Journal of Holistic Lifestyle Medicine
Vol. 1, No. 1, 2026, p. 64 – 91
https://optimumlifestylemedicine.officialnusaagency.com/jhlm

EFFECT OF EXERCISE ON DEMENTIA: A NARRATIVE LITERATURE REVIEW

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ABSTRACT

Dementia is an acquired condition affecting memory and intellectual functions due to brain disease. The number of older adults with dementia is projected to grow from 50 million worldwide in 2017 to 80 and 150 million in 2030 and 2050. Medications to improve cognitive function have contraindications and notable side effects. Exercise training stands out as one the promising non-pharmaceutical therapies to enhance cognitive health in older adults affected by all-cause dementia. Physical exercise can support healthy aging into independent body function, psychological well-being and cognition. Through a critical analysis of current research, this review provides valuable insights for healthcare professionals, researchers, and policymakers seeking effective approaches to alleviate the impact of dementia through lifestyle interventions.

Keywords : *dementia, exercise, effect*

1. Introduction

Dementia is one of the greatest global health and social care challenges of the 21st century (Chowdhary et al, 2022). The number of older adults with dementia is projected to grow from 50 million worldwide in 2017 to 80 and 150 million in 2030 and 2050 (Sanders et al, 2020; Balbim et al, 2022). Dementia is an acquired condition affecting memory and intellectual functions due to brain disease, typically not associated with impaired consciousness. Dementia refers to the disease syndrome that has various causes.

Risk factors linked to dementia include advancing age, family history, cardiovascular disease, low education attainment, social determinants, history of brain injuries, sedentary lifestyle, diabetes, smoking, abdominal obesity, and high cholesterol levels (Arvanitakis, Shah, Bennet, 2019; Meng, Lin, Zheng, 2020).

Medications to improve cognitive function have contraindications and notable side effects. Therefore, non-pharmaceutical strategies that effectively delay the progression of dementia are of particular interest in research. Exercise training stands out as one the promising non-pharmaceutical therapies to enhance cognitive health in older adults affected by all-cause dementia (Balbim et al, 2022).

In this review, our focus is on examining the impact of physical exercise as a therapeutic approach for both treating and preventing dementia.

2. Overview of Dementia

2.1. Definition and Etiology

The 5th edition of the Diagnostic & Statistical Manual of Mental Disorder (DSM-5) has updated the definition of dementia, now referred to as Major Neurocognitive Disorder (MND). MND can affect individuals at a younger age and not always indicate Alzheimer's disease as the underlying cause of cognitive decline. It is defined by a notable deterioration in at least one cognitive domain, include complex attention, executive function, memory, learning, language, social cognition, or perceptual-motor skills. This decline represents a departure from the individual's previous level of cognitive functioning, persists over time, and worsens progressively. Importantly, it is not solely linked to an episode of delirium. Together with cognitive deterioration, there must also be a decline in the individual's capability to perform daily activities and tasks.

Although most cases of dementia show progressive and irreversible declining, but if you

refer to the definition above, then dementia can also occur suddenly (for example: post stroke or head injury), and several causes of dementia can be completely reversed (e.g.: hematoma subdural, drug toxicity, depression) if being treated rapidly. Dementia can appear at any age although it appears after 65 years old. It is crucial to differentiate between dementia and delirium. Delirium is a condition marked by sudden onset confusion, typically accompanied by disruptions in memory and orientation (often with confabulation) and often manifested by abnormal movements, hallucinations, illusions, and change in affect. To differentiate from dementia, there is a decrease in the level of consciousness besides can also be hyperalert on delirium. Delirium usually fluctuates intensity and can become dementia if abnormal underlying issue is not resolved.

There are several conditions that can result in MND, with Alzheimer’s dementia being the most prevalent cause, accounting for approximately 70% of cases. The DSM-5 criteria for MND delineates thirteen etiological subtypes that are likely to cause the condition. These subtypes encompass Alzheimer’s disease, Lewy body disease, Huntington’s disease, HIV infection, Parkinson’s disease, vascular disease, frontotemporal lobe degeneration, prion disease, traumatic brain injury, substance and/or drug use, other medical conditions, multiple etiologies, and cases with unknown causes. It is possible for a patient to have multiple factors contributing to MND; for instance, they may exhibit a blend of Alzheimer’s disease and vascular disease. Additional medical conditions that may result in dementia encompass corticobasal syndrome, progressive supranuclear palsy, and multiple system atrophy (Emmady, Schoo, Tadi, 2022).

2.2.Epidemiology and risk factors

Globally, there are currently 50 million individuals living with dementia, and by 2050, this is projected to increase to 150 million (Balbim et al, 2022). The incidence of dementia has increased significantly with age. The prevalence of dementia doubles every additional five years, after the age of 65. Overall, the prevalence of dementia in the population aged over 60 years is 5.6%. In the United States, dementia affects approximately 15% of individuals over the age of 68, with Alzheimer’s disease being the primary contributor. Alzheimer’s disease ranks as the 6th main cause of death and the 5th main cause in individuals over 65 years of age. In the US and Europe, Alzheimer's disease stands as the most prevalent cause of dementia, while in Asia it is estimated vascular dementia (Arvanitakis, Shah, Bennet, 2019).

