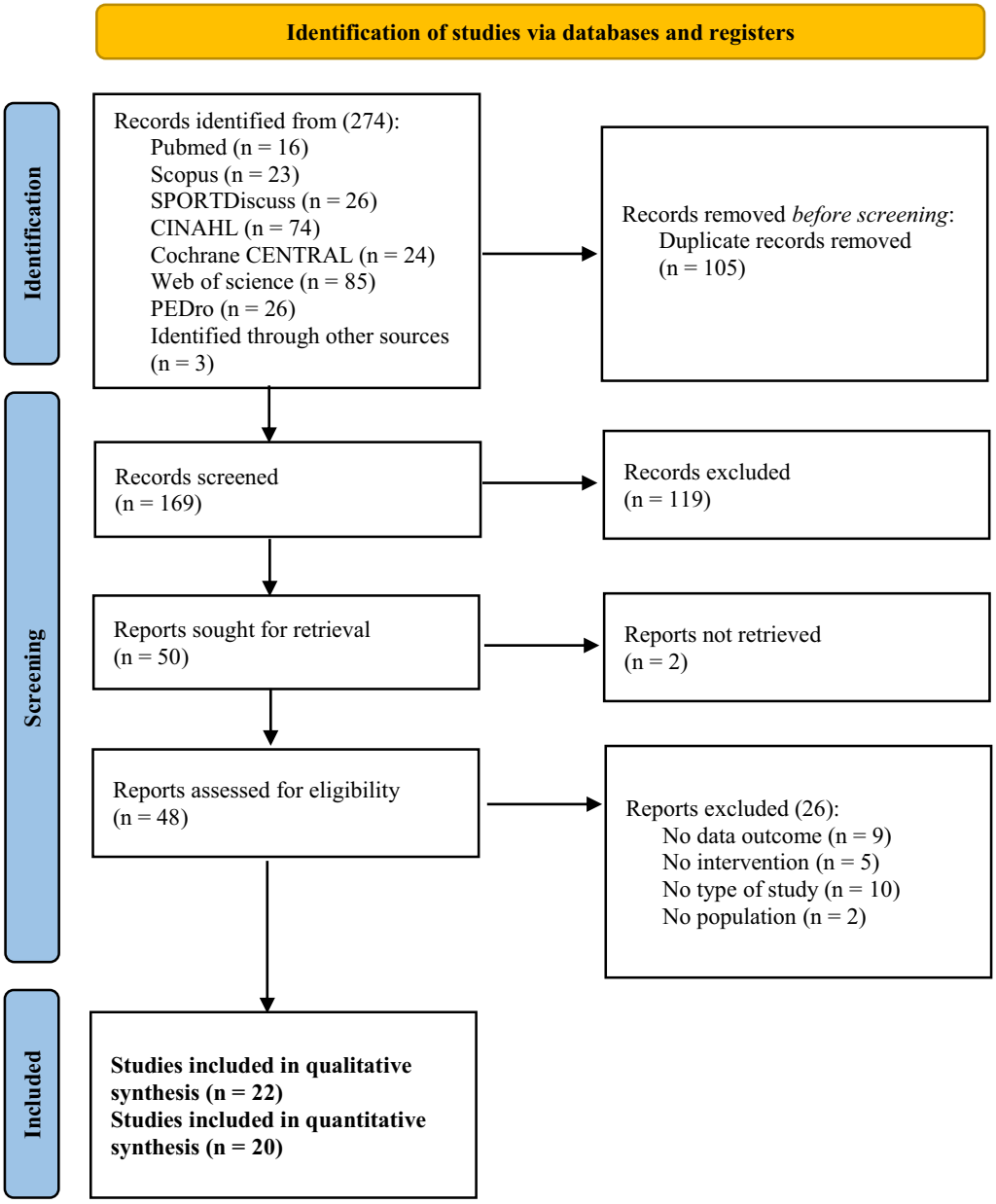

FIGURE 1 Flow diagram.

eight[20,39,40,48–51,57] were of crossover design and 14 were parallel design[19,38,41–48,53–55] (Table 1).

A total of 656 participants (34.00% female) with ages ranging between 20.4 and 79.0 years (45.12% 60 years and over) were included. Among the 19 studies included in the systematic review, eight were conducted only in men[19,38,42,44,49,50,53,54] and two only in women.[47,48] The baseline VO_2max values of the participants ranged from 16.4 to 51.77 mL/kg/min and the baseline BMI ranged from 21.78 to 38.25 kg/m^2. In addition, 16 studies were performed in a healthy population, described as subjects without specific pathology,[19,20,38–40,42–45,47–51,53,54] and six in a population with specific pathology such as poststroke,[37,41] Parkinson disease,[56] coronary artery disease,[46] Alzheimer's disease,[55] and multiple sclerosis[52] (Table 1).

3.3 | Intervention

The effect of HIIT versus control condition was estimated in 13 RCTs, where the acute effect was evaluated in seven studies[20,38,40,44,48,50,54,55] and the chronic effect in seven.[39,43,45,47,56] The effect of HIIT versus MICT was estimated in 14 RCTs; six studies evaluated the acute effect[20,37,42,48,49,51] and eight evaluated the chronic effect.[19,41,43,45,46,52,55,56] The effect of MICT versus control condition was estimated in seven RCTs; three studies

TABLE 1 General characteristics of the studies.

