

Physical Activity, Abdominal Breathing, and Other Non-Pharmaceutical Strategies for Neurodegenerative Disease Prevention and Brain Health

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Abstract

Neurodegenerative disorders (NDs) are rapidly rising worldwide with population ageing. While pharmacological treatments provide modest symptomatic benefits, they are frequently associated with serious adverse effects and offer limited disease-modifying impacts. Similarly, a large body of epidemiological, clinical, and experimental evidence indicates that lifestyle-based and other non-pharmaceutical interventions can reduce risks, delay the clinical onset, and support function in people living with or at risk of NDs. This review summarizes the global burden and treatment gaps in major NDs, outlines the concept and evidence base for non-pharmaceutical interventions and then focuses on physical activities as a central pillar of brain health promotion. The study synthesizes data on the systemic benefits of exercise, its neurobiological mechanisms, including neurotrophic signaling, neurotransmitter modulation, structural and functional brain changes, anti-inflammatory and antioxidant actions, adult hippocampal neurogenesis and the potential role of abdominal breathing. Finally, these findings are placed in the context of multidomain prevention trials, practical recommendations, and public health implications.

Keywords: Neurodegenerative disorders, Alzheimer's disease, Parkinson's disease, Physical activity, Abdominal breathing

Introduction

Dementia and other neurodegenerative diseases (NDs) have been among the leading causes of disability and dependency in older adults. Analyses from the Global Burden of Disease program estimate that more than fifty-five million people currently live with dementia worldwide, and this number may exceed one hundred fifty million by the middle of this century if current trends continue.¹ The World Alzheimer Report and related modelling studies suggest that much of this increase will occur in low-income and middle-income countries where health and social care systems are least prepared to absorb the associated costs.²

Neurological disorders as a group now rank among the leading causes of disability adjusted life years and the second leading cause of death globally, with dementia and Parkinson's disease (PD) among the fastest growing contributors.³ Successive Lancet Commissions have emphasized that up to 40% of global dementia cases may be attributable to potentially modifiable risk factors across the life course, including limited education, midlife hearing loss, hypertension, obesity, physical inactivity, diabetes, smoking, depression, social isolation, and air pollution.^{4,5} These findings have reframed dementia and other NDs not solely as the inevitable consequences of ageing but also as conditions whose incidence and

expression can be meaningfully shifted by prevention and risk reduction strategies.

This review extends the existing literature in three main ways. First, it proposes an integrated system to brain framework that links the cardiovascular, metabolic, immune, and gut microbial adaptations of physical activities to the specific central nervous system (CNS). The mechanisms of neuroprotection include neurotrophic signaling, adult hippocampal neurogenesis, and large-scale network remodeling across major NDs.⁶ Second, it introduces abdominal diaphragmatic breathing as an emerging non-pharmacological practice with plausible mechanistic links to vagal tone, heart rate variability, lymphatic clearance, and Alzheimer-related biomarkers, a topic that has received little attention in previous reviews.^{7,8} Third, it translates this mechanistic synthesis into concrete clinical and public health implications by aligning exercises and breathing prescriptions with international guidelines and multidomain prevention trials, (e.g., FINGER and related World Wide FINGERS initiatives), thereby providing a coherent non-pharmaceutical framework for brain health promotion across the life course.^{4,5,9}

Limitations of Pharmacological Treatments

Despite intensive research effort, available



pharmacological therapies for NDs remain constrained in both efficacy and tolerability. For AD, symptomatic agents (e.g., cholinesterase inhibitors and memantine) confer small average improvements in cognition and global clinical impression over six to twelve months, at the cost of gastrointestinal side effects, sleep disturbance, and bradycardia in a substantial proportion of patients.^{10,11}