Age stands as the primary risk factor for dementia (Arvanitakis, Shah, Bennet, 2019; Meng, Lin, Zheng, 2020). There is a possible minor risk, less than 1%, attributable to gene mutations,

particularly mutant amyloid precursor proteins, present in 40–65% of dementia cases, especially Alzheimer's disease, often accompanied by the APOE-e4 genetic variant. Family background could serve as an additional susceptibility element for dementia and may also be impacted by heart issues, limited educational attainment, social determinants, cognitive engagement, and prior traumatic brain injury leading to Mild Cognitive Impairment (MCI). Evidence suggests that persistent health issues, like lack of physical inactivity, smoking, diabetes, abdominal fatness, and elevated cholesterol, could heighten the likelihood of dementia onset, while social engagement and a diet low in saturated fat and high in fiber from vegetables can potentially reduce the risk.

It remains unclear whether the relationship between physical activity and dementia risk is dose-dependent; however, evidence suggests a decreased risk with increased levels of physical activity. This finding may hold significance, particularly for individuals in preliminary stages MCI or with risk factors. However, exercise offers potential benefits for individuals diagnosed with dementia (Meng, Lin, Zheng, 2020).

2.3. Pathophysiology of Dementia

The pathophysiology of dementia varies depending on its subtype as shown in table 1. Most dementia forms, except for vascular dementia, stem from the accumulation of abnormal proteins in the brain.

Table 1. Pathophysiology of Dementia Depending on Its Subtype.

Subtypes of Dementia	Pathophysiology
Alzheimer's disease	Cortical atrophy and the buildup of amyloid plaques, alongside the formation of neurofibrillary tangles containing hyperphosphorylated tau protein in neurons, contribute to their degeneration
Parkinson's disease dementia & Lewy body dementia	The intracellular buildup of Lewy bodies, aggregates of insoluble alpha-synuclein protein in the brain
Frontotemporal dementia	Multiple mutations causing the hyperphosphorylated tau proteins and deposition of ubiquitinated TDP-43 in the frontal and temporal lobes
Huntington's disease	Inherited autosomal dominant gene mutation
Prion-related dementia (include Creutzfeldt-Jakob disease and kuru)	Misfolded prions, infectious protein particles that self-propagate
HIV infection	Development of neurocognitive disorders, partly due to toxic inflammation and macrophage activation, resulting in brain neurodegeneration

Alcohol consumption (particularly in high doses and long-term use)	Various cytotoxic damage in the brain
Vascular dementia	Ischemic brain injury (e.g., stroke)

Pathological alterations of individuals with diverse types of dementia may differ in the brain. Nonetheless, there are frequently overlapping and mixed manifestations and observations across different dementia types (Emmady, Schoo, Tadi, 2022).

2.4. Diagnosis

The clinical manifestation of dementia, characterized by a progressive decline in cognitive function leading to new functional dependence, can arise from various underlying pathophysiological mechanisms. The most prevalent cause is Alzheimer's disease, accounting for 50 to 75% of cases, followed by vascular dementia (20%), Lewy bodies dementia (DLB; 5%) and frontotemporal lobar dementia (FTLD; 5%). Less common etiologies (3%) such as Huntington's disease, Creutzfeldt-Jakob disease, multiple sclerosis, and AIDS. The cognitive impairments crucial for diagnosing dementia can be categorized into 5 primary domains: executive function, memory, visuospatial abilities, language, behavior, and personality. As dementia progresses, regardless of the cause, cognitive deficits typically widen, affecting deeper, and domains, resulting in escalating functional impairment. Consequently, distinguishing between different etiologies of dementia becomes challenging in later stages. However, in the preliminary stages, identifying a predominant pattern of symptoms can aid in determining the most probable underlying disease process.

Alzheimer's disease commonly manifests with deficits in short-term memory, often characterized by repetitive questioning. A probable diagnosis of dementia stemming from Alzheimer's disease requires impairment in at least one additional cognitive domain. Atypical features may include behavioral or language disturbances indicative of frontal variants, or early visuospatial issues indicative of posterior cortical atrophy.

Vascular dementia is characterized by cognitive deficits temporally associated with stroke, along with evidence of cerebrovascular disease observed during imaging and examination tests. Lewy body diseases encompass dementia with Lewy bodies (DLB) and Parkinson's disease (PD).

Individuals with DLB may also exhibit symptoms of Parkinsonism. If dementia onset and physical PD symptoms occur within a year of each other, the diagnosis is Parkinson's disease dementia (PDD); if cognitive symptoms precede physical symptoms by more than 1 year, the diagnosis is DLB.

Early language or behavioral symptoms may be suggested by FTLD. In individuals under 65 years old, the incidence of FTLD and Alzheimer's disease is similar, unlike in older age groups where FTLD incidence is lower. Early symptoms of behavioral variant FTLD may lead to an initial diagnosis of a primary functional psychiatric disorder, which can complicate the diagnosis process. The clinical scenario often does not exclusively align with a single diagnostic criterion. Due to the accumulation of simultaneous pathophysiological processes within the brain, symptoms may reflect overlapping disease mechanisms, resulting in a diverse clinical presentation, commonly seen in Alzheimer's disease and vascular dementia.