Study characteristics		Population characteristics					Intervention characteristics
Author, year	**Country**	***n* (female)**	**Age (years)**	**Health status**	**BMI (kg/m^2)**	**Baseline VO_2max (mL/kg/min)**	**Intervention**
Boyne, 2018	USA	16 (7)	57.4 ± 9.7	Poststroke patients	27.6 ± 3.7	17.2 ± 3.3	IG-1: HIIT-treadmill IG-2: HIIT-stepper IG-3: MICT- treadmill
de Lima, 2022	Brazil	IG-1: 13 (0) IG-2: 12 (0)	IG-1: 39.46 ± 5.44 IG-2: 40.5 ± 5.63	Sedentary, overweight	IG-1: 27.76 ± 2.68 IG-2: 29.37 ± 3.61	IG-1: 45.48 ± 4.17 IG-2: 44.02 ± 5.0	IG-1: HIIT IG-2: MICT
Domínguez-Sánchez, 2018	Colombia	IG-1: 14 (0) IG-2: 12 (0) IG-3: 13 (0) CG: 12 (0)	IG-1: 24.5 ± 3.7 IG-2: 22.8 ± 3.7 IG-3: 22.2 ± 3.4 CG: 24.7 ± 3.4	Sedentary, overweight	IG-1: 27.4 ± 1.7 IG-2: 27.8 ± 1.3 IG-3: 28.1 ± 1.2 CG: 28.7 ± 2.0	IG-1: 40.6 ± 16.7 IG-2: 38.9 ± 10.5 IG-3: 37.8 ± 13.6 CG: 41.2 ± 17.3	IG-1: HIIT IG-2: Resistance training IG-3: HIIT + Resistance training CG: No exercise
Eken, 2022	Turkey	IG-1: 12 (0) IG-2: 12 (0) CG: 12 (0)	IG-1: 20.8 ± 2.3 IG-2: 22.7 ± 2.7 CC: 22.0 ± 1.65	Healthy	IG-1: 23.1 ± 3.4 IG-2: 21.9 ± 1.5 CC: 22.0 ± 2.7	NR	IG-1: HIIT IG-2: Light intensity interval training CC: No exercise
Enette, 2020	France	IG-1: 17 (11) IG-2: 14 (11) CG: 21 (11)	IG-1: 79 (75–82) IG-2: 74 (68–83) CC: 75 (75–84)	Alzheimer's disease	IG-1: 22 (20–24) IG-2: 23 (21–26) CC: 23 (21–26)	NR	IG-1: HIIT IG-2: MICT CC: Interactive information sessions around multiple-choice questionnaire
Gyorkos, 2019	USA	12 (8)	40.9 ± 20.2	Metabolic syndrome	NR	NR	IG-1: HIIT CC: No exercise
Hendy, 2022	NR	19 (10)	22.6 ± 3.0	Sedentary, healthy	NR	NR	IG-1: HIIT CC: No exercise
Hsu, 2021	Taiwan	IG-1: 10 (2) IG-2: 13 (1)	IG-1: 58.5 (49.8–67.2) IG-2: 53.1 (46.2–60.0)	Poststroke patients	IG-1: 25.5 (23.3–27.8) IG-2: 26.2 (23.7–28.6)	IG-1: 16.4 (15.0–17.8) IG-2: 17.4 (14.9–20.0)	IG-1: HIIT IG-2: MICT

			BDNF		
Frequency (days)	**Duration**	**Intensity and volume**	**Determined in:**	**Baseline levels (ng/mL)**	**Pre-post training mean difference**
1	1 day	25 min per session IG-1: repeated intervals of 30 s running at maximum tolerated speed interspersed with recovery periods IG-2: repeated intervals of 30 s cycling at maximum cadence interspersed with recovery periods IG-3·: walking at 45 ± 5% HRr	Serum	IG-1: NR IG-2: NR	IG-1: 3.20 ± 5.52 IG-2: 2.10 ± 5.32
3	8 weeks	IGF-1: 10 × 20 m sprints at 85% (weeks 1–2), 90% (weeks 3–6), 95% (week 7) or 100% (week 8) maximum velocity interspersed with 1 min of passive recovery. IG-2: running 3500–5000 m at 60% (weeks 1–2), 65% (weeks 2–6), 70% (week 7) and 75% (week 8) maximum velocity	Serum	IG-1: 1.11 ± 0.13 IG-2: 1.21 ± 0.15	IG-1: 0.73 ± 0.31 IG-2: 0.81 ± 0.27
1	1 day	IG-1: 4 × 4 min walking/running intervals at 85%–95% HRm interspersed with 4 min recovery at 75%–85% HRm; 41 min per session IG-2: 12–15 repetitions per set at 50%–70% of one repetition maximum with 60 s of recovery IG-3: IG-1 + IG-2	Serum	IG-1: 161.00 ± 86.43 CG: 176.70 ± 134.07	IG-1: 11.10 ± 127.36 CG: 1.20 ± 188.86
2	4 weeks	IG-1: 3 × 320 s exercises intervals at 85%–90% HRm (20 s × 8 exercises interspersed with 20 s recovery) interspersed with 3 min recovery; 25 min per session IG-2: 3 × 320 s exercises intervals at 57–62% HRm (20 s × 8 exercises interspersed with 20 s recovery) interspersed with 3 min recovery; 25 min per session	Serum	IG-1: 0.99 ± 0.63 CG: 0.59 ± 0.23	Chronic: IG-1: 0.75 ± 1.16 CG: 0.04 ± 0.33 Acute: G-1: 0.37 ± 1.02 CG: 0 ± 0.31
2	9 weeks	IG-1: 6 × 60 s cycling intervals at 80% HRm interspersed with 4 min recovery; 30 min per session IG-2: cycling at 70% HRm; 30 min per session	Plasma	IG-1: 0.35 ± 0.36 IG-2: 0.19 ± 0.21 CG: 0.25 ± 0.48	IG-1: 0.02 ± 0.55 IG-2: 0.14 ± 0.43 CG: 0.02 ± 0.58
3	4 weeks	IG-1: 10 × 60 s cycling intervals at ~90% HRm interspersed with 60 s of active recovery; 26 min per session	Serum	IG-1: 15.20 ± 4.30 CG: 15.40 ± 3.50	IG-1: 6.00 ± 7.71 CG: 3.10 ± 5.78
1	1 day	IG-1: 5 × 2 min cycling intervals at 80% HRm interspersed with 2 min of active recovery; 20 min per session	Plasma	IG-1: 0.36 ± 0.17 CG: 0.31 ± 0.98	IG-1: 0.09 ± 0.30 CG: −0.03 ± 0.99
2–3	36 sessions	30 min per session IG-1: 5 × 3 min cycling intervals at 80% VO_2max interspersed with 3 min of active recovery at 40% VO_2max. IG-2: cycling at 60% VO_2max	Serum	IG-1: 6.06 ± 3.65 IG-2: 7.30 ± 2.27	IG-1: 1.85 ± 4.93 IG-2: −1.42 ± 3.11

