



Review article

Effect of time-restricted eating and intermittent fasting on cognitive function and mental health in older adults: A systematic review

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ARTICLE INFO

Keywords:

Intermittent fasting
Cognition
Time restricted feeding
Mental health
Aged
Systematic review

ABSTRACT

Objective: Emerging evidence suggests that dietary interventions hold promise for promoting cognitive function and mental well-being in aging populations. This systematic review aimed to examine the potential relationship between Time-Restricted Eating (TRE) and Intermittent Fasting (IFA) with cognitive function and mental health in older adults.

Methods: A thorough exploration was undertaken on electronic databases such as PubMed, Scopus, Web of Science, Science Direct, and Google Scholar, up to October 2023, following PRISMA standards. The evaluation of the quality and potential bias in the incorporated articles involved the use of the Newcastle-Ottawa Scale and Consolidated Standards of Reporting Trials (CONSORT).

Results: From a total of 539 articles initially identified, eight studies met the eligibility criteria for inclusion in this review. Out of these eight studies, six focused on cognitive function, and 2 focused on mental health. The reviewed articles encompassed a wide range of population sizes, with the number of older adults studied varying from 10 to 1357, reflecting a diverse cohort of individuals. Conclusions.

The findings suggest that TRE and IFA may have a positive impact on cognitive function and mental health in this population. However, additional research is needed to fully comprehend this relationship. Therefore, future research should specifically examine factors such as the duration and timing of the eating window in TRE, as well as the physical condition of older adults, to provide a more nuanced understanding of the cognitive and mental health benefits of TRE and IFA in older adults.

1. Introduction

The global population of older adults is expanding at a rapid pace, with projections indicating that the number of people aged 60 years or older will reach 2.1 billion by 2050, more than double the number in 2019 (Nations, 2020). This demographic shift is largely due to advances in healthcare and living standards that have resulted in increased life expectancies (Olimid and Olimid, 2019). As the older adult population expands on a global scale, the maintenance of cognitive function and mental well-being becomes paramount for promoting healthy aging (Oschwald et al., 2019, Golja et al., 2020). Cognitive decline and mental health issues, such as depression and anxiety, can significantly impact an individual's quality of life and independence (Prabandari et al., 2020). Therefore, identifying modifiable lifestyle factors that can preserve cognitive health and mental well-being is crucial (Song et al., 2022).

Nutrition is one of the modifiable lifestyle factors that has been identified as a potential target for interventions in older adults' cognitive health and mental well-being (Jennings et al., 2020). Adequate nutrition has been demonstrated to positively influence cognitive function and mental health (Dominguez et al., 2021). However, unhealthy dietary patterns, such as a high intake of saturated and trans fats or a low intake of fruits and vegetables, have been associated with an increased risk of cognitive decline and mental health problems (Zhou et al., 2022, Melo et al., 2019).

Time Restricted Eating (TRE) and Intermittent Fasting (IFA) are two dietary approaches that have gained popularity in recent years due to their potential health benefits (Soliman, 2022). Time Restricted Eating (TRE), an approach rooted in the alignment of eating patterns with circadian rhythms, centers on limiting the span of time during which food consumption occurs each day and emphasizes the importance of

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<https://doi.org/10.1016/j.pmedr.2024.102757>

Received 30 January 2024; Received in revised form 30 April 2024; Accepted 8 May 2024

Available online 9 May 2024

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when we eat, along with underscoring the intricate interplay between nutrition and the body's internal clock within a disciplined time frame typically ranging from 8 to 12 h (Chaix et al., 2014, Longo and Panda, 2016).

On the other hand, IFA encompasses a spectrum of fasting regimens with the common thread of cycling between periods of food consumption and periods of calorie restriction or fasting (Mattson et al., 2017, Dong et al., 2020). These dietary approaches, TRE and IFA, have demonstrated their efficacy in improving metabolic health by enhancing factors such as insulin sensitivity, glucose metabolism, and lipid profiles. Additionally, these approaches have been associated with factors linked to increased longevity, including improvements in cardiovascular health and a reduction in the risk of age-related diseases (Moro et al., 2016, Hwangbo et al., 2020).

Studies have suggested that both IFA and TRE may have beneficial effects on cognitive function and mental health in older adults (Currenti et al., 2021a, Currenti et al., 2021c). The mechanisms underlying these effects are complex and multifaceted, but may involve improvements in glucose metabolism, inflammation, oxidative stress, and neuroplasticity (Selvaraji et al., 2022, Jamshed et al., 2019, McAllister et al., 2020). Both IF and TRE involve periods of fasting, which can lead to a decrease in insulin resistance and an increase in insulin sensitivity (Halberg et al., 2005). This can, in turn, improve glucose uptake in the brain, which is important for preserving cognitive function and minimizing the risk of cognitive decline (McCall, 2004). Additionally, improved glucose metabolism may have a protective effect on the brain, lowering the likelihood of neurodegenerative conditions like Alzheimer's and Parkinson's (González et al., 2022). IFA and TRE may also modulate the gut microbiome, which has been implicated in brain function and mental health (Zeb et al., 2020).