Many individuals present exhibit objective cognitive symptoms that do not meet the criteria for a dementia diagnosis. These symptoms are often indicative of MCI, which has enabled focused follow-up studies showing that 5 to 10% of MCI sufferers progress to meet the diagnostic criteria for dementia each year. These symptoms may also be attributed to psychiatric conditions, medications known to impair cognition, or temporary and spontaneously regressing factors. Apart from the criteria established by McKhann et al in 2011, there are other diagnostic criteria. The International Working Group has suggested diagnostic criteria for Alzheimer's disease primarily for research purposes. However, older scales like the Hachinski and NINDS-AIREN scales continue to be utilized to define vascular dementia. Diagnosing and distinguishing dementia necessitates a comprehensive history and examination. Patient history and additional anamnesis are necessary to identify new functional dependencies and investigate progressive cognitive impairment, as well as neuropsychiatric symptoms.

A physical examination is crucial to detect extrapyramidal or focal neurological signs. While cognition may be informally evaluated during consultations, formal testing is necessary and aids longitudinal monitoring. One of the most widely recognized formal cognitive tests is the Mini Mental State Examination (MMSE), which was first suggested in 1975. Although copyright restrictions have affected its usage in recent years, the MMSE has still become well-established and serves as a common language for those familiar with its application. The Montreal Cognitive Assessment (MoCA), initially promoted as a test for MCI and scored out of 30, has increased to

fill the void left by the limitations of the MMSE. The Addenbrooke's Cognitive Examination-III (ACE-III) offers a more comprehensive assessment, with scores calculated for each domain and totaled for a maximum score of 100. Despite the increasing diversity in existing scales, none are flawless. Inter and intra-rater reliability may restrict their usage, and all scales rely on the individual's premorbid educational capabilities. The key is to comprehend a scale, confirm its consistent application within a service, and utilize it for progress monitoring (Cunningham et al, 2015).

2.5. Treatment

Medications approved by the FDA to enhance cognitive function including memantine and cholinesterase inhibitors. Memantine acts as an NMDA antagonist, reducing glutamine activity. Cholinesterase inhibitors, such as rivastigmine, donepezil and galantamine work by preventing the breakdown of acetylcholine and aiming to delay or slow symptom deterioration. While acetylcholinesterase inhibitors elicit varied responses among patients, not all patients show benefit. Potential contraindications and significant side effects, including peptic ulcer disease, cardiovascular issues, and weight loss, must be considered with their use. Memantine may offer neuroprotective advantages by acting as a noncompetitive NMDA receptor antagonist, potentially preventing neurotoxicity and excessive calcium influx into neurons. However, the benefits of both memantine and acetylcholinesterase inhibitors are often modest, leading many individuals and healthcare providers to opt out of pharmacologic treatment.

Lifestyle adjustments aimed at optimizing cognitive function involve improving sleep quality, consuming anti-inflammatory foods, engaging in regular exercise, addressing visual or auditory impairments, stress management, and maintaining optimal blood pressure, cholesterol, and blood sugar levels. Behavioral symptoms like anxiety, depression and irritability can be managed with antidepressants and sometimes antipsychotics. Non-drug approaches such as physical exercise programs, memory training, supportive care, and mental or social stimulation should also be utilized to help control symptoms (Emmady, Schoo, Tadi, 2022).

Regular physical exercise stands out as one of the most effective methods for reducing dementia risk among all lifestyle changes studied. Numerous studies on aerobic exercise (exercise elevates the heart rate) in middle-aged or older adults have demonstrated improvements in thinking

and memory, along with decreased dementia rates. The definition of 'physical activity' or exercise utilized in exercise science research varies. According to the American College of Sport Medicine (ACSM), physical activity refers to any skeletal muscle contraction-induced body movement resulting in a substantial rise in calorie demands relative to basal metabolic rate. Exercise, a component of physical activity, comprises scheduled, regulated, and repeated body movements performed to enhance and/or sustain one or more elements of physical health (Wang et al, 2021).

3. Physical activity and dementia

For those who have cognitive decline, physical exercise can support healthy aging into independent body function, psychological well-being and cognition. In particular, exercise can also boost cognitive abilities, especially memory and executive function, independent function and psychological well-being in mild cognitive impairment/dementia (Nuzum et al. 2020). This mechanism is by encouraging not only variety of processes, such as synaptic plasticity, neurogenesis, angiogenesis and autophagy but also work as protective and preventive actions, such as enhancements in memory, cognition, mood, and sensitizes the nervous system (Yao et al. 2021). Physical activity has been shown to repair dementia patient’s general cognitive, but unfortunately not specific in cognitive domains. Certain cognitive domains in dementia patients are challenging to investigate, especially at more advanced stages of the disease. Therefore, in more advanced forms of dementia, a floor effect for these tests is anticipated (Chang 2020).

