Enhancing cognitive resilience: a narrative review of lifestyle interventions in cognitive decline prevention among older adults

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Abstract. Background: The increasing prevalence of cognitive decline and neurodegenerative disorders among ageing populations necessitates effective preventive strategies. Lifestyle interventions, including dietary modifications, cognitive training, and physical exercise, have emerged as promising avenues for enhancing cognitive resilience. This narrative review synthesizes current evidence on the efficacy of lifestyle interventions in preventing or delaying cognitive decline among older adults. Methods and Materials: A systematic search was conducted across databases, including PubMed and Google Scholar, using the PICO framework to formulate a precise research question. Inclusion criteria encompassed diverse study designs, focusing on older adults aged 65 years and above, diagnosed with mild cognitive impairment (MCI) or early-stage Alzheimer's disease (AD). Lifestyle interventions targeting cognitive health were compared against standard care or alternative non-pharmacological approaches, with primary outcomes including changes in cognitive function and activities of daily living (ADLs). Objectives: The review aimed to evaluate the effectiveness of lifestyle interventions, such as cognitive training, dietary modifications, and physical exercise, in preserving cognitive function and delaying cognitive decline among older adults. Results: The synthesis of evidence revealed significant benefits associated with lifestyle...
interventions. Dietary patterns rich in antioxidants, anti-inflammatory compounds, and essential fatty acids demonstrated neuroprotective effects and reduced cognitive decline risk. Physical exercise programs and cognitive stimulation interventions also showed promise in maintaining cognitive function. Multimodal approaches, personalized interventions, and long-term follow-ups emerged as key considerations for optimizing outcomes.

**Keywords:**
cognitive decline
lifestyle interventions
cognitive training
dietary modifications
ageing population
INTRODUCTION

Alzheimer's disease is a neurological disease that causes progressive cognitive decline, memory loss, and functional impairment. It is predicted to become increasingly prevalent as the world population ages, putting an enormous burden on society and healthcare institutions. The search for preventive measures is more important than ever because, despite substantial research, there are still limited effective pharmaceutical treatments available.

Between 2000 and 2015, mortality due to Alzheimer’s disease (AD) has increased by 123% [1]. No drugs have yet been approved to slow the progression of AD. A delay in the expression of AD of just 5 years would reduce its incidence by half [2]. Thus, novel prevention strategies that delay the onset of this disease are critical to develop.

In older adults, Alzheimer's disease (AD) is the most frequent cause of dementia, accounting for 60–80% of cases. Alzheimer's disease often begins with mild memory impairment that progresses to disrupt language, reasoning, and the capacity to do daily activities. Alzheimer's disease is characterized by the accumulation of amyloid-beta (Aβ) plaques and neurofibrillary tangles made up of hyperphosphorylated tau protein within the brain. The hippocampus and cortex, two areas of the brain linked to memory and cognition, are severely affected by these anomalies, which impair neuronal communication and cause cell death and atrophy.

A complex interaction of cellular, molecular, and genetic variables leads to the cognitive deterioration associated with Alzheimer's disease. The accumulation of amyloid-beta plaques, which are thought to impair cell-to-cell communication and trigger immunological reactions that result in chronic inflammation, is a key component of this process. Further contributing to neuronal malfunction is the creation of neurofibrillary tangles, which are caused by the hyperphosphorylation of tau protein. This instability of microtubules hinders intracellular trafficking. AD's cognitive symptoms are also significantly impacted by synaptic loss and neurotransmitter deficiencies, especially in acetylcholine. The risk of Alzheimer's disease is greatly
increased by genetic factors, including the APOE ε4 allele and mutations in the APP, PSEN1, and PSEN2 genes.

The pathophysiology of Alzheimer's disease is largely influenced by oxidative stress and inflammation. Pro-inflammatory cytokines and chemokines are released as a result of activated microglia and astrocytes in response to amyloid-beta buildup, which causes chronic neuroinflammation and exacerbates neuronal damage. This inflammatory reaction adds to tau pathology in addition to encouraging further amyloid deposition. Cellular constituents like lipids, proteins, and DNA are harmed by oxidative stress, an imbalance between the generation of reactive oxygen species (ROS) and the brain's antioxidant defences.