Monoclonal antibodies that target aggregated amyloid beta (A β), including lecanemab, have demonstrated the ability to reduce amyloid burden and produce statistically significant yet clinically modest slowing of a cognitive decline in early AD.¹² These benefits are accompanied by risks of amyloid-related imaging abnormalities (e.g., vasogenic oedema and microhemorrhages) as well as high financial and logistic burden. According to updated safety analyses, these abnormalities and related complications are more frequent in apolipoprotein E epsilon four carriers and in people receiving concomitant anticoagulation, reinforcing the need for careful risk benefit assessment.¹³

In PD, levodopa and other dopaminergic agents remain the most effective symptomatic treatments, yet long-term use is strongly associated with motor fluctuations and dyskinesias. Meta analytic work suggests that approximately 40% of patients develop troublesome motor complications after four to six years of levodopa therapy, with higher rates in those who begin treatment at a younger age.¹⁴

The pharmacological management of behavioral and psychological symptoms of dementia demonstrates another limitation. Atypical antipsychotics offer only modest reductions in aggression, agitation, and psychosis and are consistently associated with the increased risk of cerebrovascular events and death in older adults with dementia, leading to regulatory warnings in many regions.¹⁵

Collectively, these examples underscore that current drugs mainly act on downstream neurotransmitter abnormalities or single pathophysiological targets, provide limited durable benefits and can produce clinically important adverse effects. Even as disease-modifying therapeutics continue to evolve, there is a clear need for complementary approaches that can function earlier in the causal chain, carry minimal risks, and be implemented at scale.

Non-Pharmaceutical Interventions as a Framework for Brain Health

Non-pharmaceutical interventions encompass a broad set of strategies that do not rely on prescription drugs yet have measurable effects on the brain structure, brain function, and clinical outcomes. These strategies include physical activities, structured cognitive training, dietary patterns, and stress reduction, as well as the optimization of sleep and circadian rhythms, management of vascular risk factors, and enhancement of social engagement and sensory rehabilitation.

The updated Lancet Commission on dementia

prevention, intervention and care synthesized longitudinal cohort data and concluded that higher levels of physical activities, adherence to Mediterranean type diets, maintenance of social contacts, effective management of hearing loss and cardiovascular risk factors, and avoidance of smoking are associated with lower dementia incidence.⁵ Multidomain randomized trials, such as the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER), have further demonstrated that combined interventions involving diet, exercise, computer-based cognitive training, and vascular risk monitoring can preserve or improve cognitive performance in older adults at increased dementia risk.⁹ Within this multidomain framework, physical activities occupy a central place because of their strong epidemiological association with reduced neurodegenerative risks and their broad systemic and neural effects that can potentiate other interventions.

Systemic Effects of Physical Activities Relevant to Neurodegeneration

Regular physical activities exert powerful systemic actions across multiple organ systems that converge on pathways implicated in ND pathogenesis.¹⁶ At the cardiovascular level, moderate and vigorous exercises improve endothelial functions and increase nitric oxide bioavailability while reducing arterial stiffness and blood pressure, thereby attenuating both macrovascular and microvascular injuries to the brain. These adaptations arise through repeated shear stress on the vascular wall, favorable changes in lipid profiles, and reductions in chronic low-grade inflammation.

From a metabolic standpoint, exercise improves insulin sensitivity, increases skeletal muscle glucose uptake, reduces visceral adiposity, and promotes a more favorable adipokine profile. These changes decrease the risk and severity of type two diabetes and metabolic syndrome, which are both established risk factors for dementia and cerebrovascular disease.¹⁷

In the endocrine system, physical activities modulate the hypothalamic pituitary adrenal axis and the growth hormone and the insulin-like growth factor (IGF) axis, thereby supporting anabolic processes, maintaining bone mineral density, and promoting a more resilient stress response.

Exercise is also a key regulator of immune function. The repeated bouts of moderate physical activities reduce systemic concentrations of pro-inflammatory cytokines, such as interleukin (IL)-6 and tumor necrosis factor alpha, while increasing anti-inflammatory mediators, including IL-10, in part through effects on visceral fat mass and immune cell trafficking.⁹ Chronic low-grade inflammation is a recognized driver of vascular damage, insulin resistance, and neurodegeneration, so this anti-inflammatory shift is directly relevant to brain health. Emerging evidence further indicates that regular physical activities shape the composition and metabolic output of the gut microbiota, increasing microbial diversity and

favoring species associated with short chain fatty acid production and lower systemic inflammation.¹ Given links between gut microbial metabolites, immune activation, and neurodegenerative pathology, this exercise-induced remodeling of the gut brain axis may represent an additional protective mechanism.

