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Effects of Intermittent Fasting on Brain-Derived Neurotrophic Factor Levels in Adults with Overweight or Obesity: A Scoping Review

Adetunmise Oluseyi Olajide[1,2], Alejandra Gallego Rivas[1,3], Amanda Lucia Armendariz Ortiz[1,4], Ana Beatriz Sampaio Pinto de Castro[1,5], Belkis Gabriela Franco Malaver[1], Claudia Reyes Aguirre[1,6], Cristina Oliveira[1], Eugenia Rojas[1], Fatima Ramos[1,7], Felipe Marques da Costa[1,8], Gabriella Freaza[1,9], Hawraa Shwaylia[1,10], Iñaki Xavier Bizama Brahm[1,6], Jarline Esther Cruz Santana[1], Joao Victor Starling Magalhaes[1,5], Jorge Segovia[1], Jose Valenzuela[1], Letícia Sanches Kelemen[1,11], Lubna Mohammed[1], Maira Foresti[1], Maria Luiza Cunha D´avila[1,11], Marina Acevedo Zarzar de Melo[1,12,13], Roma Aguiar[1], Tomislav Rajevic Mosler[1,6], Yael Dinur Schejter[1,14], Yannick Hurni[1,15,16*]

[1]Harvard T.H. Chan School of Public Health, Boston, USA; [2]Department of Maternal and Child Health Nursing, Faculty of Nursing Sciences, Ladoke Akintola University of Technology, Ogbomoso, Oyo State, Nigeria; [3]Somer Incare Cardiovascular Center, Rionegro, Antioquia, Colombia; [4]Facultad de Medicina, Universidad Francisco Marroquin, Guatemala City, Guatemala; [5]Institution Virtú Ophthalmology, Belo Horizonte, Brazil; [6]Hospital del Trabajador ACHS Salud, Santiago, Chile; [7]Escuela de Medicina, Universidad Peruana de Ciencias Aplicadas, Lima, Peru; [8]Beneficência Portuguesa de São Paulo, São Paulo, Brazil; [9]Bahiana School of Medicine and Public Health, Salvador, Bahia, Brazil; [10]National Center for Cancer Care and Research, Hamad Medical Corporation, Doha, Qatar; [11]São Leopoldo Mandic, Campinas, Brazil; [12]Oncologia D'Or, Recife, Brazil; [13]Instituto Materno-Infantil de Pernambuco (IMIP), Recife, Brazil; [14]Division of IHOPE, Department of Pediatrics, Stollery Children's Hospital, University of Alberta, Edmonton, Canada; [15]Department of Obstetrics, Gynecology and Reproduction, Dexeus Mujer, Dexeus University Hospital, Barcelona, Spain; [16]Department of Paediatrics, Obstetrics, Gynaecology and Preventive Medicine and Public Health, Faculty of Medicine, Universidad Autonoma Barcelona, Barcelona, Spain.

Abstract

Background: *Overweight and obesity are major public health concerns. Increasing evidence links these conditions to cognitive decline and neurodegenerative disorders, potentially mediated by reduced brain-derived neurotrophic factor (BDNF). Intermittent fasting (IF) has gained attention for its potential metabolic and neuroprotective benefits, possibly increasing BDNF. However, the relationship between IF, BDNF, and cognitive outcomes in overweight and obese individuals remains unclear.*

Aims: *This scoping review aimed to systematically map and synthesize the existing evidence on the impact of various IF protocols on BDNF levels in adults with overweight or obesity.*

Methods: *Following the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines, a systematic search was conducted in five databases. Studies including adults with a body mass index* $\geq 25\,\mathrm{kg/m^2}$ *and comparing various IF protocols to continuous caloric restriction or unrestricted diets were considered. The search included studies published up to April 26, 2025. Dual independent screening, data extraction, and risk of bias assessment (RoB 2.0) were performed.*

Results: *From 22,117 records screened, 6 RCTs (n = 534; 83.5% female; ages 18–70) were identified and mapped. Trials tested alternate-day fasting, time-restricted feeding, and intermittent energy restriction protocols over 8–32 weeks. The evidence mapping revealed that three studies demonstrated significant within-group increases in BDNF, with two also reporting greater increases versus controls; the remaining three trials found no effect. Two studies assessed cognition, but results were inconsistent and showed no clear benefit attributable to IF.*

Conclusion: *This scoping review mapped heterogeneous evidence suggesting that select IF protocols may elevate BDNF in overweight and obese adults; however, the available evidence exhibits considerable methodological heterogeneity, limiting definitive conclusions. Well-powered, rigorously controlled trials with standardized protocols are warranted to clarify the clinical relevance of BDNF modulation by IF.*

Introduction

Obesity and overweight represent a growing global public health challenge. In 2022, the World Health Organization estimated that 43% of adults were overweight and 16% were obese (World Health Organization, 2024). These conditions are major risk factors for metabolic syndrome, cardiovascular disease, neurodegenerative disorders, and several cancers, generating significant clinical, social, and economic burdens (GBD 2019 Risk Factors Collaborators, 2020). Beyond systemic comorbidities, growing evidence links excess adiposity with cognitive impairment and increased risk of dementia and Alzheimer's disease (Kivipelto et al., 2005).