3.1. Effect of exercise on hippocampus and amygdala

An essential part of the limbic system, the amygdala is involved in many different facets of emotional behavior (Maurer et al. 2022). Hippocampus is separated into the dentate gyrus, cornu ammonis field 3, and cornu ammonis field 1 while amygdala is divided into the lateral amygdala, basal amygdala and central nucleus (Yao et al. 2021). It has been proposed the importance of hippocampus in learning stimuli of the factual information regarding the stimuli and the connections between contextual cues. Amygdala is crucial for emotional connection and response (Yao et al. 2021). Functional brain imaging methods, such as 18F-fluorodeoxyglucose (FDG-PET), positron emission tomography (PET) and magnetic resonance imaging (MRI), can give

important information about the anatomical and functional state of various brain regions. Regional brain atrophy patterns can be diagnosed with volumetric MRI, brain blood oxygen level and hemodynamic activity can be measured with fMRI, and early dementia stages can be identified by the results of FDG-PET by looking for hypometabolism in the precuneus and posterior cingulate cortex (Bueno-Antequera and Munguía-Izquierdo 2020).

Won et al. looked at how exercise training can affect hippocampal functional connectivity (FC) in adults with mild cognitive impairment and normal cognitive control group. They discovered that after 12 weeks of exercise training, hippocampal FC significantly increased in older adults. They also suggested that increased hippocampal FC might be a reflection of neural network plasticity linked to improvements in memory ability in mild cognitive impairment patients (Won et al. 2021). Aerobic exercise has a neuroprotective effect on brain aging, and there may be a connection between memory and aerobic exercise. Eisenstein et al. evaluated weekly aerobic activity and MRI findings showed white matter and hippocampus lesions connected memory to an active lifestyle and cardiorespiratory fitness (Eisenstein et al. 2022).

3.2. Effect exercise on total brain volume and hippocampus

The most well-known structural neuroimaging biomarker is hippocampal atrophy. Physical activity may mitigate the age-related decrease in hippocampus volume, according to new research (C. Domingos, Pêgo, and Santos 2021). Um et al. examined the effects of moderate-intensity exercise on preclinical Alzheimer's disease on cortical thickness and subcortical volumes, finding that the exercise group had greater cortical thickness and volumes than the non-exercise group. A study by Domingos et al. also showed that longer periods of intense exercise were linked to bigger volumes of the right and left hippocampal gyrises. Additionally, the functional connectome study showed that for light, moderate and total physical activity time, there was a greater functional connectivity (FC) between the frontal gyrus, cingulate gyrus and occipital inferior lobe; while conversely, sedentary time was linked with a reduced FC in the same networks (Célia Domingos et al. 2021). In older adults with minor cognitive impairment, aerobic dancing may enhance episodic memory and raise the sizes of the right and total hippocampus regions. An enhanced hippocampal activation that appears to be involved in memory consolidation during locomotion, was caused by the aerobic dance's physical movements, which required a lot of spatial stimulation.

This process involves repetitive logical learning and review (Zhu et al. 2022). There are correlations between changes in hippocampus volumes over time and changes in physical activity levels in long-term follow-up (up to 12 years). The left hippocampal region showed a yearly volume decline, while the right hippocampal region did not. In middle age, a 0.33% higher hippocampus volume was linked to every 10 metabolic equivalents (METs, approximately 2 hours of moderate exercise) increase in weekly physical activity (equal to approximately 1 year of usual aging). Each extra MET was linked to a 0.05% increase in hippocampus volume in older age; however, the effects decreased with aging by 0.005% annually (Fraser et al. 2022). Furthermore, after controlling for confounders, Moored et al. studied the relationships between enriching early-life activities (EELAs) and hippocampus and amygdala volumes revealed that each extra EELA was linked to a higher amygdala volume. Every extra EELA in men was linked to a larger hippocampus volume. Compared to the thalamus, associations were exclusive to these locations (Moored et al. 2020). In community-dwelling older individuals with cognitive decline, Baduanjin exercise intervention in 24 weeks can effectively enhanced cognitive capacity and decreased physical frailty. The mechanism may be due to modifying the structural plasticity of the hippocampus subregion. The eight low-to-medium intensity movements of the Baduanjin exercise are among the most well-liked ancient mind-body exercises in China. They are distinguished by symmetrical body postures and motions, breathing control, a meditative state of mind and mental focus (Wan et al. 2022).

3.3.Exercise to improve mitochondrial dysfunction

Following physical activity, enhanced energy metabolism and protein expression were documented in the majority of studies examining mitochondrial function. Notably, there was an increase in glycogen content in the hippocampal region. They are still challenging to apply to illnesses involving mitochondrial malfunction, though. Exercise boosted mitochondrial respiration in both healthy older persons and patients with peripheral vascular disease, supporting these findings (da Costa Daniele et al. 2020).