Neurobiological Mechanisms of Physical Activities in the Central Nervous System

Neurotrophic Signaling and Synaptic Plasticity

One of the most consistently replicated findings in exercise neuroscience is the upregulation of neurotrophic factors that support neuronal survival, synaptic plasticity, and neurogenesis. Aerobic training increases the expression of brain-derived neurotrophic factor (BDNF) in hippocampus and cortex in animal models and increases circulating and possibly central BDNF in humans.¹⁸ It is noteworthy that BDNF binds to the tropomyosin-related kinase B receptor and activates intracellular cascades, including phosphatidylinositol three kinase, mitogen activated protein kinase, and phospholipase C gamma pathways, which collectively promote dendritic growth, synapse formation, and long-term potentiation.

Exercise also enhances the production and uptake of IGF-1. Peripheral IGF-1 generated by skeletal muscle and liver during exercise can cross the blood brain barrier and is critical for exercise-induced increases in neurogenesis and angiogenesis within the hippocampus.¹⁹ The vascular endothelial growth factor produced by endothelial cells and astrocytes in response to exercise supports angiogenesis, increases cerebral perfusion, and provides additional trophic support to neurons and progenitor cells.²⁰

Myokines released from contracting skeletal muscles (e.g., irisin, which is cleaved from the precursor FNDC5) further link peripheral activities with central plasticity. Experimental studies suggest that irisin can increase BDNF expression in the hippocampus and may contribute to the cognitive benefits of exercise, although human data remain more limited.²⁰

Neurotransmitter Modulation and Mood Regulation

Physical activities also modulate multiple neurotransmitter systems that are important for cognition, motivation, and mood.²¹ Moreover, repeated exercises increase dopamine synthesis and turnover in mesocorticolimbic and nigrostriatal pathways, enhance dopamine receptor availability, and improve signaling efficiency. These changes may underpin improved executive function and motivation in physically active individuals and can be particularly relevant in PD, where dopaminergic neurons degenerate.

Additionally, exercise elevates serotonin levels and alters receptor expression in several brain regions, contributing to reductions in the symptoms of depression and anxiety observed in trials of exercise interventions.²² Noradrenergic activities arising from the locus coeruleus are similarly increased, supporting enhanced arousal,

attention, and stress resilience. Likewise, acute and chronic exercises stimulate the release of endogenous opioids and endocannabinoids, which are associated with analgesia, positive affect, and reductions in perceived stress.²³

Structural and Functional Brain Changes

Neuroimaging studies in older adults have demonstrated that regular aerobic exercise can increase or preserve brain volume in regions that are particularly vulnerable to ageing and neurodegeneration. In a landmark randomized trial, one year of moderate-intensity walking in previously sedentary older adults led to significant increases in hippocampal volume compared with the stretching control group, accompanied by improvements in spatial memory performance.²⁴ Subsequent research confirmed the beneficial effects of aerobic and resistance training on hippocampal and prefrontal volume, white matter integrity, and functional connectivity within networks that support memory and executive control.²⁴

Furthermore, functional magnetic resonance imaging and electrophysiological studies demonstrate that exercise enhances long-term potentiation (e.g., plasticity), increases task-related activation in frontal and parietal regions during cognitive tasks, and improves the efficiency of large-scale brain networks. These neural changes parallel improvements in processing speed, attention, working memory, and cognitive flexibility observed in behavioral assessments.^{24,25}

Anti-Inflammatory and Antioxidant Effects in the Brain

Neuroinflammation and oxidative stress are the central features of various NDs, including AD and PD. The microglial activation, astrocytic reactivity, and chronic elevation of pro-inflammatory cytokines contribute to synaptic dysfunction, impaired clearance of misfolded proteins, and neuronal death.^{25,26}