Intermittent fasting (IF) has emerged as a promising dietary strategy with benefits extending beyond weight loss (de Cabo & Mattson, 2019). It is defined as a temporal eating regimen characterized by recurrent cycles of energy intake and caloric restriction or abstinence, with fasting intervals typically ranging from several hours to multiple consecutive days. Although the precise mechanisms remain incompletely understood, IF may positively influence metabolic pathways implicated in obesity-related comorbidities, including insulin sensitivity, lipid metabolism, and systemic inflammation reduction (Yuan et al., 2022). Notably, IF may also exert neuroprotective effects by modulating oxidative stress pathways, enhancing synaptic plasticity, and promoting neuronal resilience (Brocchi et al., 2022). A key molecular mediator in this process could be brain-derived neurotrophic factor (BDNF), a protein predominantly synthesized in the central nervous system. BDNF plays a crucial role in neuronal growth, synaptic plasticity, and differentiation, as well as in cognitive functions such as learning and memory, and the regulation of appetite and energy homeostasis (Brocchi et al., 2022; Huang & Reichardt, 2001). In individuals with obesity, BDNF levels are often reduced due to chronic inflammation, insulin resistance, and poor lifestyle habits (Chaldakov et al., 2007). IF may increase BDNF by inducing mild metabolic stress, improving insulin sensitivity, reducing inflammation, and shifting brain metabolism to ketones, potentially enhancing both metabolic and cognitive function (Brocchi et al., 2022).

Despite growing interest in IF and its potential neuroprotective effects, evidence regarding its impact on BDNF levels and cognitive outcomes in individuals with excess weight remains limited and inconclusive. Moreover, the comparative efficacy of different IF protocols and the mechanisms by which they may influence neurotrophic and cognitive outcomes are not well established. Existing studies are few and methodologically heterogeneous, with substantial variability in populations, fasting regimens, and outcome definitions. To explore and map this emerging field, we conducted a scoping review to systematically describe the available evidence on the effects of various IF regimens on BDNF levels and cognitive outcomes in adults with overweight or obesity, aiming to clarify the extent and nature of the literature and to highlight areas requiring further, more rigorous investigation.

Materials and Methods

This study was conducted as a scoping review, following the methodological guidance outlined in the PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews) checklist (Tricco et al. 2018). We aimed to map existing evidence on the effects of IF on levels of BDNF in adults with overweight or obesity. This review was guided by the question of how various IF protocols affect BDNF levels in adults with overweight or obesity, compared to diets without time restriction.

Search Strategy

A comprehensive search was conducted in PubMed, Scopus, Embase, the Cochrane Library, and Web of Science from the database's inception to April 26, 2025. The strategy combined controlled vocabulary (e.g., Medical Subject Headings [MeSH]) and free-text terms covering three key concepts: the population ("overweight," "obesity," "obese," "excess weight," "body mass index," "BMI"), the interventions ("intermittent fasting," "time restricted feeding," "alternate day fasting," "fasting mimicking diet," "periodic fasting," "Ramadan fasting"), and the outcomes ("brain-derived neurotrophic factor," "BDNF," "cognition," "cognitive function," "memory," "neuroplasticity"). Searches were run in all available fields for each database. The full database-specific search strings are reported in Supplementary Material 1. We also manually screened the reference lists of included studies and relevant reviews to identify additional eligible articles. Grey literature sources, trial registries, and unpublished data were not included.

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Inclusion and Exclusion Criteria

Included studies enrolled adults ($\geq$ 18 years) with a BMI $\geq 25\,\mathrm{kg/m^2}$, with or without metabolic comorbidities. All intermittent fasting (IF) protocols (e.g., time-restricted eating, periodic fasting, alternate-day fasting, Ramadan-style fasting), alone or combined with physical activity, were eligible. Comparison groups received either non-restricted or continuous caloric restriction diets. Studies were included only if they reported serum or plasma brain-derived neurotrophic factor (BDNF) concentrations both before and after the intervention. Eligible studies were interventional or observational, published in English, Spanish, or Portuguese, with no time restrictions.