3.4. Exercise to reduce markers inflammation

Inflammation and mitochondrial dysfunction are correlated on both sides. Inflammation is a byproduct of mitochondrial failure, which in turn causes inflammation. In neurodegenerative diseases, mitochondrial dysfunction and neuroinflammation are frequently observed (da Costa Daniele et al. 2020). Training in physical exercise may be a safe and efficient way to slow Alzheimer's disease progression and enhance antioxidant and anti-inflammatory systems; therapy may also be monitored by particular evaluated biomarkers. According to Farias et al., after physical training, patients with Alzheimer's disease showed increases in interleukin-4 and nitrite levels and a decrease in catalase activity and ROS levels (de Farias et al. 2021). Aerobic, strength, balance, and postural exercises are all included in multicomponent training (MT), which has the potential to be a useful training method for improving cognitive function as well as functional ability in dementia patients. Papenberg et al. found that, regardless of IL-12p40 levels, individuals with low activity and high levels of inflammatory marker had reduced volumes of the lateral prefrontal cortex and hippocampus in comparison to those who were more physically active (Papenberg et al. 2016). Strength training has been shown to reduce leukocyte and lymphocyte counts and increase hemoglobin, mean cell volume, and mean cell hemoglobin concentration in older women with cognitive impairment. Chupel et al. conducted another study to examine the effects of strength training on inflammatory cytokines and hematological markers. (Chupel et al. 2017). Liu and colleagues discovered that a rigorous 4-week exercise regimen, involving both strength and aerobic training, significantly improves the plasma monocyte chemotactic protein-1 levels of elderly dementia patients. Additionally, patients who underwent aerobic training also showed improvements in their serum levels of brain neurotrophic factor (Liu et al. 2020)

Area of interest	Study	Sample size	Physical activity	Assestment	Findings
Brain volume & hippocampus	Um et al (2020)	63 preclinical Alzheimer	moderate aerobic activity intensity (dance, swimming,	MRI	When compared to the exercise group, the non-exercise group's

	disease subjects	mountain climbing) greater than one hour five days a week		cortical thickness and volumes were less.
Domingos et al (2021)	120 community-dwelling older adults	Gait speed and handgrip strength	MRI scan	Greater sizes of the right hippocampal and left parahippocampal gyrus are correlated with longer periods of intense PA.
Zhu et al (2022)	33 patients aged 50-85 years	3 months Moderate-intensity group aerobic dance	MRI	Seniors with MCI may benefit from aerobic dance since it can boost their right and total hippocampus volumes and enhance their episodic memory.
Fraser et al (2022)	411 middle age and 375	A physical activity	MRI Scan Acquisition	There was a drop in volume on the left but

		older age adults	recall questionnaire		not the right. hippocampal
	Moored et al (2020)	123 participants	The Hopkins EELA inventory	MRI acquisition	Higher EELA was linked to a larger volume of the hippocampus and amygdala.
	Wan et al (2022)	102 community-dwelling adults	Baduanjin exercise consists of eight low-medium intensity movements	MRI data acquisition	Frequent Baduanjin treatments may improve the resting function link between the prefrontal lobe and bilateral hippocampal regions.
Hippocampus function	Won et al (2021)	35 community-dwelling older adults	Gait speed and handgrip strength	Neurocognitive testing	Exercise training for 12 weeks causes a considerable boost in hippocampal function connectivity in older persons.
	Eisenstein et al (2022)	50 participants (aged 65–80)	active lifestyle and cardiorespiratory fitness	MRI	Pathways link including white matter and hippocampus

					lesions that connect memory to an active lifestyle and cardiorespiratory fitness
Marker inflammation	Farias et al (2021)	15 women	22 training sessions, twice a week	Neurotrophin, Cytokine Levels, Antioxidant and Pro-oxidant Serum	While nitrite and interleukin-4 levels were elevated, ROS and catalase activity were downregulated.
	Papenberg et al (2016)	555 patients age 60–87 years	Self-administered questionnaire	Blood Serum Markers of Inflammation	Individuals with low levels of physical activity and elevated levels of IL-12p40 had reduced sizes of the lateral prefrontal cortex and hippocampus in comparison to those with higher levels of physical activity, regardless of IL-12p40 levels.

	Chupel et al (2017)	33 women	28 weeks strength training program	Blood Serum Markers of Inflammation	Strength training can raise hemoglobin, mean cell volume, and mean cell hemoglobin concentration while lowering leukocyte and lymphocyte numbers.
	Liu et al (2020)	80 participants	4 weeks strength or aerobic training	Serum brain neurotrophic factor, insulin-like growth factor-1, and plasma monocyte chemotactic protein-1 levels	Patients who underwent strength and aerobic exercise showed improvement in brain neurotrophic factor and plasma monocyte chemotactic protein-1 serum levels