A typical characteristic of AD is mitochondrial malfunction, which increases the generation of ROS and feeds the vicious cycle of oxidative damage and neuronal impairment. When combined, these mechanisms in Alzheimer's disease exacerbate neurodegeneration and quicken cognitive decline [1].

Cognitive decline and neurodegenerative disorders, such as Alzheimer's disease (AD), pose significant challenges to global healthcare systems and societal well-being. As the aging population continues to expand, the urgency to identify effective preventive strategies intensifies. This manuscript aims to delve into the realm of lifestyle interventions, specifically focusing on cognitive training, dietary modifications, and cognitive stimulation programs, to evaluate their role in preventing or delaying cognitive decline among older adults.

The foundation of this research endeavor lies in the formulation of a precise research question using the PICO (Population, Intervention, Comparison, Outcome) framework. Through a rigorous systematic search encompassing databases such as PubMed and Google Scholar, studies were meticulously scrutinized against a comprehensive set of inclusion and exclusion criteria to ensure methodological rigor and relevance to the review's objectives.

The inclusion criteria encompassed diverse study designs, including randomized controlled trials (RCTs), cohort studies, and systematic reviews/meta-analyses, to capture a
breadth of evidence. Studies focusing on older adults aged 65 years and above, diagnosed with mild cognitive impairment (MCI) or early-stage AD, were included, with a keen emphasis on longitudinal studies with a minimum follow-up period of 6 months. Lifestyle interventions targeting cognitive health, ranging from cognitive training programs and dietary modifications to physical exercise regimens and social engagement activities, constituted the core intervention criteria. These interventions were compared against standard care, placebo interventions, or alternative non-pharmacological approaches, ensuring robust comparison groups. Primary outcomes encompassed changes in cognitive function, activities of daily living (ADLs), and biomarkers of cognitive decline, while secondary outcomes included adherence to interventions and safety profiles.

Conversely, exclusion criteria filtered out studies lacking methodological robustness, focusing on younger populations, or deviating from the core focus on lifestyle interventions and cognitive outcomes. The methodological rigor was underscored by the adherence to SANRA guidelines throughout the review process, ensuring systematic data extraction, contemplation, and synthesis.

This manuscript embarks on a comprehensive exploration of dietary interventions, shedding light on the intricate interplay between nutrition, brain health, and cognitive resilience. The growing body of evidence underscores the pivotal role of diet in preserving cognitive function and potentially mitigating the onset or progression of neurodegenerative disorders like AD. Insights from observational studies, case-control analyses, and cohort investigations elucidate the nuances of dietary patterns, nutrients, and dietary indices that wield neuroprotective effects and bolster cognitive well-being.

Furthermore, lifestyle interventions extend beyond dietary paradigms to encompass broader lifestyle factors encompassing physical activity, cognitive stimulation, and psychosocial engagement. The multifaceted nature of these interventions calls for a nuanced understanding of their differential impacts on cognitive outcomes across diverse populations and disease spectrums, from primary prevention in
cognitively healthy individuals to tertiary prevention in those with established cognitive impairments.

As we traverse through the intricacies of lifestyle interventions in cognitive health, this manuscript endeavours to illuminate pathways for promoting cognitive resilience, delaying cognitive decline, and potentially reshaping the trajectory of neurodegenerative disorders in the ageing population.

METHODOLOGY

A research question was created using the PICO framework. The studies identified through a systematic search were comprehensively read to assess their appropriateness for incorporation into the review based on the following criteria.