Exclusion criteria included studies performed on patients with cognitive-impairing neurological or psychiatric conditions, pregnant or lactating women, animal studies, and studies involving additional interventions such as medications or surgical procedures.

Selection of Studies, Screening Process, and Data Extraction

All references were managed in Covidence (Veritas Health Innovation, Melbourne, Australia). Title/abstract screening and full-text assessment were performed by pairs of independent reviewers from the review team, with a third reviewer resolving disagreements. A standardized extraction form was used to ensure consistency. Data were extracted independently by two reviewers per study; discrepancies were resolved by consensus.

Primary and Secondary Outcomes and Data Synthesis

The primary outcome was a change in serum or plasma BDNF from baseline. Secondary outcomes included cognitive performance, anthropometric measures, glucose/insulin metabolism, and lipid profile. Data were synthesized using a qualitative, narrative approach, as heterogeneity in IF protocols, intervention duration, study populations, and BDNF measurement methods precluded a quantitative meta-analysis.

Risk of Bias Assessment

As only parallel-group RCTs met the eligibility criteria, risk of bias was assessed using the Cochrane RoB 2.0 tool (Sterne et al., 2019), which evaluates five domains: randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of the reported result. The assessment was conducted by two independent reviewers, with disagreements resolved by a third.

Results

Description of Studies

The systematic search retrieved 22,108 records from the five electronic databases, and an additional nine records were identified through manual screening of the reference lists of relevant publications, for a total of 22,117 records. After duplicate removal and screening, 46 full-text articles were assessed for eligibility. Following full-text review, 6 studies met the inclusion criteria and were included in this scoping review (Figure 1). All included studies were randomized controlled trials (RCTs). The trials were conducted across five countries—the United Kingdom, the United States, Germany, Iran, and Thailand—and all took place in single-center outpatient settings, with one study also involving a research facility (Table 1).

Population

The six included studies enrolled a total of 534 adults who were overweight or obese. The overall study population was predominantly female (83.5%), with individual trial samples ranging from 50% to 100% women. Participants were aged between 18 and 70 years and were free from major neurological or psychiatric conditions. Notably, specific inclusion criteria varied and included subgroups such as premenopausal women (Harvie et al., 2011), postmenopausal women (Keawtep et al., 2024), or individuals with some features of the metabolic syndrome (Bartholomew et al., 2021)(Table 1).

Intermittent Fasting Interventions, Controls, and Measured Outcomes

Among the six included studies, IF protocols varied considerably: four employed weekly intermittent energy restriction (Harvie et al., 2011; Schübel et al. 2018; Keawtep et al. 2024; Bartholomew et al. 2021), differing in fasting day frequency, caloric intake (ranging from 0% to 75% of daily needs), and schedule progression; one study adopted alternate-day fasting with total caloric abstinence (Catenacci et al., 2016); and one used a daily time-restricted feeding protocol with a fixed 10-hour eating window (Irani et al., 2024) (Table 2).

Control groups also varied considerably. Four trials compared IF with continuous caloric restriction