3.5. Exercise Mode in Reducing the Risk of Dementia Development

Senile dementia, also known as dementia, is the diminishing mental capabilities associated with getting older. It involves a decrease in cognitive functions, challenges in concentration, and notably, the hindrance of higher cerebral cortex functions, such as memory, judgment, abstract thinking, as well as alterations in personality and behavior. Essentially, dementia presents as a decline in mental and intellectual functions due to brain diseases in mature adults, affecting their overall life and work capabilities (Wang et al., 2021a). The majority of dementia instances stem from Alzheimer's disease (AD) and multiple infarct dementia, which is alternatively termed vascular dementia or multi-infarct dementia. Alzheimer's disease is marked by the reduction, depletion, and deterioration of brain cells, and its progression is linked to the aging process. The occurrence of dementia is relatively infrequent prior to the age of 65 but increases in prevalence beyond that age. Due to the generally longer lifespan of women compared to men, a greater percentage of women experience the impact of Alzheimer's disease (*Exercise and Dementia: What Should We Be Recommending?*, n.d.). Dementia resulting from multiple cerebral infarctions is caused by the interruption of blood supply in various brain regions, leading to impaired functioning of the cerebral cortex. Despite ongoing global efforts to prevent Alzheimer's disease, finding definitive solutions remains challenging. Nonetheless, research proposes that specific actions can be taken to reduce the risk. According to prospective studies, even light to moderate physical activity can lower the likelihood of developing dementia and Alzheimer's disease. Exercise is suggested as a potential lifestyle intervention to minimize the occurrence of these conditions. Customized exercise routines can be formulated based on individual physical conditions. In general, consistent participation in exercise over a period of 6-8 weeks has been shown to decrease the risk of developing dementia ("The Effect of Exercise Intervention on Cognitive Performance in Persons at Risk of, or with, Dementia: A Systematic Review and Meta-Analysis," 2014).

Dementia's multifaceted nature necessitates comprehensive strategies for prevention and management. This section explores the impact of different exercise modes on reducing the risk of dementia development. Aerobic exercise, resistance training, and combination exercises will be discussed, emphasizing their unique contributions to cognitive health. Relevant studies and clinical trials will be reviewed to provide a nuanced understanding of the connection between exercise mode and dementia prevention. Recent research suggests that aerobic exercise, such as brisk

walking, jogging, and swimming, has profound effects on cognitive function. It promotes neuroplasticity, enhances cerebral blood flow, and stimulates the release of neurotrophic factors. On the other hand, resistance training, involving muscle-strengthening activities, may influence cognitive performance through its impact on muscle-nerve connections. The combination of aerobic and resistance exercises may offer synergistic benefits. This section will present a critical analysis of these findings, discussing the underlying mechanisms and potential implications for designing effective exercise interventions. The role of exercise mode in dementia prevention is complex and multifaceted. While aerobic exercise, resistance training, and combination exercises show promise, further research is needed to tailor exercise prescriptions for different populations and stages of dementia.

3.6. Exercise Duration in Reducing the Risk of Dementia

In 2018, the US Department of Health and Human Services unveiled a primary set of recommendations concerning physical activity for adults and the elderly. The focal point revolves around specific guidelines regarding the duration of physical activity. Adults and older individuals are urged to participate in a minimum of 150 minutes (2 hours and 30 minutes) of moderate-intensity aerobic physical activity per week. Alternatively, they can choose to engage in 75 minutes (1 hour and 15 minutes) to 150 minutes (2 hours and 30 minutes) of vigorous-intensity aerobic physical activity on a weekly basis. Another option involves undertaking a blend of moderate- and vigorous-intensity aerobic activities that are deemed equivalent. It is recommended to spread aerobic activities across the entire week. For individuals with chronic conditions who find it challenging to meet the 150-minute guideline, it is advised to tailor their physical activity to align with their capabilities and health conditions (Wang et al., 2021b). Numerous prior inquiries have delved into exploring the relationship between engaging in physical activities and the development of dementia, scrutinizing the association between the duration of physical activity and the onset of dementia. In a research endeavor led by Najar et al., participants were categorized into four distinct groups based on their levels of activity, investigating the correlation between cognitive and physical activities and the occurrence of dementia. The findings suggested that the period of physical activity in midlife was associated with a reduced risk of both mixed dementia and dementia with cerebrovascular disease. Furthermore, a meta-analysis concentrating on the

influence of physical activity on individuals with Alzheimer's disease discovered that interventions lasting an average of 40 minutes per session over 12 to 24 weeks could improve cognitive function in elderly individuals with Alzheimer's (Demurtas et al., 2020). Maass et al. delved into the impact of physical activity on cognitive performance among older individuals, but failed to establish a significant correlation with cognitive functions. Nevertheless, this research employed a shorter exercise duration of 30 minutes, differing from others that spanned between 60 to 90 minutes. The study highlighted the potential significance of exercise duration in shaping cognitive outcomes. Prior investigations have assessed physical activity using diverse approaches, exploring various types, intensities, durations, and frequencies. Although not presenting an optimal exercise prescription for brain health, function, or dementia risk reduction, these findings suggest that a variety of physical exercises and activities collectively contribute to enhancing brain health and cognitive function (Digitalcommons@uri & Saul, n.d.).