Implementing specific dietary patterns emerges as a cost-effective and accessible yet highly valuable intervention within the realm of geriatric care (Black and Bowman, 2020). Educating older adults on tailored diet patterns not only presents a pragmatic and economical approach but also holds profound significance in fostering their overall well-being (Bojang and Manchana, 2023). By imparting knowledge about nutrition tailored to the unique needs of older individuals, healthcare practitioners can empower them to make informed choices that positively influence their health. This intervention aligns with the principle of prevention and holistic care, acknowledging the intrinsic connection between dietary habits and various facets of health, including cognitive function (Chen et al., 2019). Thus, advocating for specific diet patterns stands as a pragmatic and impactful good practice intervention, embodying a commitment to enhancing the quality of care for the older adult population.

Aligned with the emphasis on targeted dietary approaches, this systematic review aims to investigate the potential relationship between TRE, IFA, and cognitive function and mental health in the older adult population. By synthesizing findings from multiple studies, the review seeks to provide a comprehensive understanding of the potential benefits and limitations of TRE and IFA as interventions for preserving cognitive health and mental well-being in older adults. The practical implications of these findings extend to healthcare professionals and older adults contemplating the adoption of TRE or IFA as dietary strategies.

2. Methodology

In October 2023, we conducted an initial search for this systematic review across five prominent databases, namely PubMed, Google Scholar, Science Direct, Web of Science, and Scopus. Our search strategy involved using the keywords "Time-Restricted Eating," "Time-Restricted Feeding," "Intermittent Fasting," "older adults," "cognitive function," and "mental health" (Table 1). No restrictions were placed on the publication year of the articles to expand the search results. Subsequently, following that, the acquired results were imported into an information

Table 1

Database search terms used in the systematic review.

	Search terms
Intervention	"Intermittent Fasting" OR "Time-Restricted Eating" OR "Time-Restricted Feeding" OR "Fasting"
Outcome	"Cognition" OR "cognitive function" OR "cognitive impairment" OR "mental health" OR "depression" OR "stress" OR "anxiety" OR "mental well-being"
Population	"older adults" OR "older people" OR "older age" OR "aged" OR "elderly"

management program, specifically Endnote, to facilitate effective organization and referencing. Additionally, we manually reviewed datasets and other relevant sources to identify a larger number of articles related to our study.

2.1. Inclusion and exclusion criteria

Inclusion criteria for selecting the articles were as follows: Studies investigating the relationship between TRE and IFA on Cognitive Function and Mental Health of older adults were included. Cognitive function refers to a broad range of mental processes that encompass memory, attention, executive functions, and overall cognitive abilities, including both healthy cognition and cognitive impairment. Mental health, in this context, includes psychological well-being, emotional health, and the presence or absence of conditions such as depression, anxiety, and other mental health disorders commonly associated with older adults. Additionally, only studies providing full access to the entire text were considered for inclusion. Furthermore, research carried out on human participants in the old age period, defined as individuals aged 60 years or older (or, if the age range did not start from 60, studies with an average participant age of 60 years or above were also eligible), were included. Moreover, study design, including RCT, cross-sectional, cohort, and longitudinal studies, were included. Regarding fasting periods, studies reporting various fasting durations and patterns, such as 14–18 h of fasting per day, 8–10 h TRE compared to no time restriction, or fewer hours of TRE, were considered. Finally, studies published in English were considered for inclusion. Conversely, studies categorized as review studies, replication studies, or those written in a language different from English were excluded from the review according to the exclusion criteria.

2.2. Study selection

The selection of studies for this research adhered to the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021). Duplicate studies sourced from various search databases were excluded from this study to ensure the inclusion of only unique and relevant articles. Initial screening involved examining the titles and abstracts of the articles to assess their compatibility with the inclusion criteria. Subsequently, the entire text of the articles was reviewed, and irrelevant studies were excluded based on the predetermined inclusion and exclusion criteria. In order to mitigate potential bias, two independent researchers carried out all stages of data analysis and extraction. In the event of any disagreements between the researchers, a third reviewer was consulted to ensure the accuracy and consistency of the results.

2.3. Quality assessment and risk of bias

Two authors independently assessed the quality of the studies using a modified version of the Newcastle-Ottawa Scale (NOS) for cohort studies (Peterson et al., 2011). Recognizing the inclusion of cross-sectional studies in our systematic review, we adapted the assessment criteria to align with the unique characteristics of this study design. This adaptation aligns with a precedent established by previous research

(Brandenberger et al., 2019) to ensure the appropriateness of the quality assessment for each study type. The modified NOS comprised six items, categorized into three dimensions: Selection, Comparability, and Outcome. Each item had predefined response options, and we utilized a star system. A maximum of one star was assigned for each Selection and Outcome item, while a maximum of two stars were awarded for the Comparability item to identify high-quality studies.

At the same time, for clinical trial studies, the Consolidated Standards of Reporting Trials (CONSORT) tool was employed (Cuschieri, 2019). The CONSORT tool provides a structured framework to evaluate the quality of reporting in randomized controlled trials. By examining the various components of the CONSORT checklist, encompassing vital aspects such as trial design, participant enrollment, interventions, outcome assessments, statistical analyses, and the presentation of results, the rigor and transparency of trial studies can be systematically gauged.