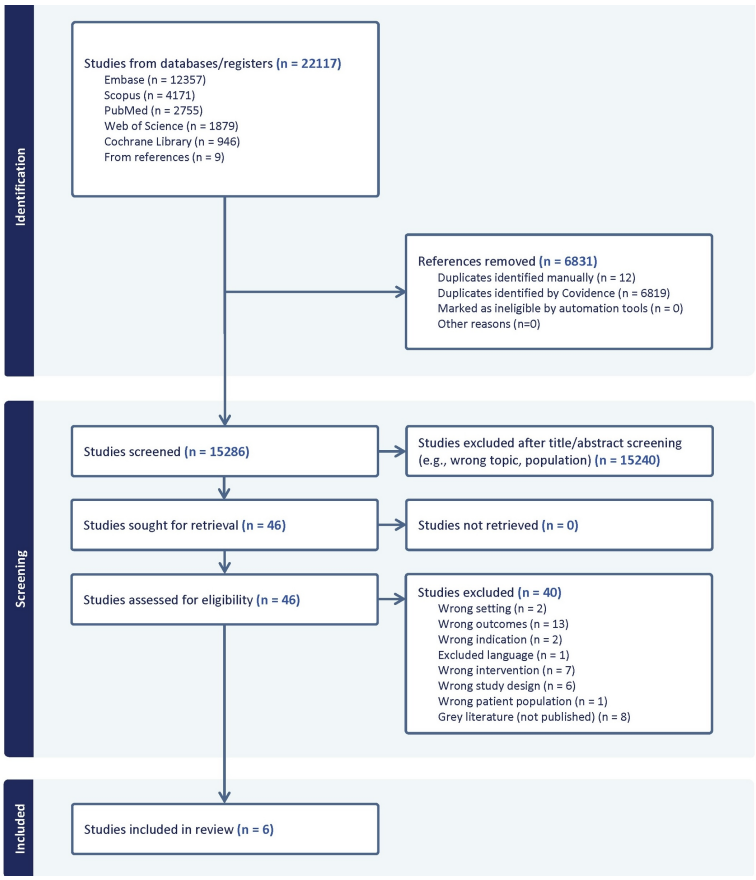

Figure 1: *PRISMA flow diagram of the study selection process.*

protocols (Harvie et al., 2011; Catenacci et al. 2016; Schübel et al. 2018; Irani et al. 2024). In contrast, other studies used non-dietary comparators, such as physical-cognitive exercise with or without dietary changes (Keawtep et al. 2024), or no intervention at all (Bartholomew et al. 2021; Schübel et al. 2018; Keawtep et al. 2024).

BDNF levels and cognitive functions were the primary outcomes in one study (Keawtep et al. 2024). In the remaining five studies, these outcomes were considered secondary endpoints, with the main focus placed on lipid profiles, anthropometric characteristics, insulin sensitivity, or adipose tissue gene expression.

BDNF was measured in serum (Harvie et al. 2011; Schübel et al. 2018; Irani et al. 2024) or plasma (Catenacci et al. 2016; Bartholomew et al. 2021; Keawtep et al. 2024), and assessed at baseline and at the end of the study in all six trials. BDNF concentrations were quantified using enzyme-linked immunosorbent assay (ELISA) in all studies, although different commercial kits were employed. Notably, the specific sampling time was not reported in one study (Schübel et al. 2018); in the remaining studies, blood samples were collected in the morning following a fasting period of $\geq$ 10–12 hours.

Main Outcomes

Impact on BDNF

Three RCTs reported significant within-group increases in BDNF levels (pre- vs. post-intervention) (Catenacci et al., 2016; Irani et al., 2024; Keawtep et al., 2024). In two of these (Catenacci et al., 2016; Irani et al., 2024), between-group comparisons also showed a greater increase in the IF group compared to controls. In the study by Keawtep et al. (2024), BDNF levels increased significantly in both the IF-only and IF combined with exercise groups relative to the no-intervention control; however, no significant differences were observed when compared to the exercise-only group. The remaining three studies (Harvie et al., 2011; Schübel et al., 2018; Bartholomew et al., 2021) did not report significant changes in BDNF levels (Table 2 and Supplementary Table 2).

In the study by Catenacci et al., no differences in BDNF were observed between alternate-day fasting and daily caloric restriction after 8 weeks. However, after 24 weeks of unsupervised follow-up, BDNF significantly increased in the IF group ($+4.80 \pm 2.48$ ng/mL) and decreased in the caloric restriction group (-4.23 ± 2.45 ng/mL), with a significant between-group difference ($p = 0.016$) (Catenacci et

First Author, Year	Country	Study Type and Design	Setting	Subjects characteristics	Sample Size (IF / Control)	Female (%)	Age (mean ± SD) (years)	BMI (mean ± SD) (kg/m²)
Harvie, 2011	UK	Single-center RCT (Parallel)	Outpatient	Premenopausal, overweight or obese healthy women aged 30–45	IF: 54 Control: 53	100%	IF: 40.1±4.1 Control: 40.0±3.9	IF: 30.7±5.0 Control: 30.5±5.2
Catenacci, 2016	USA	Single-center RCT (Parallel)	Outpatient	Obese, non-smoking, healthy adults aged 18–55	IF: 14 Control: 12	76%	IF: 39.6±9.5 Control: 42.7±7.9	IF: 35.8±3.7 Control: 39.5±6.0
Schübel, 2018	Germany	Single-center RCT (Parallel)	Outpatient	Overweight and obese, healthy, non-smoking adults aged 35–65	IF: 50 Control 1: 50 Control 2: 50	50%	IF: 49.4±9.0 Control 1: 50.5±8.0 Control 2: 50.7±7.1	IF: 32.0±3.8 Control 1: 31.2±4.0 Control 2: 31.1±3.6
Bartholomew, 2021	USA	Single-center RCT (Parallel)	Mixed: Outpatient and Research Center	Overweight or obese, healthy adults with a modest increase in LDL-C, ≥1 metabolic syndrome component and/or type 1 diabetes mellitus, aged 21–70	IF: 50 Control: 53	66%	IF: 49.3±12.0 Control: 47.0±9.8	IF: 35.1±8.2 Control: 34.0±7.3
Irani, 2024	Iran	Single-center RCT (Parallel)	Outpatient	Overweight or obese women aged 20–65	IF: 29 Control: 27	100%	IF: 43.6±9.3 Control: 41.0±8.3	IF: 30.8±3.2 Control: 31.8±3.8
Keawtep, 2024	Thailand	Single-center RCT (Parallel)	Outpatient	Postmenopausal obese women with no history of hormone therapy, aged 45–59	IF 1: 23 IF 2: 23 Control 1: 23 Control 2: 23	100%	IF 1: 52.9±3.9 IF 2: 52.2±3.4 Control 1: 53.6±2.8 Control 2: 52.7±3.6	IF 1: 28.3±2.8 IF 2: 29.7±4.6 Control 1: 29.2±2.9 Control 2: 29.1±2.9