(Continues)

TABLE 1 (Continued)

Study characteristics		Population characteristics					Intervention characteristics
Author, year	**Country**	***n* (female)**	**Age (years)**	**Health status**	**BMI (kg/m^2)**	**Baseline VO_2max (mL/kg/min)**	**Intervention**
Inoue, 2020	Brazil	IG-1: 10 (0) IG-2: 10 (0)	30.0 ± 5.4	Obese	IG-1: 34.1 ± 3.6 IG-2: 34.6 ± 3.7	NR	IG-1: HIIT IG-2: MICT
Kovacevic, 2019	Canada	IG-1: 21 (14) IG-2: 20 (10) CC: 23 (15)	IG-1: 72.4 ± 4.4 IG-2: 72.0 ± 6.2 CC: 71.5 ± 6.6	Sedentary, healthy	IG-1: 27.0 ± 4.0 IG-2: 28.0 ± 4.0 CC: 30.0 ± 6.0	IG-1: 25.0 ± 6.2 IG-2: 24.9 ± 5.5 CG: 19.2 ± 6.7	IG-1: HIIT IG-2: MICT CC: nonaerobic seated and standing stretches
Kujach, 2020	Poland	IG-1: 20 (0) CC: 16 (0)	IG-1: 21.0 ± 0.9 CC: 21.7 ± 1.3	Healthy	IG-1: 24.2 ± 2.0 CC: 24.6 ± 2.5	IG-1: 48.6 ± 5.1 CC: 49.4 ± 6.2	IG-1: HIIT CC: No exercise
Li, 2021	China	IG-1: 10 (3) IG-2: 10 (4) CC: 9 (4)	IG-1: 64.9 ± 3.45 IG-2: 66.4 ± 4.5 CG: 63.9 ± 3.95	Sedentary, overweight and obese	IG-1: 27.8 ± 1.04 IG-2: 27.7 ± 2.84 CC: 27.1 ± 1.5	IG-1: 19.47 ± 3.8 IG-2: 18.03 ± 2.21 CC: 18.04 ± 1.63	IG-1: HIIT IG-2: MICT CC: No exercise
O'Callaghan, 2020	England	IG-1: 9 (5) IG-2: 13 (9) CG (for IG-1): 8 (4) CG (for IG-2): 14 (6)	1G-1: 68.8 ± 7.9 IG-2: 70.4 ± 7.2 CG (for IG-1): 69.0 ± 6.6 CG (for IG-2): 64.6 ± 8.6	Parkinson disease	NR	IG-1: 20.5 ± 3.34 IG-2: 20.1 ± 4.91 CG (for IG-1): 22.5 ± 6.49 CG (for IG-2): 18.8 ± 5.38	IG-1: HIIT IG-2: MICT CG (for IG-1 and IG-2): No exercise
Reed, 2022	Canada	IG-1: 43 (7) IG-2: 44 (6)	IG-1: 61 ± 7 IG-2: 60 ± 7	Coronary artery disease patients	IG-1: 29.0 ± 5.8 IG-2: 30.1 ± 6.4	NR	IG-1: HIIT IG-2: MICT
Rentería, 2019	Mexico	IG-1: 9 (9) CG: 8 (8)	IG-1: 22.0 ± 1.6 CC: 21.0 ± 0.8	Healthy	IG-1: 25.3 ± 2.2 CC: 23.0 ± 1.4	NR	IG-1: HIIT CC: No exercise
Reycraft, 2019	Canada	8 (0)	23.1 ± 3.0	Healthy	24.8 ± 2.3	51.2 ± 4.4	IG-1: SIT IG-2: MICT IG-3: VICT CC: No exercise
Rodriguez, 2018	USA	Obese: 6 (0) Normal-weight: 6 (0)	Obese: 25.54 ± 1.67 Normal-weight: 22.58 ± 0.69	Obese and normal-weight	Obese: 38.25 ± 1.36 Normal-weight: 21.78 ± 0.74	Obese: 33.88 ± 2.09 Normal-weight: 51.77 ± 1.94	IG-1: HIIT IG-2: MICT
Schmolesky, 2013	USA	IG-1: 8 (0) IG-2: 9 (0) IG-3: 9 (0) IG-4: 9 (0) CG: 10 (0)	IG-1: 21.1 ± 2.6 IG-2: 21.1 ± 2.9 IG-3: 21.6 ± 2.6 IG-4: 20.9 ± 2.4 CG: 20.4 ± 2.0	Healthy	NR	NR	IG-1: MICT IG-2: MICT IG-3: VICT IG-4: VICT CG: No exercise