2.4. Data extraction

Two scholars (S. Sh and K.B) performed data extraction using a predefined checklist that encompassed diverse factors, including the primary author's identity, the year of publication, study site, sample size, age group of the participants, examination instruments used to assess Time Restricted Eating and Intermittent Fasting, assessment tools

employed to evaluate cognitive performance, as well as a summary of the notable findings. Due to the considerable heterogeneity among the differing definitions and measures of TRE and IFA, cognitive outcomes evaluated, and methods of analysis used, a meta-analysis was considered unsuitable for deriving significant conclusions, in accordance with Section 9 of the Cochrane handbook's recommendations. Therefore, a narrative synthesis method was employed to analyze and interpret the data extracted from the selected studies, with the findings presented in a descriptive and comprehensive manner. This approach allowed for a thorough examination of the available evidence while also acknowledging the limitations of the studies and the heterogeneity of the data. We gathered and organized the effect size of each study separately, focusing on their results related to cognitive performance and mental health. Then, we created a visual representation of these effects using Stata 17 software, presenting them in a forest plot.

2.5. Ethical compliance

This systematic review was based on publicly available anonymized data and is therefore exempt from ethical compliance.

3. Results

This systematic review aimed to comprehensively evaluate the

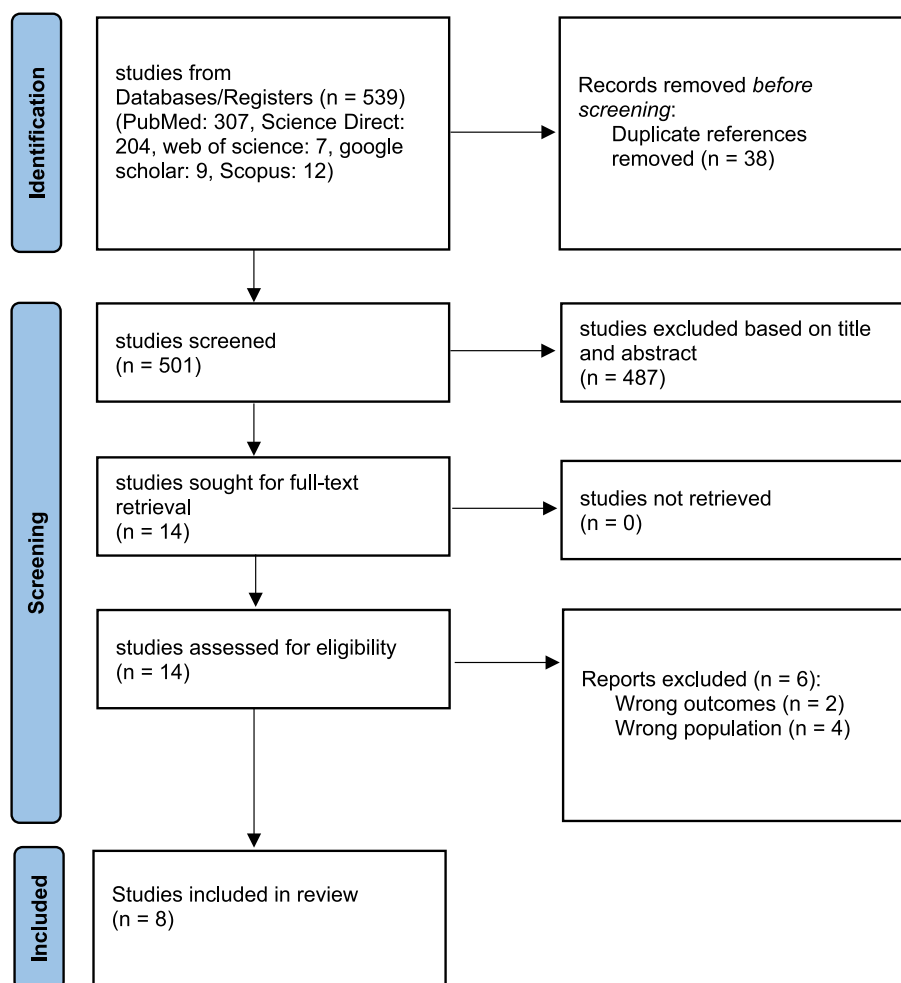


Fig. 1. The flowchart on the stages of including the studies in the systematic review (PRISMA 2020). **Fig. 1.** PRISMA flowchart illustrating the search and selection process for the systematic review examining Effect of Time-Restricted Eating and Intermittent Fasting on Cognitive Function and Mental Health in older adults. A total of 539 articles were identified and managed through the Endnote software, with 38 articles being removed due to duplication. After reviewing the titles and abstracts, 487 articles were excluded based on inclusion and exclusion criteria, leaving 14 studies for full review. Six articles were eliminated during the full review stage based on the inclusion and exclusion criteria.

relationship between TRE and IFA on Cognitive Function and Mental Health of older adults, while adhering to the guidelines outlined in the PRISMA guidelines. A preliminary identification and management of 539 articles were undertaken using the Endnote software, wherein 38 articles were subsequently excluded during the selection stage due to duplication. Subsequently, the titles and abstracts of the remaining articles underwent scrutiny in accordance with the established inclusion and exclusion criteria, resulting in the exclusion of 487 articles from the review. The full review stage involved the evaluation of 14 articles, with 6 studies being excluded based on the inclusion and exclusion criteria. After the selection process, a comprehensive evaluation was conducted on a total of 8 articles that met the eligibility criteria for the final stage. The PRISMA flowchart, depicted in Fig. 1, outlines the search and selection procedures, and detailed information about the included 8 articles is presented in Table 2.