IF= intermittent fasting; SD = standard deviation; BMI = body mass index; RCT = randomized controlled trial

Table 1: *Characteristics of the included randomized controlled trials.*

al., 2016).

In the study by Irani et al., participants in the time-restricted feeding group (10-hour eating window) showed a substantial increase in serum BDNF compared to the low-calorie diet control group (1.44 ± 1.34 ng/mL vs. 0.14 ± 0.49 ng/mL; $p < 0.001$) (Irani et al., 2024).

Conversely, in the study by Keawtep et al. (2024), BDNF increased significantly in all intervention groups—IF alone, exercise alone, and their combination—compared to controls ($p < 0.05$). The greatest increase was observed in the combined group (from 3.79 ± 2.17 to 4.72 ± 2.25 ng/mL), followed by the exercise-only group (4.01 ± 2.23 to 4.67 ± 2.15 ng/mL), and the IF-only group (3.21 ± 2.43 to 4.39 ± 1.80 ng/mL). However, no significant differences were found among the three interventions, suggesting that the BDNF increase may not be attributable specifically to IF.

Impact on Cognitive Functions

Only two trials assessed cognitive function as an outcome. In Keawtep et al. (2024), the IF group did not show statistically significant improvements in cognitive performance compared to either the control or other intervention groups, as measured by the Montreal Cognitive Assessment, Verbal Fluency Test, Digit Span Test, and Trail Making Test A and B. Although some improvements were observed in the exercise and combined groups, no cognitive benefit could be specifically attributed to the dietary intervention alone (Keawtep et al., 2024). Using the MicroCog GCPi score as a measure of global cognitive function, Bartholomew et al. found no significant between-group differences in cognitive outcomes following the fasting intervention (Bartholomew et al., 2021) (Table 2 and Supplementary Table 2).

Impact on Anthropometric Characteristics, Glucose/Insulin Metabolism and Lipid Profile

Among the six studies reviewed, three (Irani et al., 2024; Keawtep et al., 2024; Harvie et al., 2011) reported significant reductions in body weight and BMI following IF interventions compared to controls. Irani et al. observed a significant decrease in both parameters in the time-restricted feeding group versus the chronic caloric restriction group (BMI: -1.70 ± 0.86 vs. -1.41 ± 0.48 kg/m^2, $p = 0.009$; weight: -4.42 ± 2.16 vs. -3.72 ± 1.32 kg, $p = 0.01$) (Irani et al., 2024). Although Keawtep et al. (2024) and Harvie et al. (2011) reported significant reductions within groups following IF, no between-group differences emerged for either BMI or weight. No significant effects were found in the remaining studies.

Significant improvements in glucose–insulin metabolism were observed in only two studies, with IF showing improved insulin sensitivity compared to controls (Harvie et al., 2011; Bartholomew et al., 2021), whereas Keawtep et al. (2024) reported improved insulin sensitivity only in the combined and exercise intervention groups (Keawtep et al., 2024).

Keawtep et al. (2024) observed improvements in blood cholesterol in the IF groups compared to non-intervention controls, but not compared to the other intervention groups (Keawtep et al., 2024). The remaining studies reported no significant between-group differences in lipid parameters (Table 2 and Supplementary Table 2).