			BDNF		
Frequency (days)	**Duration**	**Intensity and volume**	**Determined in:**	**Baseline levels (ng/mL)**	**Pre-post training mean difference**
3	6 weeks	40 min per session IG-1: 10 × 1 min running on treadmill al 100% of VO_2max interspersed with 1 min of passive recovery IG-2: supervised walking/running at 65% VO_2max	Serum proBDNF and mBDNF	IG-1: 9.89 ± 5.02 IG-2: 6.24 ± 3.42	IG-1: 2.36 ± 7.60 IG-2: 1.90 ± 5.64
3	12 weeks	IG-1: 4 × 4 min walking at 90%–95% HRmax interspersed with 3 min of active recovery at 50%–70% HRm IG-2: walking at 70%–75% HRmax; 47 min per session	Serum	IG-1: 29.50 ± 6.80 IG-2: 29.1 ± 7.9 CG: 24.6 ± 10.4	IG-1: −1.90 ± 8.48 IG-2: −3.1 ± 10.50 CG: 0.4 ± 12.63
1	1 day	IG-1: 6 × 30 s of all out cycling exercise interspersed with 4.5 min of active recovery	Serum	IG-1: 14.19 ± 2.64 CG: 8.45 ± 5.89	IG-1: 13.41 ± 4.38 CG: 0.7 ± 8.01
3	12 weeks	45 min per session IG-1: 4 × 3 min cycling at 90% VO_2max interspersed with 3 min of active recovery at 60% IG-2: 25 min cycling at 70% VO_2max	Serum	IG-1: 1.04 ± 0.27 IG-2: 1.05 ± 0.26 CG: 1.08 ± 0.26	IG-1: 0.38 ± 0.44 IG-2: 0.28 ± 0.41 CG: 0.01 ± 0.38
NR	12 weeks	45–60 min per session IG-1: 4–6 × 4 min at ≥85 HRmax interspersed with 3.5 min of recovery. IG-2: aerobic and resistance exercise at 60–80 HRmax.	Serum	IG-1: 685.00 ± 65.97 IG-2: 1300.10 ± 671.53 CG (for IG-1): 699.90 ± 199.58 CG (for IG-2): 1470.30 ± 1372.86	IG-1: 7.4 ± 126.54 IG-2: 263.30 ± 1731.27 CG (for IG-1): −72 ± 824.47 CG (for IG-2): −608.9 ± 1810.01
2	12 weeks	IG-1: 4 × 4 min at 85%–95% HRmax interspersed with 3 min of active recovery at 60–70% HRmax; 45 min per session IG-2: 10–15 min of continuous aerobic conditioning for the first 1–3 weeks, progressing to 30 min for the remaining weeks; 60 min per session	Plasma	IG-1: 31.9 ± 17 IG-2: 29.6 ± 10.1	IG-1: −1.3 ± 23.62 IG-2: 0.2 ± 14.93
3	4 weeks	IG-1: 1–5 × 30 s at 80% W interspersed with 4 min of active recovery at 40% W	Serum	IG-1: 19.50 ± 0.57 CG: 17.53 ± 0.62	IG-1: 2.44 ± 0.61 CG: 1.97 ± 1.00
1	1 day	IG-1: 4 × 30 s running all-out interspersed with 4 min of passive recovery IG-2: at 65% VO_2max IG-3: at 85% VO_2max	Plasma	IG-1: 3.23 ± 0.36 IG-2: 4.74 ± 1.09 CG: 4.90 ± 1.09	IG-1: 6.25 ± 2.06 IG-2: 2.71 ± 1.99 CG: 0.05 ± 1.86
1	1 day	IG-1: 4 × 4 min running or jogging at 80%–90% VO2max interspersed with 3 min of active recovery at 50%–60% VO_2max; 33 min per session IG-2: walking or jogging at 50%–60% VO_2max; 43 min per session	Serum	IG-1: Obese: 40.22 ± 4.28 Normal-weight: 28.86 ± 5.35 IG-2: Obese: 44.59 ± 10.71 Normal-weight: 25.36 ± 7.50	IG-1: Obese: 9.18 ± 9.58 Normal-weight: 3.50 ± 9.21 IG-2: Obese: −7.43 ± 15.14 Normal-weight: −1.75 ± 13.08
1	1 day	Cycling IG-1: at 60% HR reserve; 40 min per session IG-2: at 60% HR reserve; 20 min per session IG-3: at 80% HR reserve; 40 min per session IG-4: at 80% HR reserve; 20 min per session		IG-1: NR IG-2: NR CG: NR	IG-1: NR IG-2: NR CG: NR

(Continues)

TABLE 1 (Continued)

Study characteristics		Population characteristics					Intervention characteristics
Author, year	Country	*n* (female)	Age (years)	Health status	BMI (kg/m^2)	Baseline VO_2max (mL/kg/min)	Intervention
Slusher, 2018	USA	13 (0)	23.62 ± 1.06	Healthy	24.21 ± 0.88	43.62 ± 2.5	IG-1: HIIT CC: No exercise
Tsai, 2021	Taiwan	21 (11)	60.62 ± 4.96	Healthy	24.15 ± 2.23	NR	IG-1: HIIT IG-2: MICT CC: No exercise
Weaver, 2021	United Kingdom	24 (9)	23 ± 5	Healthy	23.0 ± 11.1	43.9 ± 6.4	IG-1: HIIT IG-2: SIT IG-3: MICT
Zimmer, 2017	Switzerland	IG-1: 27 (20) IG-2: 30 (18)	IG-1: 51 ± 9.9 IG-2: 48 ± 12.1	Multiple Sclerosis	IG-1: 22.55 ± 2.65 IG-2: 23.73 ± 4.8	IG-1: 20.03 ± 5.88 IG-2: 19.03 ± 6.14	IG-1: HIIT IG-2: MICT

Abbreviations: BDNF, brain-derived neurotrophic factor; CC, control condition; HIIT, high-intensity interval training; HRmax, maximum heart rate; IG, intervention group MICT, moderate-intensity continuous training; NR, No reported; RCT, randomized controlled trials; SD, standard deviation; SIT, sprint interval training; VO_2max, maximal volume of oxygen; W, watts.

evaluated the acute effect[20,48,53] and four evaluated the chronic effect.[43,45,55,56]