Geographically, the included studies displayed variation in their origin; three emanated from Malaysia, two from Italy, with one originating from the United States, Tunisia, and China respectively.

Table 2
Summary of characteristics of included studies in the systematic review.

study	participants	Design	Time Restricted Feeding Defined/ Intervention	cognitive function Outcome Measures	Results
Anton et al. (2019), USA	N = 10, Age > 65, Mean age = 77.1, 6 women and 4 men	Pilot trial study	Participants fasted for 16 h per day (target range: 14–18 h) for four weeks, with adherence to the study intervention measured using food diaries. Compliance was defined as fasting between 14 and 18 h per day during weeks 2–4.	The Montreal Cognitive Assessment (MoCA) was administered at baseline assessments and the week four follow-up.	No Significant changes in cognitive function and health-related quality of life observed.
Currenti et al. (2021a,b), Italy*	N = 1572, Mean age = 46.5, 660 men and 912 women	Cross-sectional study	Food frequency questionnaires: 8-h TRF vs. no time restriction	Mental health status assessed using Pittsburgh Sleep Quality Index, Perceived Stress Scale, and CES-D-10	Individuals practicing TRF were less likely to exhibit signs of mental health distress, especially in those older than 70 years.
Currenti et al. (2021a,b), Italy	N = 883, Mean age = 65 (S.D = 9.6), 382 men and 501 women	Observational study	Food frequency questionnaires: 10-h TRF vs. less than 10 h TRF	Short Portable Mental Status Questionnaire (SPMSQ)	Adherence to TRF associated with a reduced likelihood of cognitive impairment.
Choon Ooi et al. (2020), Malaysia	N = 99, mean age = 68.66 (S.D = 5.08), 53 men and 46 women	Cohort study	Intermittent Fasting Grouping: regularly practicing IF, irregularly practicing IF, or not practicing IF	The Malay version of the Mini Mental State Examination, Montreal Cognitive Assessment, Rey Auditory Verbal Learning Test, Digit Span Test, and Digit Symbol were administered at baseline and again 36 months later.	More individuals in the regularly practicing IF group reverted to successful aging with no cognitive impairment and diseases compared to irregular and non-practicing IF groups.
Ooi et al. (2022), Malaysia	N = 99, mean age = 68.66 (S.D = 5.08), 53 men and 46 women	Cohort study	Intermittent Fasting Grouping: regularly practicing IF, irregularly practicing IF, or not practicing IF	The Mini Mental Examination State, Montreal Cognitive Assessment, Rey Auditory Verbal Learning Test, Digit Span Test, and Digit Symbol were administered at baseline and again 36 months later.	IF practice was associated with improved cognitive function. Partial mediation observed through higher SOD activity, lower DNA damage, lower CRP levels, and higher HDL-cholesterol levels.
Boujelbane et al. (2022), Tunisia	N = 58, Mean age = 62.9, S.D = 3.9	Experimental design	Participants assessed 2 weeks before Ramadan (non-fasting condition) and during the fourth week of Ramadan (fasting condition). During Ramadan, participants in the active group continued to train in a fasted state at the same time as before Ramadan, while the control group did not perform any physical training program.	The Neurotrack digital cognitive battery was administered two weeks prior to Ramadan and during the fourth week of Ramadan's fast.	Physically active individuals showed improvement in executive function, attention, inhibition, associative memory, and recognition memory during Ramadan, while sedentary individuals experienced a decline in associative learning performance.
Li et al. (2023), China	N = 1353, Mean age: 73.38 ± 6.16 years, 563 men and 790 women	Cross-sectional study	10-h TRE vs. less than 10 h TRE	Chinese-version of Mini Mental State Examination	TRE was associated with a higher prevalence of cognitive impairment in the domains of orientation to place and attention/calculation.
Hussin et al. (2013), Malaysia	N = 31 men, Mean age: 59.7, SD: 6.3	Randomized controlled trial (RCT)	Calorie-restricted dietary regime with intermittent fasting during a 3-month period	The Beck Depression Inventory-II and Geriatric Depression Scale-15 were measured at baseline, as well as at weeks 6 and 12 of the study.	Significant decreases in tension, anger, confusion, and total mood disturbance were observed in participants in the fasting group compared to the control group. No significant changes in mean depression scores were noted.

Note: The study marked with an asterisk (*) included participants under 60 years old; however, it separately analyzed the age group of 70 years and above, which aligns with our research focus on older adults.