First Author, Year	Intermittent fasting protocol	Control	Duration	BDNF change vs. baseline	BDNF change vs. control	Cognitive Impact	Anthropometric Characteristics	Glucose / Insulin Profile	Lipid Profile
Harvie, 2011	Intermittent energy restriction (2 days/week, ~25% of needs). No restrictions on other days.	Continuous caloric restriction (~75% of needs)	26 weeks	No differences	No differences	Not assessed	Significant body weight and BMI reduction in both groups. No intergroup differences.	Improved insulin sensitivity in both groups; significantly better results in the IF group.	Improved lipid profile in both groups. No intergroup differences.
Catenacci, 2016	Alternate-day fasting (0 kcal on fasting days). No restrictions on other days.	Continuous caloric restriction (400 kcal deficit)	8 weeks followed by a 24-week unsupervised follow-up	Increased	BDNF levels increased compared with control at week 32	Not assessed	Significant body weight and BMI reduction in both groups. No intergroup differences.	No differences.	Improved lipid profile in both groups. No intergroup differences.
Schübel, 2018	Intermittent energy restriction (2 days/week, ~25% of needs). No restrictions on other days.	Control 1: Continuous caloric restriction (~75% of needs) Control 2: No restrictions	12 weeks	No differences	No differences	Not assessed	Significant reductions in body weight and BMI were observed in all groups. The IF group showed significantly greater improvements compared to Control 2, and Control 1 outperformed Control 2. No significant difference between IF and Control 1.	Improved insulin sensitivity in all groups. No intergroup differences.	Improved lipid profile in all groups. No intergroup differences.
Bartholomew, 2021	Intermittent energy restriction (2 days/week; 0 kcal during 4 weeks, followed by 1 day/week for 22 weeks). No restrictions on other days.	No restrictions	26 weeks	No differences	No differences	No differences (MicroCog)	No differences.	Improved insulin sensitivity in the IF group; significantly better than the control group.	No differences.
Irani, 2024	Time-restricted feeding (10-h eating window: 10am–8pm) with 300–500 kcal deficit.	Continuous caloric restriction (300–500 kcal deficit)	8 weeks	Increased	Significantly higher BDNF levels in IF group compared to the control group.	Not assessed	Significant reductions in body weight and BMI in the IF group, both pre-post and compared to the control.	Not assessed	Not assessed
Keawtep, 2024	IF1: Intermittent energy restriction (2 days/week, progressive calorie restriction: ~75% of needs during 4 weeks, ~50% for 4 weeks, and ~25% for 4 weeks). No restrictions on other days IF2: as IF 1 + physical activity	Control 1: Physical activity only. No dietary restrictions. Control 2: No dietary restrictions	12 weeks	Increased for both IF1 and IF2	Significantly higher BDNF levels in IF1, IF2, and Control 1 than in Control 2. No significant differences among IF1, IF2, and Control 1.	IF1, IF2, and Control 1 performed significantly better than Control 2 on all tests. No significant differences between IF1, IF2, and Control 1 (MoCA, VFT, DST, TMT-A/B).	Significant reduction in weight and BMI in IF1, IF2, and Control 1 vs baseline. IF2 and Control 1 (but not IF1) showed significant reduction compared to Control 2. No differences between IF1, IF2, and Control 1.	Improved insulin sensitivity in IF1 and IF2 compared to Control 2; no significant difference between IF1 and IF2.	Total cholesterol significantly decreased in IF1, IF2 compared with Control 2. Triglyceride levels did not differ between groups.

IF = Intermittent Fasting; BDNF = Brain-Derived Neurotrophic Factor; BMI = Body Mass Index; MoCA = Montreal Cognitive Assessment; VFT = Verbal Fluency Test; DST = Digit Span Test; TMT-A/B = Trail Making Test, Part A and B; HOMA-IR = Homeostatic Model Assessment of Insulin Resistance; TG = Triglycerides; TC = Total Cholesterol; LDL-C = Low-Density Lipoprotein Cholesterol; HDL-C = High-Density Lipoprotein Cholesterol; GCPi = General Cognitive Proficiency Index

Table 2: *Summary of intermittent fasting protocols and main outcomes.*

Assessment of Risk Bias in Individual Studies

The risk of bias across the six included trials is summarized in Figure 2. One study (Catenacci et al. 2016) was judged to be at high overall risk of bias, primarily due to major concerns regarding deviations from the intended intervention. In comparison, four studies (Harvie et al. 2011; Bartholomew et al. 2021; Irani et al. 2024; Keawtep et al. 2024) were rated as having some concerns, often related to the randomization process or selective reporting. Only one study (Schübel et al. 2018) was judged to be at low risk of bias across all domains.

Discussion

BDNF, a neurotrophin essential for neuroplasticity, energy homeostasis, and cognitive function (Bathina & Das, 2015), has been implicated in the pathogenesis of neurodegenerative disorders (Scalzo et al., 2010; Sohrabji & Lewis, 2006; Mughal et al., 2011) and metabolic dysregulation (Lebrun et al., 2006). In individuals with overweight or obesity, reduced BDNF levels have been associated with cognitive deficits, suggesting that therapeutic strategies aimed at restoring its expression may confer neurocognitive benefits (Chaldakov et al., 2007; Ceylan et al., 2024). This scoping review synthesized evidence from six RCTs investigating the effects of various IF protocols on BDNF levels, cognitive function, and metabolic parameters in overweight or obese adults. The findings suggest that while IF may enhance BDNF levels and improve metabolic outcomes, results across studies remain heterogeneous and limited, particularly concerning cognitive benefits. The substantial heterogeneity among the included RCTs precluded a meaningful synthesis of subgroup results; each study differed in terms of participants, IF regimen, intervention duration, and BDNF measurement methods. Due to this diversity, we were limited to providing a descriptive synthesis of the available evidence rather than a structured or pooled analysis.