HIIT volume and intensity ranged from 1 to 10 intervals of 30 s to 5.30 min of exercise at 75%–100% of VO_2max or HRmax and 1–4.50 min of recovery (active or inactive) at 40%–70% VO_2max or HRmax. The volume and intensity of the MICT ranged from 25 to 60 min per session at 45%–75% VO_2max or HRmax. The length of the exercise programs, in which the chronic effect of training was evaluated, ranged from 3 to 12 weeks, and the frequency ranged from 2 to 5 days per week, prevailing 3 days per week in eight studies.[19,39,41–43,45,47,52] HIIT sessions were performed primarily on cycle ergometer in 10 studies,[20,39–41,44,45,47,51,52,55] followed by treadmill in seven studies,[19,38,42,43,48,49,57] seated stepper in one study,[57] one study in a Speedflex machine,[56] lower body ergometer in one study,[45] different types of exercises (squat jump, inchworm, walk down-shoulder tap, plank get ups, goblet squats, jackknife crunch, and burpee mountain climbing movements) in one study[54] and various aerobic exercise equipment (e.g., treadmill, cycle ergometer, elliptical, etc.) or dance/movement-based routines in one study.[46] MICT sessions were performed mainly on treadmill[42,43,48,49,57] and cycle ergometer,[20,41,51–53] on a track in one study[19] and on aerobic equipment or walking on an indoor track in one study.[46] The control groups did not exercise except in one study that performed static stretches in seated and standing positions.[43]

3.4 | Outcome

Seventeen studies determined BDNF levels in serum[19,20,38,39,41–45,47,49,50,52–54,56,57] and five in plasma.[40,46,48,51] In all studies, BDNF samples were analyzed by enzyme-linked immunosorbent assay according to the clinical standards of the laboratory or the manufacturer's guidelines.

The baseline peripheral levels of BDNF for the chronic effect ranged from 1.04 to 685 ng/mL in the HIIT intervention, from 0.19 to 1300.10 ng/mL in the MICT intervention and from 0.25 to 1470.30 ng/mL in the control condition. For the acute effect, BDNF values ranged between 0.36 and 161.00 ng/mL in the HIIT intervention, between 1.13 and 44.59 ng/mL in the MICT intervention and between 0.31 and 176.70 ng/mL in the control condition. Respect to the pre-post training mean differences, for the chronic effect ranged from −1.90 to 7.40 ng/mL in the HIIT intervention, from −3.10

			BDNF		
Frequency (days)	**Duration**	**Intensity and volume**	**Determined in:**	**Baseline levels (ng/mL)**	**Pre-post training mean difference**
1	1 day	IG-1: 10 × 20 s cycling all out interspersed with 10 s of active recovery; 20 min per session	Plasma and serum	IG-1: NR CG: NR	IG-1: NR CG: NR
1	1 day	30 min per session IG-1: 10 intervals of 1 min cycling at 70–75% HRmax interspersed with 2 min of active recovery IG-2: cycling at 50–55% HRmax	Serum	IG-1: 4.78 ± 1.68 IG-2: 4.95 ± 1.73 CG: 4.99 ± 1.169	IG-1: 0.86 ± 2.57 IG-2: 1.13 ± 2.75 CG: −0.18 ± 2.48
1	1 day	IG-1: 4 × 4 min cycling at 85% HRmax interspersed with 3 min of active recovery; 36 min per session IG-2: 4 × 30 s cycling at 100% of Wmax interspersed with 4.5 min of active recovery; 28 min per session IG-3: cycling at 65% of VO_2max; 38 min per session	Plasma	IG-1: 1.34 ± 0.92 IG-2: 1.35 ± 1.05 IG-3: 1.13 ± 0.76	IG-1: 0.68 ± 1.67 IG-2: 1.15 ± 3.21 IG-3: 0.75 ± 1.83
IG-1: 3 IG-2: 5	3 weeks	IG-1: 5 × 3 min cycling intervals at 80% VO_2max or 90% HRmax interspersed with 1.5 min of active recovery at 40% VO_2max; 20 min per session IG-2: cycling at 65% VO_2max or 70% HRmax; 30 min per session	Serum	IG-1: 20.97 ± 10.61 CG: 19.29 ± 11.23	IG-1: 3.70 ± 16.79 CG: 1.57 ± 15.15

to 263.30 ng/mL in the MICT intervention and from −608.90 to 3.10 ng/mL in the control condition. For the acute effect, BDNF values ranged from 0.09 to 13.41 ng/mL in the HIIT intervention, from −7.43 to 1.90 ng/mL in the MICT intervention and from −0.18 to 1.20 ng/mL in the control condition (Table 1).

3.5 | Risk of bias

According to the RoB 2.0 Cochrane tool,[24] one study scored at "low risk of bias",[55] four studies scored at "high risk of bias",[19,43,48,50] whereas the remaining 17 studies rated "some concerns"[20,38–42,44–47,49,51–54,56,57] (Figure S1). By domain, the randomization process was the highest rated as "high risk of bias" (13.6%), and the selection of the reported outcome was the highest rated as "some concerns" (81.8%).

3.6 | GRADE evidence quality

Evidence quality of the chronic effect of HIIT versus control condition, HIIT versus MICT and MICT versus control condition, assessed according to GRADE, is "very low." The acute effect of HIIT versus control condition, HIIT versus. MICT and MICT versus control condition is "moderate," "low," and "very low," respectively (Table S5).