SELECTION CRITERIA

Inclusion Criteria

1. Study Design
   - Randomized controlled trials (RCTs), quasi-experimental studies, cohort studies, case-control studies, and systematic reviews/meta-analyses.
   - Longitudinal studies with a minimum follow-up period of 6 months to assess cognitive outcomes.
   - Studies published in peer-reviewed journals.
2. Participants
   - Older adults aged 65 years and above.
   - Individuals diagnosed with mild cognitive impairment (MCI), early-stage Alzheimer's disease, or at risk of cognitive decline based on validated cognitive screening tools (e.g., Mini-Mental State Examination).
   - Exclusion of participants with severe cognitive impairment, advanced dementia, or neurological disorders other than Alzheimer's disease.
3. Interventions
   - Lifestyle interventions targeting cognitive health, including but not limited to:
     - Cognitive training programs (e.g., memory exercises, problem-solving tasks, brain training software).
     - Dietary modifications or nutritional interventions aimed at improving brain health (e.g., Mediterranean diet, supplementation with omega-3 fatty acids, antioxidants).
     - Physical exercise programs with a cognitive component
(e.g., aerobic exercise, strength training, yoga, tai chi).
- Social engagement activities or interventions promoting cognitive stimulation and social interaction.
4. Comparison Group
- Studies comparing lifestyle interventions with standard care, usual activities, placebo interventions, or alternative non-pharmacological interventions.
- Studies with clearly defined control groups or comparison arms.
5. Outcomes
- Primary outcomes:
  a. Changes in cognitive function measured by validated neuropsychological tests (e.g., Montreal Cognitive Assessment, Trail Making Test, Rey Auditory Verbal Learning Test).
  b. Maintenance or improvement in activities of daily living (ADLs) and instrumental activities of daily living (IADLs) related to cognitive function.
- Secondary outcomes:
  a. Changes in biomarkers of cognitive decline (e.g., amyloid-beta levels, brain imaging findings).
  b. Adherence to lifestyle interventions and acceptability among participants.
  c. Adverse events or safety outcomes related to interventions.

Exclusion Criteria
1. Study Design
- Case reports, case series, editorials, letters to the editor, conference abstracts, and non-peer-reviewed publications.
- Studies lacking adequate methodological quality or clear reporting of intervention protocols and outcomes.
2. Participants
- Studies focusing primarily on pediatric populations, younger adults (below 65 years), or individuals without documented risk factors for cognitive decline.
- Studies including participants with significant comorbidities or medical conditions that may confound cognitive outcomes (e.g., severe cardiovascular disease, uncontrolled diabetes).
3. Interventions
- Pharmacological interventions (e.g., medications for cognitive enhancement, herbal supplements) without concurrent lifestyle interventions.
- Interventions targeting only one aspect of lifestyle (e.g., dietary supplements without dietary modifications, physical exercise without cognitive training).

4. Comparison Group
- Studies lacking appropriate control groups or comparison arms for evaluating the effects of lifestyle interventions on cognitive outcomes.
- Studies with control groups receiving pharmacological treatments or interventions not relevant to cognitive health.

5. Outcomes
- Studies with incomplete or insufficient data on cognitive outcomes, ADLs, IADLs, or biomarkers of cognitive decline.
- Studies focusing solely on surrogate outcomes (e.g., biomarker changes without clinical correlation, subjective self-reported cognitive improvements without objective measures).

The manuscript has been drafted based on SANRA guidelines to search, compile, contemplate, and extract data. Investigators independently searched PubMed, and Google Scholar following the protocol mentioned in the literature.

DIETARY INTERVENTIONS
There is growing evidence that lifestyle factors—especially diet—are important for preserving cognitive function and may even lower the incidence of Alzheimer's disease. Nutritional neuroscience has identified several dietary patterns and certain nutrients that may have neuroprotective effects. Diets high in antioxidants, anti-inflammatory chemicals, and essential fatty acids are of particular interest because they have the potential to improve brain health through a variety of pathways, including lowering oxidative stress, inflammation, and amyloid-beta buildup.

Numerous studies have demonstrated the influence of nutrition on brain function and the risk of cognitive decline, demonstrating the close relationship between diet and
cognitive health. In addition to supporting general brain health, a balanced diet rich in a variety of nutrient-dense foods may be able to postpone the beginning of neurodegenerative disorders such as Alzheimer's. Important food ingredients including omega-3 fatty acids, vitamins, minerals, and antioxidants are essential for preserving the integrity of neurons, lowering inflammation, and fending off oxidative stress—all of which are crucial for cognitive performance. Diets high in fruits, vegetables, whole grains, nuts, and lean proteins—like the MIND and Mediterranean diets, for example—have been linked to improved cognitive function and a lower risk of dementia.

These diets are rich in bioactive substances that support vascular health, improve synaptic plasticity, and boost neuroprotection—all of which help to maintain cognitive capacities as we age. Consequently, one of the most important components of attempts to maintain cognitive health and reduce the risks of cognitive decline is making educated food choices.