Among the included studies, only three trials demonstrated significant increases in BDNF following IF interventions. However, the patterns of BDNF change varied across protocols. In Catenacci et al. (2016), significant BDNF elevation emerged only after a prolonged unsupervised follow-up, suggesting possible delayed or sustained effects of alternate-day fasting. Irani et al. (2024) observed that a daily 10-hour time-restricted feeding regimen led to increased BDNF levels compared to caloric restriction with equivalent energy deficits. Keawtep et al. (2024) demonstrated BDNF increases across both IF and physical-cognitive exercise groups, suggesting that exercise may confound or enhance IF-related effects.

Several factors likely contribute to these discrepancies. Variations in study population, IF protocols, duration, caloric intake control, study length, and body composition changes introduce substantial heterogeneity across studies. Among these, the degree of adipose tissue reduction may be particularly relevant, as some studies reported that greater fat loss correlated with increases in BDNF levels (Irani et al., 2024; Catenacci et al., 2016; Keawtep et al., 2024). This raises the possibility that the observed BDNF increases may be, at least in part, a consequence of weight loss rather than a direct effect of the fasting regimen (Carneiro & Pellerin, 2022; Guo et al., 2023).

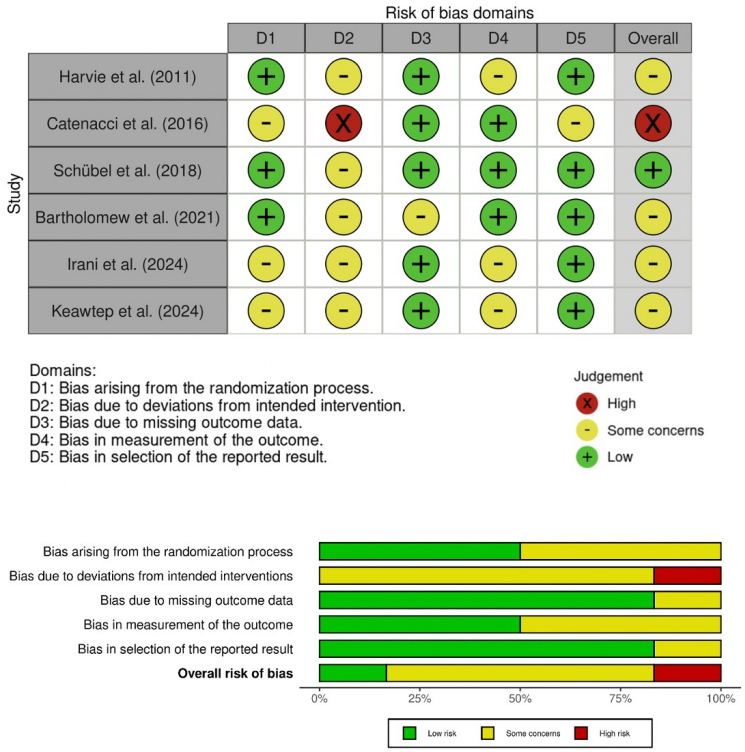

Figure 2: *Risk of bias assessment of the included randomized controlled trials using the RoB 2.0 tool.*

Moreover, the predominance of female participants across varying hormonal states may have introduced a confounding factor. Given that sex hormones modulate BDNF regulation (Glud et al., 2019; Begliuomini et al., 2007), this may contribute to heterogeneity and limit the generalizability of the results.

In addition to these sources of heterogeneity, the biological significance of the observed BDNF changes warrants consideration. Peripheral BDNF concentrations in adults typically range widely, with serum levels often in the tens of ng/mL (median values around 20–30 ng/mL) and broad interindividual variability, whereas plasma levels tend to be lower and more variable owing to preanalytical and methodological factors (Naegelin et al., 2018). The BDNF changes observed across the included RCTs—generally in the range of 1–5 ng/mL—thus represent relatively small to moderate shifts when considered against these background levels, and their clinical relevance remains uncertain. Interpretation is further complicated by (i) heterogeneity in sample matrix and assay methodology (serum vs. plasma, different ELISA platforms), which can markedly influence absolute values, and (ii) the absence of an established minimal clinically important difference for BDNF with respect to cognitive outcomes. These limitations further challenge the ability to determine whether the observed changes are sufficient to translate into meaningful neurocognitive effects. Consequently, current evidence linking IF-induced changes in peripheral BDNF to cognitive outcomes remains indirect and preliminary.