Understanding the optimal duration of exercise for dementia prevention is crucial for developing practical and sustainable interventions. This section investigates the relationship between exercise duration and the reduction of dementia risk. It examines both short-term and long-term effects, considering the cumulative impact of regular exercise on cognitive health. Studies exploring the effects of short-duration, high-intensity exercises, as well as longer-duration moderate-intensity exercises, will be reviewed. The time-dependent nature of exercise-induced neurobiological changes will be discussed, emphasizing the importance of consistency and adherence to exercise regimens. Additionally, the potential role of varying exercise durations in different stages of dementia will be explored. Balancing the optimal duration of exercise with individual preferences and capabilities is crucial for maximizing the benefits in dementia prevention. This section will conclude with recommendations for tailoring exercise duration based on current evidence and the need for personalized approaches in dementia management.

3.7.Exercise Intensity in Reducing the Risk of Dementia

This segment is obligatory and relates to the energy utilized during physical activity, commonly known as exercise intensity. The parameter frequently employed to evaluate exercise intensity is the pulse rate, serving as an indicator of how the cardiovascular system reacts to the demands imposed by physical activity. Determining the suitable exercise intensity presents a

notable challenge in formulating an exercise regimen. The primary methods for prescribing and overseeing exercise intensity encompass heart rate (HR) and the perceived exertion rating (RPE). HR is employed to establish a spectrum of exercise intensity due to its direct correlation with the percentage of functional capacity VO2. Generally, it is advised that the younger demographic partake in exercise intensities ranging from 60% to 80%, while older individuals often experience advantages from an exercise intensity of 40% of HR reserve, showcasing aerobic and functional training adaptations (Jia et al., 2019). The Dementia and Physical Activity (DAPA) trial, initiated by the National Institute for Health Research (NIHR), sought to contribute to discussions regarding the potential cognitive advantages of physical exercise for individuals with dementia. A preceding research effort, which analyzed longitudinal data from 16,700 Europeans aged 54 to 75 over a 13-year span, found that engaging in regular moderate physical activity directly safeguards against cognitive decline and dementia. Notably, women appeared to derive greater benefits than men. Examples of activities falling under the categories of moderate and vigorous exercise include brisk walking, running, or circuit training. A study from 2019, featured in the journal Applied Physiology, Nutrition, and Metabolism, explored the correlation between the intensity of physical workouts and improvements in memory. While high-intensity interval training showed the most pronounced enhancement in memory, the study concluded that exercise intensity had no significant impact on executive functioning, as positive trends were evident in both exercise groups. Overall, enhanced fitness levels were associated with improved memory performance (Steichele et al., 2022). Research findings suggest that the crucial factor lies in the intensity of physical activity. Older individuals who partake in short, intense bursts of physical activity may witness a significant 30% improvement in memory performance, while those engaged in moderate workouts generally do not experience any enhancement. A study involving eleven young men (average age of 25) and ten older men (average age of 69) revealed that interval exercise leads to a more notable overall change in the total volume of blood flow during both exercise and recovery for individuals in both age groups compared to steady-state exercise. Given that age-related declines in brain blood flow are linked to a higher risk of cognitive decline, including dementia, the increased brain blood flow resulting from interval exercise could potentially be beneficial for future brain health. The essential indicators of exercise intensity vary across research methodologies in interventions targeting dementia reduction, spanning from moderate to high intensity (Chung et al., 2023).

The intensity of exercise is a key factor influencing physiological adaptations and, consequently, cognitive outcomes. This section investigates the impact of exercise intensity on reducing the risk of dementia, examining both moderate and high-intensity exercise regimens. The neurobiological mechanisms underlying the relationship between exercise intensity and cognitive function will be explored. Research studies comparing the cognitive benefits of moderate-intensity aerobic exercise with those of high-intensity interval training (HIIT) will be critically analyzed. The potential role of exercise intensity in enhancing neuroplasticity, neurotrophic factor release, and mitochondrial function will be discussed. Moreover, considerations for individual variations in response to different exercise intensities will be addressed. Determining the optimal exercise intensity for dementia prevention requires a nuanced understanding of individual factors and underlying neurobiological processes. This section will conclude with recommendations for tailoring exercise intensity based on individual profiles and considerations for long-term adherence.

3.8. Differential Effects of Open Skill Exercise and Close Skill Exercise on the Prevention of Dementia

Emerging findings suggest that engagement in physical activity has a positive impact on the release of neurotrophic factors and myokines. Nonetheless, conclusive evidence regarding the most effective type of physical exercise to stimulate these releases remains elusive. This research aimed to evaluate the immediate and prolonged effects of open-skill exercise (OSE) compared to closed-skill exercise (CSE) on the serum and plasma levels of brain-derived neurotrophic factor (BDNF), including both full-length (BDNFS) and truncated (BDNFP) forms, as well as serum levels of insulin-like growth factor 1 (IGF-1) and interleukin 6 (IL-6) in healthy older individuals. For the immediate effects, thirty-eight participants were randomly assigned to either an intervention group (participating in badminton (aOSE) and bicycling (aCSE), n = 24, mean age 65.83 ± 5.98 years) or a control group (reading (CG), n = 14, mean age 67.07 ± 2.37 years). Blood samples were collected immediately before and 5 minutes after each condition, with heart rate monitored during each session. The mean heart rate for aOSE and aCSE was identical (65 ± 5% of heart rate reserve). In a subsequent 12-week training intervention, twenty-two participants were randomly assigned to either a sport-games group (cOSE, n = 6, mean age 64.50 ± 6.32) or a

strength-endurance training group (cCSE, n = 9, mean age 64.89 ± 3.51) to assess long-term effects. Training intensity for both groups was adjusted based on subjective perceived exertion using the CR-10 scale (value 7). Blood samples were taken within one day after the training intervention. BDNFS, BDNFP, IGF-1, and IL-6 levels increased after a single 30-minute exercise session. After 12 weeks of training, BDNFS and IL-6 levels were elevated, while IGF-1 levels were reduced in both groups. However, only in the cOSE group were these changes statistically significant. No notable distinctions were identified between the exercise modalities (Sanders et al., 2020).