The total number of participants across these 8 studies ranges from 10 to 1572, resulting in a combined total of 4006 participants. Among these studies, two examined mental health using assessments such as the Perceived Stress Scale, Center for the Epidemiological Studies of Depression Short Form, Geriatric Depression Scale-15, and Beck Depression Inventory-II. The remaining six studies focused on cognitive performance, employing measures such as the Mini Mental State Examination, Neurotrack digital cognitive battery, Montreal Cognitive Assessment (MoCA), Rey Auditory Verbal Learning Test, Digit Span Test, Digit Symbol and Short Portable Mental Status Questionnaire (SPMSQ).

3.1. Quality assessment

Out of the pool of 5 observational studies subjected to assessment using the NOS tool for quality evaluation, the entirety of these studies achieved commendable scores of 7 or above, reflecting an elevated level of quality ranging from medium to high. Regarding the 3 studies that underwent evaluation through the CONSORT tool, each of these studies

demonstrated low, medium, and high levels of quality (Table 3).

3.2. Cognitive function

Out of the six studies examining cognition outcomes, only one study did not find a significant association between TRE and IFA with cognitive function in older adults (Fig. 2).

3.2.1. Cross-sectional studies

Currenti et al. (2021a,b) discovered that individuals who maintained a 10-hour TRE regimen exhibited a reduced likelihood of experiencing cognitive impairment, as evidenced by an odds ratio (OR) of 0.28 and a 95 % confidence interval (CI) ranging from 0.07 to 0.90 (Currenti et al., 2021b). This association remained robust even after adjusting for baseline characteristics through multivariate logistic regression analysis. The adjustment incorporated various factors, including age, gender, marital status, educational and occupational background, smoking, and alcohol consumption patterns. It also took into account levels of physical activity.

Furthermore, Li et al. (2023) reported that a 10-hour TRE was associated with impairment in orientation to place and attention/calculation. After adjusting for covariates, including age, male gender, BMI, Instrumental Activities of Daily Living (IADL), illiteracy, widowhood, living alone, farming occupation, smoking and drinking habits, night-time feeding, International Physical Activity Questionnaire (IPAQ) score, type-2 diabetes, hypertension, dyslipidemia, stroke, heart disease, and cancer, The study revealed that TRE had a negative impact on the “Orientation to place” ($P < 0.001$) and “Attention/calculation” ($P < 0.001$) functions within six cognitive domains.. The analysis also pointed out that older age, hypertension, and stroke were positively associated with participation in the TRE group. Moreover, the results indicated that TRE was negatively related to the Mini-Mental State Examination (MMSE) score ($P < 0.001$) in addition to the specific cognitive functions mentioned earlier (Li et al., 2023).

3.2.2. Cohort studies

In the study by Ooi et al. (2020), individuals with mild cognitive impairment practicing IFA demonstrated enhanced cognitive function and a more successful aging process. Specifically, the mean Mini-Mental State Examination (MMSE) scores were significantly higher in both the regularly practicing IF group (19.59 ± 2.05 vs. 24.05 ± 3.25) and the irregularly practicing IFA group (18.60 ± 2.38 vs. 22.40 ± 3.38) compared to the mean MMSE score in the non-fasting group over time (18.73 ± 1.48 vs. 16.33 ± 4.11). In terms of the Montreal Cognitive Assessment (MoCA), the research revealed that the group practicing regular IFA (16.82 ± 4.10 vs. 19.43 ± 4.45) and the group with irregular IFA practices (15.84 ± 2.73 vs. 19.00 ± 2.04) achieved significantly higher scores compared to the non-IFA group across the observation period (Ooi et al., 2020).

Ooi et al. (2022) reported an association between IFA and improved cognitive function in older adults with mild cognitive impairment. When

comparing the regular-IFA and n-IFA groups, the analysis shows That the practice of intermittent fasting was correlated with a reduced Malondialdehyde (MDA) level [$b = 49.19$, $t(87) = 10.29$, $p = <0.001$], higher Superoxide Dismutase (SOD) activity [$b = -38.91$, $t(87) = -6.84$, $p = <0.001$], lower percentage of DNA in tail [$b = 8.19$, $t(87) = 11.36$, $p = <0.001$], and lower CRP level [$b = 1.39$, $t(87) = 13.01$, $p = <0.001$]. Furthermore, the mediating influence of reduced DNA damage, lower CRP levels, and higher levels of high-density lipoprotein (HDL) on cognitive function suggests potential pathways through which intermittent fasting may exert its cognitive benefits (Ooi et al., 2022).

3.2.3. Experimental studies

Boujelbane et al. (2022) observed that physically active individuals who underwent four weeks of fasting exhibited improved cognitive performance, while sedentary individuals experienced a decline in cognitive abilities. During Ramadan (fasting period), the physically active group showed significant enhancements in executive function ($p = 0.035$), attention ($p = 0.005$), inhibition ($p = 0.02$), associative memory ($p = 0.041$), and recognition memory ($p = 0.025$). In contrast, the sedentary group experienced a decrease in associative learning performance ($p = 0.041$). Meanwhile the other cognitive domains showed no changes throughout fasting period (Boujelbane et al., 2022).