Cognitive outcomes were assessed in only two studies. Keawtep et al. (2024) reported global cognitive improvements across all intervention groups, but these improvements were not specifically attributable to IF. Bartholomew et al. found no significant cognitive changes. These findings should therefore be interpreted as preliminary and exploratory, reflecting the paucity of well-designed trials with cognition as a prespecified primary endpoint. Although preclinical and observational data suggest that elevated BDNF may support cognitive resilience (Alkurd et al., 2024), current human evidence is limited. Future research should include adequately powered, randomized trials that incorporate standardized neurocognitive batteries as primary outcomes, ideally alongside harmonized BDNF assessment, to clarify whether IF can produce meaningful cognitive benefit.

Secondary metabolic outcomes demonstrated more consistent trends. Three trials reported significant reductions in body weight and BMI following IF interventions (Irani et al., 2024; Keawtep et al., 2024; Harvie et al., 2011), though not all between-group differences reached significance. Moreover, even when statistically significant, the absolute differences were often modest, raising questions about their clinical relevance. Improvements in insulin sensitivity were observed in multiple studies (Harvie et al., 2011; Bartholomew et al., 2021; Keawtep et al., 2024), con-

sistent with known metabolic benefits of IF (Polacchini et al., 2015). However, lipid profile responses were inconsistent, contrasting with previous meta-analyses (Polacchini et al., 2015). Variability in baseline lipid status, intervention length, and caloric control may account for these mixed results.

Significant methodological limitations undermine confidence in these findings. Most studies were small, single-center trials with heterogeneous designs, and many did not designate BDNF as a primary endpoint, limiting statistical power. Additional challenges arise from variability in BDNF measurement methods (e.g., serum vs. plasma, assay differences), which further complicates interpretation (Dinoff et al., 2016). Notably, trials reporting more favorable BDNF changes had methodological concerns, including small sample sizes, unclear randomization, and incomplete outcome reporting. In contrast, the trial with the lowest risk of bias (Schübel et al., 2018) did not show significant BDNF changes, underscoring the uncertainty of the positive signals. Overall, confidence in the evidence is limited by these risks of bias, the high inconsistency across protocols and populations, and the indirectness of using peripheral BDNF as a surrogate for cognitive outcomes. As a result, the certainty with which these findings can inform clinical practice remains low. Due to these important limitations, no firm clinical recommendations can currently be made regarding the use of IF for cognitive benefits in overweight or obese individuals. Well-designed, adequately powered trials with standardized protocols and comprehensive cognitive assessments are needed to clarify these relationships.

This review has some limitations that should be acknowledged. First, although unlikely, the exclusion of grey literature and unpublished studies may have resulted in the omission of relevant data, introducing a potential publication bias. Second, substantial heterogeneity in study designs, populations, interventions, comparators, and BDNF assessment methods precluded quantitative synthesis, limiting the ability to draw definitive conclusions. Finally, as intrinsic to scoping reviews, this analysis was designed to map existing evidence rather than formally evaluate the efficacy of interventions.

Despite these limitations, this review has important methodological strengths. The search strategy was comprehensive, encompassing multiple major databases with no time restrictions within predefined eligibility criteria. Study selection, data extraction, and risk of bias assessment were conducted independently by pairs of reviewers using standardized protocols and validated tools, minimizing selection and extraction bias. Adherence to PRISMA-ScR guidelines further enhances the transparency and reproducibility of this synthesis. Additionally, the inclusion of BDNF as a biomarker provides mechanistic insight into the potential neurocognitive effects of IF, representing a key strength that adds biological plausibility to the clinical outcomes assessed.

Conclusions

This scoping review provides the most comprehensive synthesis to date of studies investigating the effects of IF on BDNF levels in overweight and obese adults, highlighting important gaps in the current knowledge. IF may potentially influence BDNF levels and, consequently, cognitive outcomes in overweight and obese individuals; however, the current body of evidence remains limited, heterogeneous, and inconclusive. Further well-designed, adequately powered studies are needed to clarify the effects of IF on neurotrophic and cognitive outcomes and to determine its potential role in clinical practice.

Author's Contributions

All authors contributed equally to the conceptualization, design, formal analysis, methodology, data interpretation, writing, and critical revision of the original draft, and approved the final version to be published. Therefore, the authorship order was determined alphabetically using the first name of each author.

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Supplementary Materials

Full search strategy for all databases; numerical outcomes for primary and secondary endpoints in included studies.

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Conflicts of Interest

The authors declare no conflict of interest.

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