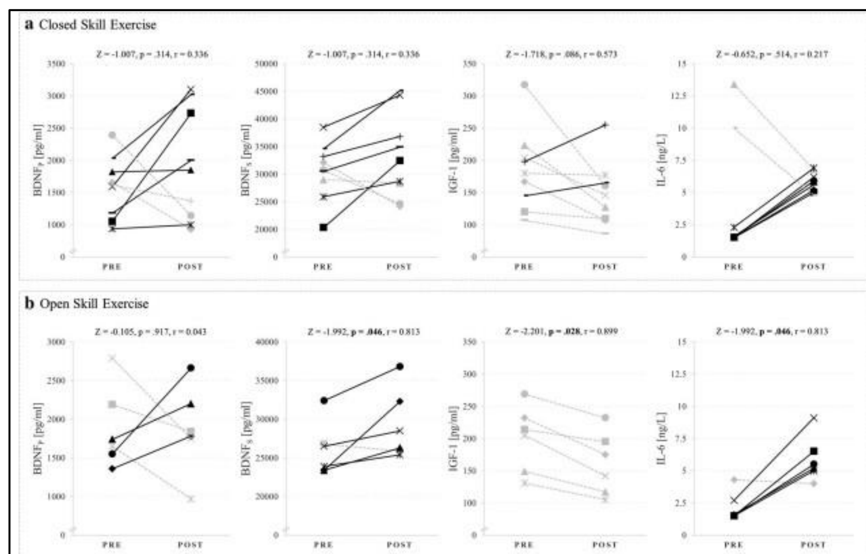

Fig. 1 Illustrates the absolute values of BDNFP, BDNFS, serum IGF-1, and serum IL-6, spanning from pre-test (T1: before intervention) to post-test (T3: after 12 weeks of intervention) for both the cOSE-group (a) and the cCSE-group (b). The symbols in both a and b correspond to the same individual.

Physical activities can be divided into open and closed skill tasks, each imposing unique cognitive requirements. This segment delves into the potential variations in the impact of open and closed skill exercises on dementia prevention. The cognitive and neural adaptations linked with each exercise type will be explored. The cognitive challenges associated with open skill activities, like sports and dance, and closed skill exercises, such as weightlifting and yoga, will be examined concerning their influence on cognitive function and reducing the risk of dementia. Findings from studies comparing the cognitive outcomes of these exercise categories will be presented, underscoring the importance of considering the specific cognitive demands within exercise

interventions. Comprehending the intricate effects of open and closed skill exercises on cognitive well-being offers valuable insights for creating targeted and efficient exercise strategies for dementia prevention. This portion will wrap up with suggestions to incorporate diverse activities addressing various cognitive demands, promoting overall brain health. To sum up, this thorough exploration of exercise's impact on dementia provides valuable insights for formulating evidence-based prevention and management strategies. The nuanced discussion on exercise mode, duration, intensity, and the differential effects of open and closed skill exercises contributes to the expanding knowledge in neurology and geriatrics. Ongoing research is essential to fine-tune and personalize exercise recommendations, considering the variety of dementia subtypes and the individual needs of affected individuals (Behrendt et al., 2021).

CONCLUSION

The comprehensive review on the impact of physical activity on dementia presents a plethora of evidence affirming the beneficial effects of exercise on cognitive function and the prevention of dementia. The literature examined consistently indicates that engaging in regular physical activity is linked to a decreased risk of developing dementia and may potentially decelerate cognitive decline in individuals already affected by the condition. Various forms of exercise, such as aerobic and resistance training, along with activities that enhance balance and coordination, have been proven to contribute positively to cognitive health. Mechanisms underlying these benefits include enhanced blood flow to the brain, the release of neurotrophic factors, and a reduction in risk factors like hypertension and diabetes. Furthermore, the review underscores the significance of integrating exercise into lifestyle interventions for those at risk of or already dealing with dementia. The results highlight the potential for exercise to serve as an economical and accessible preventive measure against cognitive decline. However, it is crucial to recognize the diversity in study designs, participant characteristics, and exercise interventions throughout the literature. Future research should strive to standardize methodologies and investigate the prolonged effects of various exercise modalities on specific subtypes of dementia. In summary, the existing wealth of evidence strongly advocates for the pivotal role of exercise in promoting cognitive health and averting dementia. Encouraging regular physical activity should be a fundamental element of global public health initiatives addressing the challenge of dementia.

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