3.7 | Effect of HIIT, MICT, and control condition on peripheral BDNF

Network maps of included comparisons testing the chronic and acute effects of HIIT, MICT and control condition on peripheral BDNF are shown in Figure 2. Table 2 shows the pairwise (upper diagonal; Figure S2) and network meta-analysis (lower diagonal; Figure 3) SMD estimates. In the chronic effect, in the pairwise analysis, only the SMD for HIIT versus control condition was significant (0.35, 95% CI: 0.03, 0.67). Whereas, network SDM estimates were not significant for any comparison. In the acute effect, in the pairwise analysis, the SDM estimates were significant for HIIT versus control condition (0.57, 95% CI: 0.27, 0.87), HIIT versus MICT (0.35, 95% CI: 0.08, 0.61), and MICT versus control condition (0.86, 95% CI: 0.01, 1.72). Network SMD estimates were significant for HIIT versus control condition (1.49, 95% CI: 0.61, 2.38) and MICT versus control condition (1.08, 95% CI: 0.04, 2.12; Figure S3).

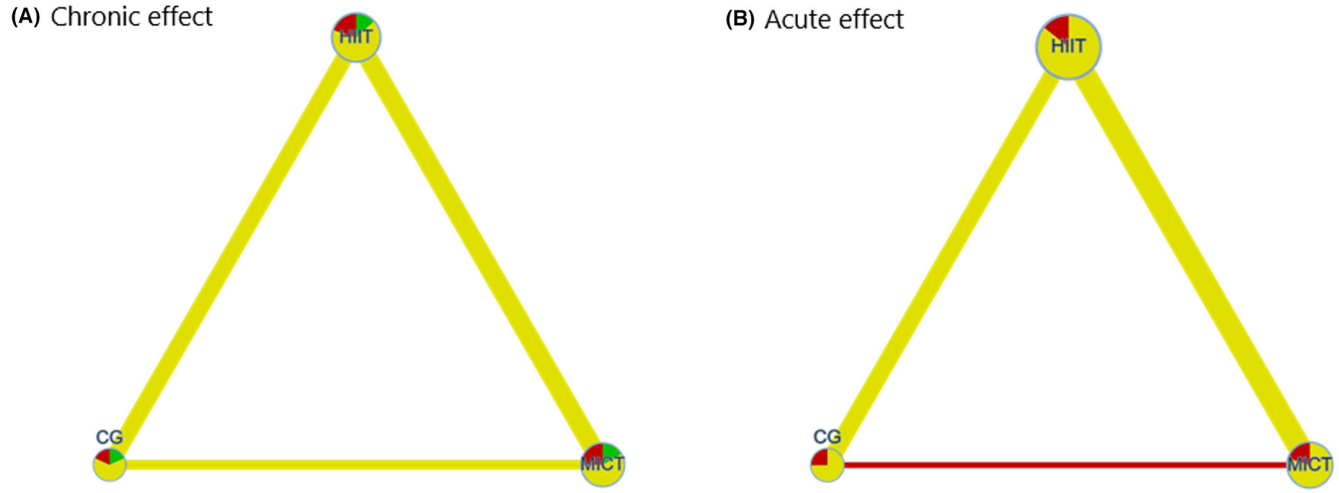

FIGURE 2 Network of available comparisons between interventions on BDNF levels for chronic (A) and acute (B) effect. The size of the node is proportional to number of trial participants, and thickness of the continuous line connecting nodes is proportional to number of participants randomized in trials directly comparing the two treatments. Areas correspond with the proportion of studies for each node with respect to risk of bias assessment as follows: green for low risk, yellow for some concerns, and red for high risk of bias. The color of the lines corresponds with the average of the risk of bias assessment of the studies directly comparing the two interventions.

3.8 | Transitivity

There was no statistically significant difference at baseline in mean age and BMI between HIIT, MICT, and control condition in the chronic and acute effect. The transitivity study is detailed in Table S6.

3.9 | Probabilities

High-intensity interval training showed a higher probability of being the best intervention (74.9% for the chronic effect and 84.9% for the acute effect) (Figure 3). The SUCRA value was higher for HIIT for the chronic effect (85.7%) and for the acute effect (92.4%).

The HIIT versus MICT comparison showed significant substantial heterogeneity for chronic effect ($I^2 = 72.2\%$, $\tau^2 = 0.27$; Table S7).

3.10 | Sensitivity analysis

For the chronic effect, the pooled SMD estimate in BDNF levels was significantly modified in magnitude or direction when removing, for HIIT versus control condition: Eken and Emin Kafkas,[54] Gyorkos et al.,[39] Li et al.,[45] O'Callagham et al.,[56] and Rentería et al.,[47]; for MICT versus control condition: Kovacevic et al.[43] The pooled SMD estimate was not significantly modified for HIIT versus MICT.

For the acute effect, the pooled SMD estimate in BDNF levels was significantly modified in magnitude or direction when removing, for HIIT versus MICT: Boyne[37]; for MICT versus control condition: Reycraft.[48] The pooled SMD estimate was not significantly modified for HIIT versus control condition.

TABLE 2 Results for direct pairwise comparisons and network meta-analysis.

(A) Chronic effect		
HIIT	0.29 (−0.14, 0.73)	**0.35 (0.03, 0.67)**
0.7 (−0.20, 0.35)	MICT	0.23 (−0.19, 0.64)
0.21 (−0.11, 0.54)	0.14 (−0.20, 0.48)	Control condition
(B) Acute effect		
HIIT	**0.35 (0.08, 0.61)**	**0.57 (0.27, 0.87)**
0.41 (−0.37, 1.19)	MICT	**0.86 (0.01, 1.72)**
1.49 (0.61, 2.38)	**1.08 (0.04, 2.12)**	Control condition

Note: Data are effect sizes (95% confidence intervals). Standardized mean differences in bold are statistically significant. Upper right triangle gives pooled standardized mean differences from pairwise comparisons (column intervention relative to row); lower left triangle gives pooled standardized mean differences from the network meta-analysis (row intervention relative to column).

Abbreviations: BMI, high-intensity interval training; MICT, moderate-intensity continuous training.