Anton et al. (2019) conducted a pilot trial study, where the association between TRE with cognitive function was explored. Results indicated that TRE and IFA were not significantly associated with cognitive function in older adults (Anton et al., 2019).

3.3. Mental health

3.3.1. Cross-sectional study

Based on the findings of Currenti et al. (2021a,b), it was observed that older individuals (aged 70 years and above) who adhered to an 8-hour TRE regimen exhibited a lower likelihood of experiencing symptoms associated with mental health distress [OR = 0.14, CI: 0.03–0.65]. However, it is noteworthy that, while the initial model revealed a negative correlation between TRE and indicators of psychological distress (Odds Ratio [OR] = 0.65, 95 % Confidence Interval [CI]: 0.44–0.95), subsequent analyses, incorporating adjustments for potential confounding variables across the entire study cohort ($n = 1,572$), failed to identify any significant associations (Currenti et al., 2021d).

3.3.2. Experimental study

A study by Hussin et al. (2013) indicated significant reductions in tension, anger, confusion, and overall mood disturbance, as well as improvements in vigor among participants in the FCR (Fasting and Calorie Restriction) group compared to the control group. However, there was no statistically significant change in depression scores [OR = 0.11, CI: -0.30 – 0.52] (Hussin et al., 2013).

Table3

Quality Assessment of Included Studies: Observational Studies (NOS) and Randomized Controlled Trials (CONSORT).

Study	Selection				Comparability	Outcome			Score/ Total
	Item 1	Item 2	Item 3	Item 4		Item 3	Item 4	Item 5	
Li et al. (2023)	*	*	*	*	**	*	*	–	7/10
Currenti et al. (2021a,b)	*	*	*	*	*	*	*	–	7/10
Currenti et al. (2021a,b)	*	*	*	*	*	*	*	–	7/10
Choon Ooi et al. (2020)	*	*	*	*	**	*	*	*	8/10
Ooi et al. (2022), CONSORT	*	*	*	*	*	*	*	*	7/10
	Random Sequence Generation	Allocation Concealment			Blinding	Incomplete Outcome	Selective Reporting	Total Quality	
Anton et al. (2019)	No	No			Yes	No	No	Low	
Boujelbane et al. (2022)	Unclear	No			Yes	No	No	Medium	
Hussin et al. (2013)	Yes	Yes			Yes	No	No	High	