By means of observational studies, including case-control and cohort studies, scientists have pinpointed distinct dietary patterns and nutrients that could potentially impact the likelihood of developing AD. Additionally, nutritional epidemiology looks at the relationship between dietary practices and molecular markers of AD, including tau and amyloid-beta protein levels, oxidative stress, and inflammation.

These findings highlight the significance of a balanced, nutrient-rich diet in preserving cognitive health and preventing neurodegeneration, and they offer critical insights into potential dietary interventions and public health measures targeted at reducing the burden of Alzheimer's disease.

Plant-based diets are known for their beneficial effects on diseases like type 2 DM [3], obesity [4, 5], coronary artery disease [6], and reducing the risk of mortality [7]. Such diets have been shown to have various metabolic effects such as improved weight and glycemic control, reduction in the levels of blood lipids and in blood pressure, and reversal of atherosclerosis. [8] Since cardiovascular and
neurodegenerative diseases like Alzheimer’s share similar pathophysiologic mechanisms (inflammation, vascular damage & oxidative stress), it is suggested that a Plant-Based diet might lead to a reduction in cognitive decline with progressing age.

A study was conducted to evaluate the association between a plant-based diet and the rate of cognitive decline in African American adults and white adults. The quality of a plant-based diet index was evaluated by an overall Plant-based diet index (PDI), healthful Plant-based diet index (hPDI), and unhealthful Plant-based diet index (uPDI). It was observed that in African American adults, higher hPDI was associated with a lesser rate of decline in global cognition, episodic memory and perceptual speed. This was not observed in white adults. There was also a proportional relationship observed between participants with higher hPDI and a slower rate of decline of cognition, episodic memory and speed of perception. No association was seen between uPDI and PDI with a decline in cognition in either racial group. A healthy plant-based diet includes whole grains, fruits, vegetables, nuts, legumes, vegetable oils, tea and coffee [9]

Another study conducted on Taiwanese adults found that vegetarians were associated with a reduced risk of clinical dementia as compared to those who eat non-veg. [10] In a study, it was found that higher levels of plasma A-Carotene, lutein and zeaxanthin were associated with improved global cognition and semantic memory in individuals at risk of cognitive decline. Moreover, individuals with higher levels of A-carotene have better global cognition. These levels represent a greater intake of fruits, green leafy and other vegetables, and cheese and less intake of butter, margarine, meat and fried foods. [11]

An interesting study found that adherence to a prudent diet led to lesser cognitive decline as compared to the higher cognitive decline in individuals who were adherent to a Western-type diet. Also, the decline in Western-type diet (which includes red meat, refined grains, high-fat dairy products and sugar) [12] was attenuated when it was accompanied by adherence to a diet having prudent patterns, rich in fruits and vegetables This highlights the importance
of the cumulative effect that various nutrients in a whole diet have on cognitive function which might differ from the effect that a single nutrient or food component has individually since many people eat a combination of healthy and non-healthy foods; the impact of this mixed dietary pattern on the risk of conditions like Alzheimer’s however, remains unknown. [12, 14, 15]

A study conducted by Krikorian et al showed that consumption of a diet that induced ketosis, even in the short term, can lead to improved memory in older adults with Mild Cognitive Impairment. Such a diet composed of very low carbohydrates (10-14% of total calories), was supposed to correct hyperinsulinemia and induce ketosis which led to a reduction in inflammation and an enhancement of the energy metabolism, thus correcting the underlying disorders that might have led to neurodegeneration [16].

It has been observed that the receptors for insulin are expressed in a high concentration in various regions of the brain, which are very much vulnerable to neurodegeneration, which mediates memory (long-term and working memory). However, the capacity to synthesize insulin in the brain is limited. Hence, it must be transported from the peripheral bloodstream into the brain. Paradoxically, in individuals with hyperinsulinemia due to insulin resistance, due to the saturation of blood-brain barrier transport mechanisms, central (brain) hypoinsulinemia occurs. Moreover, it has been found that individuals with Alzheimer’s have a lower CSF to plasma insulin ratio as compared to healthy older adults. [17, 18]

Mediterranean diet is rich in antioxidants and protects against oxidative stress. Secondly, it also exerts an anti-inflammatory effect due to the high content of omega-3 fatty acids in the form of fish and olive oil along with the dietary fibres present in fruits and vegetables. Additionally, red wine reduced CRP levels and IL17 levels. This diet is also one of the most nutritionally adequate diets in Europe and people following this diet have better nutritional status than people following other diets. It has nutrients like zinc, iron, vitamin B12, vitamin D, folic acid, calcium, selenium and iodine; most of these improve cognition and lower the
risk of AD [19].