3.11 | Subgroup analysis and meta-regression models

Regarding exercise intervention characteristics, >30 min of session (SMD: 0.63, 95% CI: 0.06, 1.20) and ≤6 weeks of exercise program duration (SMD: 0.62, 95% CI: 0.16, 1.07) resulted in a significant chronic effect when comparing HIIT versus control condition. The health status

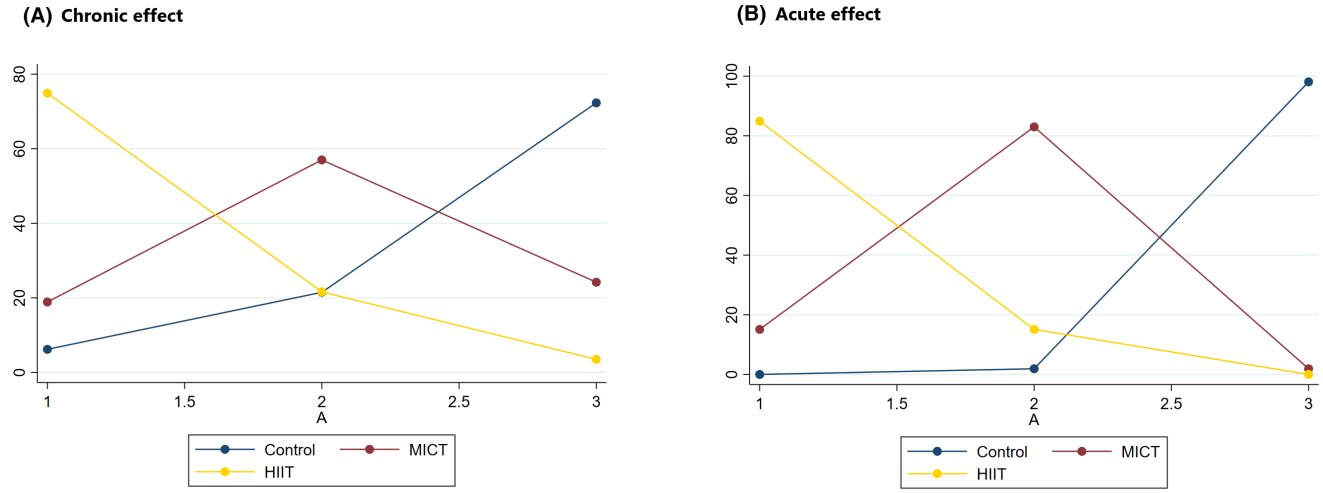

FIGURE 3 Relative rankings for interventions on BDNF levels for chronic (A) and acute (B) effect.

of the subjects did not show to influence the association (Table S8).

An acute effect of HIIT versus the control condition on BDNF concentration was observed in healthy subjects (SMD: 0.57, 95% CI: 0.27, 0.87) with ≥5 bouts (SMD: 0.62, 95% CI: 0.25, 1.00) of ≤2 min duration (SMD: 0.70, 95% CI: 0.34, 1.05), and with a session time ≤ 30 min (SMD: 0.46, 95% CI: 0.09, 0.83). While a significant effect was observed for HIIT versus MICT when performing <5 bouts (SMD: 0.45, 95% CI: 0.02, 0.89) of ≤2 min duration (SMD: 0.32, 95% CI: 0.03, 0.61; Table S8).

Random-effects meta-regression models for the chronic effect of HIIT versus control condition and for the acute effect of HIIT versus control condition and HIIT versus MICT showed that baseline age, VO_2max, BMI, percentage of females and baseline levels of BDNF were not related to pooled SMD estimates (Table S9).

Subgroup analysis and meta-regression models for MICT versus control condition could not be performed due to the limited number of studies.

3.12 | Publication bias

Finally, evidence of publication bias was found by Egger's test and funnel plot asymmetry for the chronic effect of HIIT versus control condition ($p = 0.005$) and MICT versus control condition ($p = 0.060$) but not for the rest (Figures S4 and S5).

4 | DISCUSSION

To our knowledge, this is the first systematic review and network meta-analysis that provides an integrated synthesis of the effectiveness of HIIT and MICT on peripheral BDNF in adults. Our study suggests that the intervention with most promising short-term (acute) effects on peripheral BDNF was HIIT followed by MICT, although our network estimates did not show significant differences between them in our network estimates. Pairwise comparison only for HIIT versus control condition resulted in a significant effect for long-term improvements (chronic effects) in BDNF concentrations.

4.1 | HIIT versus control condition

According to previous evidence, we found that interval training, as well as high-intensity exercise, has a moderate short-term effect on BDNF levels in young adults, suggesting that the intensity may be associated with the BDNF response to exercise.[22,27] In contrast, our network estimates did not support a long-term effect of this modality of exercise on BDNF, probably due to the scarcity of studies evaluating this comparison, as we found a publication bias, so this evidence should be interpreted with caution. Moreover, our results suggest that an increase in its concentration would only be achieved with sessions of >30 min and programs with a duration of ≤6 weeks.

Alternatively, performing HIIT across time would improve cognition,[58–60] and this may be determined by the physiological effects induced by a single HIIT session on cognition-related factors such as BDNF,[61] since it seems that the improvement in short-term memory would be related to the acute increase in BDNF.[62] Moreover, an association between the intensity of exercise and its acute effects on peripheral BDNF concentrations, with high intensity and graded exercise tests leading to greater increases in

plasma BDNF concentration.[63] Our data corroborate previous evidence in healthy subjects, with the dose required to achieve this acute beneficial effect corresponding to sessions of ≤30 min per session that included ≥5 bouts of a duration ≤2 min, regardless of rest time.