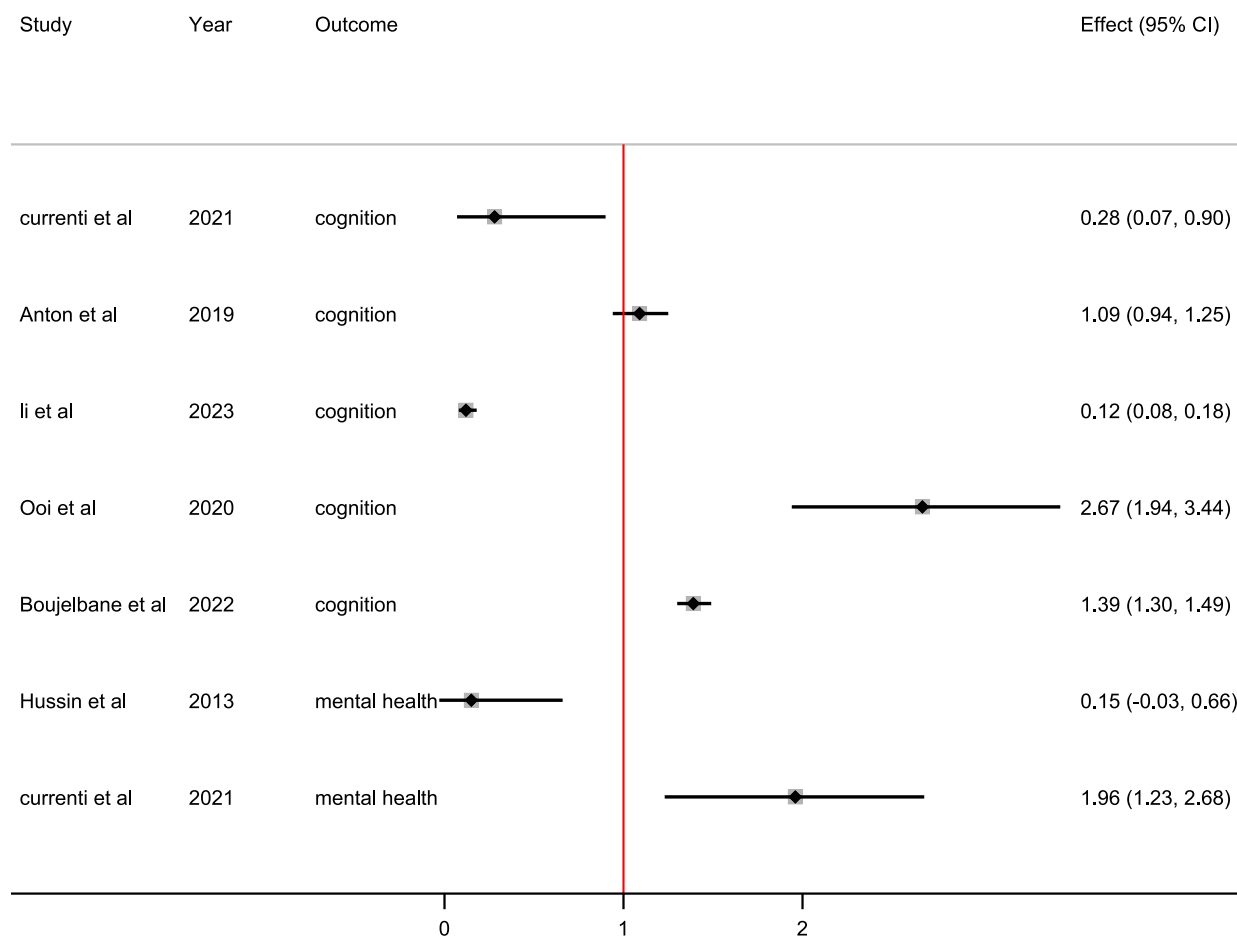


Fig. 2. Associations between TRF/IF and cognitive function and mental health. The vertical line represents the null effect.

4. Discussion

The primary objective of this systematic review was to investigate the relationship between TRE and IFA and their potential impact on cognition and mental health in older adults, specifically targeting individuals aged 60 years and older. To our knowledge, this systematic review represents the first comprehensive exploration within this specific age group. Recent studies have delved into the association between TRE, cognitive function, and mental health in older adults, yielding somewhat mixed results. While our findings suggest a relationship between TRE and IFA practices and cognitive function and mental health among older adults, it is important to acknowledge the complexity of this relationship. Various factors, including the duration and timing of the eating window and the physical condition of older adults, or even specific subgroups like those aged 70 years and older, can influence the outcomes.

The systematic review encompasses a range of study designs, each offering unique insights into the effects of fasting interventions on cognitive function and mental health in older adults. Cross-sectional studies revealed that individuals practicing TRE were less likely to exhibit signs of mental health distress, particularly those aged over 70 years. Experimental designs provided preliminary evidence regarding the feasibility and potential efficacy of fasting interventions. Cohort studies tracked participants over time and found that individuals regularly practicing IFA were more likely to revert to successful aging with no cognitive impairment compared to those with irregular or no IFA practice.

Consistent with these findings, a review study has highlighted the potential of IFA in reducing depression scores within the general

population, albeit without significant effects on anxiety or mood (Fernández-Rodríguez et al., 2022). In another review study, preliminary indications propose that TRE exhibits potential for eliciting neuroprotective effects on cognitive function and mitigating neuro-inflammatory markers linked to Alzheimer's disease in human subjects (Ezzati and Pak, 2022).

The outcomes of TRE in humans appear to be contingent on the temporal placement of the eating window, rather than solely on the duration of fasting (Carlson et al., 2007, Gill and Panda, 2015, Stote et al., 2007, Tinsley et al., 2017). In point of fact, investigations have demonstrated that constraining dietary intake to the first half of the day (omitting dinner) has been associated with reductions in adiposity, fasting glucose, insulin resistance, hyperlipidemia, and inflammation (Moro et al., 2016, Gill and Panda, 2015) which are factors that have been linked to cognitive function (Ma et al., 2015, Tangestani Fard and Stough, 2019).

Zeb and colleagues have shown that time-restricted eating has the potential to influence the composition of the gut microbiota and increase its relative abundance, which can influence the host's metabolic status and nutritional well-being (Zeb et al., 2020). The imbalance of gut microbiota has been linked to various diseases related to inflammation, the immune system, and the nervous system through the microbiome-brain axis communication pathway (Salvucci, 2019). This pathway is also known to affect brain development and function (Ceppa et al., 2019).

A wealth of scientific research has highlighted the potential of IFA to promote improvements in synaptic plasticity, neurogenesis, and neuroprotection, particularly through the upregulation of brain-derived neurotrophic factor (BDNF) (Kaptan et al., 2015, Fusco and Pani,

2013). Notably,

BDNF has been identified as a significant modulator of neural precursor cells (NPCs) situated within the dentate gyrus of the hippocampus, playing a crucial role in the generation of newly-formed neurons that integrate into the hippocampal circuitry. The hippocampus is a region of the brain that is crucial for learning and memory, and spatial pattern separation is a fundamental aspect of these cognitive processes (Marosi and Mattson, 2014, Mattson et al., 2001, Vivar and Van Praag, 2013). The involvement of BDNF in the regulation of hippocampal neurogenesis underscores its potential as a promising therapeutic target for the treatment of various neurological and neuropsychiatric disorders that are associated with impaired cognitive function and synaptic plasticity.