A study found that when compared with a group of people with low adherence to MedDiet, the high-adherence MedDiet group was associated with better Learning and Memory performance and an increase in the size of dentate gyri [31]. As discussed earlier, a prudent diet could lead to attenuation of cognitive decline in individuals consuming a Western diet. In contrast, a study found that MedDiet attenuated cognitive decline only in individuals with a low Western Diet score and not in those individuals with a high Western Diet score. Hence, increased consumption of components of the Western Diet decreases the beneficial association of MedDiet on cognition [20].

Many studies found that adherence to MedDiet was positively associated with a slower rate of decline in global cognition and a higher percentage of adherence to MedDiet was associated with a slower rate of decline as compared to a lower percentage of adherence to MedDiet [21, 22]. Other studies found that better adherence to MedDiet was associated with a lower level of hs-CRP and a reduced risk of developing MCI and its further progression into AD [20].

Some studies found that higher adherence to MedDiet was associated with reduced mortality risk, showing that adherence to MedDiet may not only affect the risk of Alzheimer’s but also the subsequent disease course [23]. The MIND diet has been shown to reduce depressive symptoms over time as compared to Western Diet [24]. Similarly, the DASH Diet along with MedDiet were found to be consistently associated with higher levels of cognitive function in elderly men and women [25]. MIND Diet was also associated with a lesser rate of cognitive decline in adults with MCI [26].

Limiting the consumption of sugar-filled drinks, processed meals, and saturated and trans fats may also help lower the risk of cognitive decline. In general, maintaining social ties, eating a balanced and diverse diet, regulating other lifestyle factors, and engaging in physical and mental activity can all help to promote brain health and potentially reduce the incidence of Alzheimer's disease in at-risk groups.

**LIFESTYLE INTERVENTIONS**

Lifestyle factors include vascular and metabolic factors
high blood pressure and cholesterol, obesity, diabetes, impaired glucose metabolism, smoking [28], excessive use of alcohol [27], depression [30], as well as other psychosocial factors, such as work-related stress, depression, and infrequent social contacts and are associated with increased dementia risk. Protective factors for cognitive impairment, dementia and Alzheimer's include interventions such as regular physical activity having a higher formal education, engaging in cognitively and mentally stimulating leisure activities, having a rich social network etc.

A systematic review by [29], predicts that people with diabetes have a 1.5-fold decline in cognitive function and a 1.6-fold greater risk of future Alzheimer's. Likewise, a study by [31] found an emergence of an intriguing relationship between hypertension and AD, raising the prospect that a chronic elevation in BP aggravates AD pathology, contributing to dementia and no strong evidence explains the relationship between cognitive improvement and antihypertensive treatment. A study by [32] emphasized that long-term exercise training had a positive impact by delaying the onset of physiologic memory loss.

Though engaging in physical exercise programs seems to be effective, it is not enough and studies that examine multimodal interventions hypothesize that an integrated approach to addressing multiple risk factors for AD may be more successful than single-component interventions in producing benefits.

A Study by the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) in 2013 revealed the importance of multi-domain lifestyle modification which successfully improved the cognitive functions in the elderly and hence, can facilitate the reduction of dementia risk by addressing the multifactorial, complex, heterogeneous nature of late-life cognitive impairment and AD and offers prevention potential on a large scale, with possibilities for worldwide implementation [32].

COGNITIVE INTERVENTIONS

Cognitive interventions in MCI/AD may be classified into the following three types: cognitive stimulation (CS), cognitive training (CT) and cognitive rehabilitation (CR). CS
may be defined as the participation in a variety of group activities and group discussions intended to improve overall cognitive and social functioning. CT may be defined as a guided practice on a series of standard tasks to develop a specific cognitive domain while CR may be defined as a tailored method focused on increasing performance in activities of daily living to reach predetermined personal goals [33].