Moreover, a single session of HIIT results in an increase in executive function,[64] which is accompanied by the stimulation of the circulating levels of peripheral exercise-related factors, such as systemic lactate.[65] This myokine accumulates in the blood during acute exercise depending on the intensity and duration of the exercise and is able to cross the blood–brain barrier.[66,67] Lactate synthesized as a result of exercise is used to satisfy the energy demands of neurons[68] and, as a neuronal signaling molecule, to increase BDNF expression.[69] Therefore, HIIT programs would result in a peak accumulation of lactate in the blood, which is responsible for augmented BDNF expression in the brain.[68]

4.2 | HIIT versus MICT

Previous studies have shown that continuous exercise increases BDNF levels, but the evidence as to whether its effect is equal to that of HIIT is controversial, mainly in those studies that aim to determine which of the two types of exercise is more effective. Fernandez et al.,[27] in a meta-analysis to evaluate the acute effect, reported that there was no difference between HIIT and noninterval exercise in young adults, collapsing in their analyses moderate- and low-intensity continuous training as a single category. Thus, the results of an experimental study conducted in eight healthy adults suggested that intensity is a key factor in determining the acute response to functional fitness training, such that functional fitness training performed at all out resulted in a more pronounced acute increase in BDNF than a self-regulated intensity based on perceived exertion.[70]

Consistent evidence supports the role of BDNF as a primary mediator of synaptic plasticity, which is related to cortical volume, neurogenesis, and neural activities such as long-term potentiation and memory consolidation.[71] Accordingly, our findings are consistent with previous studies reporting that the acute effect of HIIT was sufficient to modulate cortical excitability and neuroplasticity, whereas MICT was not.[72,73] Thus, Hugues et al.[59] reported that a single session of HIIT, in contrast to moderate-intensity exercise, accelerates vocabulary learning in student athletes and that BDNF could play a mediating role in enhancing retention of new vocabulary through HIIT. In fact, HIIT seems to be more effective than MICT in improving cognitive performance in young adults and in severe mental illness.[61]

4.3 | Influence of cardiorespiratory fitness on the effect of HIIT interventions

It has been reported that resting serum BDNF levels are significantly lower in middle-aged trained men than in sedentary controls, increasing immediately after exercise and then decreasing to lower levels than in sedentary individuals.[74] Conversely, our analyses show that the baseline cardiorespiratory fitness of the subjects does not influence the effect of HIIT; moreover, in our study, the variability of the characteristics of the HIIT interventions has a negligible effect on peripheral BDNF levels. Therefore, to improve brain functioning and considering that, in the short term, HIIT is a more efficient option than MICT to increase BDNF, along with other physiological adaptations such as a decrease in oxidative stress and inflammation,[75,76] it would be of interest to prescribe the usual HIIT programs to adult people regardless of their baseline levels of fitness but rather guided by their preferences in terms of working time, resting time, number of bouts, intensity (at least 75% VO_2max or HRmax) and session time.

4.4 | Limitations

Some limitations of our systematic review and meta-analysis should be acknowledged; some of them are common to this type of synthesis study, but others are not. First, the low sample size of the included studies undermine the reliability of their estimates. Second, it has been shown that baseline levels of serum BDNF can be stable individually but may differ widely across subjects.[77] However, this meta-analysis has examined interstudy variability and non inter participants variability. Instead of it, the influence of baseline peripheral BDNF concentration was explored using meta-regression models. Third, HIIT programs were heterogeneous across studies, however, they have been pooled in a way that can provide conclusive results in relation to the dose–response. Fourth, circulating BDNF in blood was measured across serum and plasma, which could introduce a bias from one study to another, as it is well established that higher concentrations of BDNF are observed in serum than in plasma.[78] In the coagulation process, platelet activation causes a release of BDNF from platelets into serum, whereas plasma is obtained from blood samples collected in tubes containing anticoagulants, which prevents coagulation and, as a consequence, platelet action and BDNF release.[79] Finally, comparisons of HIIT and MICT versus control condition for the chronic effect showed publication bias, which could affect the

reliability of direct and indirect estimates for such comparisons, requiring further research. Future RCTs evaluating the effect of HIIT on peripheral BDNF levels, with a larger sample size, in populations with different age groups and health conditions are needed to produce more consistent evidence that can be incorporated into clinical guidelines.

4.5 | Perspective

These findings show the effectiveness of HIIT to improve acutely peripheral BDNF in healthy adults. These results were similar those shown in previous systematic reviews which studied high-intensity exercise in young adults, as well as those studying the effect of low/moderate-intensity intervallic exercise in young and older adults. Furthermore, although MICT influences positively peripheral BDNF levels, the acute benefits of HIIT are superior to those of MICT. Thus, the prescription of HIIT programs could have cognitive protective effects.

5 | CONCLUSION

HIIT is an effective training method for acutely increasing peripheral BDNF levels in healthy adults, requiring sessions of ≤30 min including ≥5 bouts of duration ≤2 min, regardless of resting time. Their benefits in terms of BDNF levels are higher than those of MICT and, because this exercise modality involves shorter training time, regardless of sex, BMI, and baseline fitness, the prescription of HIIT programs may have protective effects on mental health and cardiac function. Additionally, further studies evaluating the chronic effect of these interventions versus control condition are required to corroborate our results.

AUTHOR CONTRIBUTIONS

Eva Rodríguez-Gutiérrez participated in the design of the study and contributed to data collection and data reduction/analysis; Ana Torres-Costoso and María José Guzmán-Pavón participated in the design of the study; Bruno Bizzozero-Peroni participated in the design of the study and contributed to data collection; Mairena Sánchez-López and Alicia Saz-Lara contributed to data reduction/analysis; Vicente Martínez-Vizcaíno contributed to data analysis and interpretation of results. All authors contributed to the manuscript writing. All authors have read and approved the final version of the manuscript and agree with the order of presentation of the author.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Additional supporting information can be found online in the Supporting Information section at the end of this article.

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