Aging is associated with a gradual diminution of synaptic connections in specific regions of the human brain, leading to impaired Inter-neuronal communication, increased inflammation, and oxidative stress (Johnson and Johnson, 2015). The demonstrated effect of IFA involves augmenting neuronal resilience to excitotoxic stress, averting learning deficits attributed to hippocampal cell demise, stimulate neurogenesis, and increase the expression of synaptic proteins that regulate calcium homeostasis (Qiu et al., 2012, Arumugam et al., 2010). IFA may also exert neuroprotective effects by improving mitochondrial respiratory function through the upregulation of PGC1 α , which contributes to mitochondrial biogenesis and detoxification (Cerqueira et al., 2012, Liang and Ward, 2006). The modulation of nitric oxide (NO) expression, facilitated by this upregulation, manifests antioxidant and protective properties within the endothelium, potentially preserving the microvasculature of the brain (Borniquel et al., 2006).

Notably, investigations into time-restricted eating protocols have yielded intriguing results, unveiling a reduction in the production of reactive oxygen species (ROS) and an enhancement in endothelial function (Headland et al., 2018). Additionally, these protocols seem to lead to a decline in the levels of pro-inflammatory cytokines like TNF α , IL-1 β , and IL-6 (Arumugam et al., 2010). The therapeutic potential of such observations is particularly interesting in the context of neurodegenerative diseases, where the accelerated aging-associated changes prompt consideration of interventions like intermittent fasting (Longo and Mattson, 2014).

The reviewed studies exhibit notable heterogeneity not only in the fasting interventions employed but also in the methodologies used to investigate their impact on cognitive function and mental health in older adults. These methodologies include cross-sectional studies, experimental designs, cohort studies, and pilot trials. While some studies focused on TRE with varying daily fasting durations, others explored IFA in different forms, such as regular, irregular, or no practice of IFA. Additionally, there were variations in the fasting periods within TRE, ranging from 8 to 16 h per day, and the choice of outcome measures, including cognitive function and mental health indicators. This variability in fasting protocols and measures may contribute to the observed differences in study outcomes. These methodological differences pose several limitations. First, the lack of standardized definitions and protocols for TRE and IFA makes it challenging to compare findings across studies accurately. Second, the diverse outcome measures used across studies may hinder the synthesis of results and limit the generalizability of findings. Third, variations in participant characteristics, such as age, gender, and health status, further complicate the interpretation of results. Therefore, future research efforts should aim to establish standardized protocols for TRE and IFA interventions and utilize consistent outcome measures to facilitate better comparability and synthesis of findings in this field.

One noteworthy limitation observed across the reviewed studies pertains to the relatively small sample sizes within two trial studies. This factor has the potential to compromise the statistical power and, consequently, the generalizability of their findings. Furthermore, a common constraint shared by both these studies lies in the relatively abbreviated duration of the interventions. The short-term nature of

these interventions might hinder the comprehensive exploration of their longer-term impacts. Additionally, a distinct limitation across several studies in this review is the utilization of self-reported Intermittent Fasting (IFA) practices. The reliance on self-reporting introduces the possibility of bias, thereby warranting cautious interpretation of the reported associations.

A potential limitation of this systematic review is the restricted scope of the included studies to those published in English, resulting in the possibility of overlooking relevant studies in other languages. Additionally, the omission of unpublished studies and gray literature might impact the comprehensiveness of the findings. Moreover, the reliance on the available data within the included studies might constrain a more nuanced analysis of the heterogeneous effects of TRE across different populations.

While this systematic review provides valuable insights into the relationship between TRE and IFA with cognitive function and mental health in older adults, several avenues for future research warrant exploration. Firstly, addressing the limitation of small sample sizes in certain trial studies is crucial. Future investigations should prioritize larger, more diverse participant groups to enhance statistical power and strengthen the generalizability of findings. Additionally, extending the duration of fasting interventions beyond short-term assessments could shed light on the longer-term impacts and sustainability of TRE and IF practices in older populations.

5. Conclusion

This systematic review suggests that Time-Restricted Eating (TRE) and Intermittent Fasting (IFA) hold promise for enhancing cognitive function and mental health in older adults. However, the limited number of randomized controlled trials (RCTs) in the current literature warrants cautious interpretation of the findings. Future research should focus on conducting rigorous RCTs to elucidate the effects of TRE and IFA, explore optimal feeding window durations, and investigate potential risks and side effects. These endeavors are vital for developing targeted dietary interventions to promote cognitive health and mental well-being in older adults.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

SS conceptualized and designed the systematic review. SS and KB conducted the database searches, abstract, full-text screening, and data extraction. SS conducted the narrative synthesis and MR reviewed the data extraction and narrative synthesis results. The first draft of the manuscript was written by SS, KB and FR. All authors commented on the manuscript and read and approved the final manuscript.

CRediT authorship contribution statement

Sina Sharifi: Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Conceptualization. **Fatemeh Rostami:** Writing – review & editing. **Kimia Babaei Khorzoughi:** Writing – review & editing, Writing – original draft, Methodology. **Mahmoud Rahmati:** Writing – review & editing, Writing – original draft, Investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

Acknowledgements

We acknowledge the Student Research Committee of Kermanshah University of Medical Sciences for its assistance, in support of this research.

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