Gómez-Soria et al., [33] found that CS can improve overall cognitive functioning in elderly individuals with intact cognition and those with MCI/AD. Sun et al., [34] and Saragih et al., [35] also found improved cognition in patients with AD. CS has been shown to improve mini-mental state examination (MMSE) scores and Montreal Cognitive Assessment (MoCA) scores in elderly individuals with normal cognition and those with MCI/AD. Regarding individual cognitive domains, Gómez-Soria et al., [33] found that CS resulted in higher scores in memory, praxis, calculation and orientation domains in cognitively healthy elderly individuals. MCI patients, in addition, showed improvements in verbal and language domains [33]. In terms of program duration, short-term and long-term CS have been shown to increase cognitive performance. Short-term cognitive stimulation appears to increase memory and orientation, whereas long-term CS appears to improve language. In terms of CS session duration, it was discovered that 45 minutes per session improves overall cognitive performance, memory, executive function, and verbal fluency. Personalized/adapted CS has been found to greatly enhance overall cognitive functioning, orientation and praxis. However, non-personalized/adapted CS has also been shown to considerably improve overall cognitive functioning, memory, language, and verbal fluency [33].

Butler et al., [36] found that in otherwise healthy elderly individuals CT improved testing performance specific to the cognitive domain being tested. These findings were corroborated by Gates et al., [37] who found moderate-sized improvements in memory performance and global cognitive measures post-CT in cognitively healthy elderly participants. While CT shows promising results for otherwise healthy elderly individuals, the same could not be said for patients of
MCI/AD. Butler et al., [38] found that patients of MCI showed either no improvement or mixed results following intervention with CT. Bahar-Fuchs et al., [39] and Clare et al., [40] found that patients with vascular dementia and early-stage AD did not show any improvement following CT.

While CS and CT can be used for primary prevention (to prevent disease incidence in cognitively healthy individuals) and secondary prevention (to reduce MCI conversion to dementia), the role of CR is mainly in tertiary prevention (to reduce disability in patients with mild-to-moderate dementia) [37, 41]. Kudlicka et al., [41] found that in patients of mild-to-moderate dementia treated with CR, at the medium-term follow-up, auditory selective attention and sustained attention showed an improvement whereas general functional ability, memory and anxiety showed worsening. They also found strong evidence suggesting an improvement in self-efficacy and immediate recall at the end of the treatment [41]. Sustained attention, delayed recall, memory and general functioning showed no improvement at the end of treatment while self-efficacy, immediate recall and verbal fluency showed no improvement at the medium-term follow-up [41].

DISCUSSIONS

The synthesis of evidence underscores the complex interplay between lifestyle factors, cognitive function, and neurodegenerative processes. The efficacy of dietary interventions, notably the Mediterranean diet and plant-based diets, in preserving cognitive function emerges as a prominent theme. Studies highlighted the neuroprotective effects of antioxidants, anti-inflammatory compounds, and essential fatty acids, supporting the hypothesis that diet plays a pivotal role in brain health. Additionally, the observed association between higher adherence to these diets and reduced risk of cognitive decline reinforces the importance of dietary choices in mitigating cognitive impairment.

Physical exercise programs, cognitive training, and cognitive stimulation interventions also exhibit potential benefits in maintaining cognitive function and delaying decline. The multifaceted nature of these interventions, particularly when integrated into multimodal approaches, underscores the importance of holistic lifestyle strategies.
in promoting cognitive resilience.

Notably, the discussion delves into the nuances of intervention duration, personalized approaches, and the differential impacts on cognitive domains. While some interventions show promise in certain cognitive domains or populations, the heterogeneous nature of cognitive decline necessitates tailored interventions and ongoing research to optimize outcomes.

The limitations of the reviewed studies, such as variability in intervention protocols, outcome measures, and participant characteristics, are acknowledged. Future research directions, including large-scale randomized controlled trials with long-term follow-ups, standardized outcome assessments, and diverse participant cohorts, are proposed to further elucidate the efficacy and mechanisms of lifestyle interventions in cognitive decline prevention.

Overall, this discussion synthesizes the current evidence base, underscores the potential of lifestyle interventions in preserving cognitive health, and delineates avenues for advancing research and clinical practice in this critical area.

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