Regular physical activities attenuate these processes at several levels. Systemically, as outlined earlier, exercise reduces circulating pro-inflammatory mediators and shifts immune cell populations toward a less inflammatory profile.^{27,28} Within the CNS, experimental studies indicate that exercise can reduce microglial activation and the expression of inducible nitric oxide synthase and nicotinamide adenine dinucleotide phosphate oxidase while increasing antioxidant enzyme activities, including superoxide dismutase and catalase. These changes limit oxidative damage to lipids, proteins, and DNA, supporting a more favorable microenvironment for neuronal survival and plasticity.²⁵

Adult Hippocampal Neurogenesis

The discovery that new neurons are generated throughout life in the dentate gyrus of the hippocampus has important implications for understanding how lifestyle factors influence cognition and mood. Voluntary running in rodents robustly increases the proliferation, survival, and integration of neural progenitor cells in the dentate gyrus,

an effect that is partly dependent on BDNF, IGF-1 and vascular endothelial growth factor signaling.²⁹

Exercise-induced adult hippocampal neurogenesis appears to contribute to improvements in pattern separation, spatial memory, and stress resilience in animal models. In humans, direct measurement of neurogenesis is challenging; however, converging evidence from neuroimaging, blood-based biomarkers, and post-mortem work suggests that long-term physical activity is associated with the preservation of hippocampal structure and function and may promote ongoing circuit remodeling in this region.²⁴

Abdominal Breathing and Brain Health

According to the emerging evidence, diaphragmatic or abdominal breathing is a simple non-pharmaceutical technique that may complement physical exercises in protecting brain function and potentially modulating risk pathways relevant to NDs.³⁰ Diaphragmatic breathing is characterized by slow nasal inhalation with outward abdominal expansion, followed by prolonged exhalation. This pattern increases tidal volume and activates vagal afferents, thereby enhancing parasympathetic activities, raising heart rate variability, and reducing hypothalamic pituitary adrenal axis activation.³¹

Narrative reviews and randomized trials indicate that regular diaphragmatic breathing can reduce perceived stress and anxiety, lower cortisol concentrations, and improve sustained attention and working memory in healthy adults and clinical populations.^{31,32} In older adults, higher resting vagally mediated heart rate variability is associated with better executive functioning and predicts slower functional decline, whereas reduced heart rate variability is observed in mild cognitive impairments and early AD.⁸ Considering that slow abdominal breathing reliably increases heart rate variability, it is proposed as a low burden strategy to support prefrontal and limbic circuitry involved in emotion regulation and cognitive control.

Furthermore, mechanistic research demonstrates that breathing-based interventions can influence molecular pathways directly relevant to AD.³³ In a recent trial, heart rate variability biofeedback protocols that used slow-paced breathing to drive large oscillations in heart rate reduced the plasma concentrations of A β forty and A β forty-two and modified tau-related biomarkers in younger and older adults.⁷ In addition, magnetic resonance imaging studies have confirmed that yogic breathing practices with a focus on abdominal movement acutely increase respiratory contributions to cerebrospinal fluid pulsatility at the foramen magnum, which may enhance the glymphatic clearance of metabolic waste products including amyloid and tau species.⁷

Although direct intervention trials in patients with established ND remain scarce, preliminary work in neurological and psychiatric populations indicates that integrating structured diaphragmatic breathing into multimodal lifestyle programs can improve sleep

quality, reduce depressive symptoms, decrease perceived cognitive fatigue, and enhance quality of life.^{31,34} Overall, these findings support the consideration of abdominal breathing as a safe, accessible adjunct that can be combined with physical activities, cognitive training, and dietary interventions in prevention and rehabilitation strategies targeting brain ageing and neurodegeneration.

Evidence From Epidemiology, Trials, and Multidomain Interventions

Large observational cohorts consistently report that higher levels of physical activities are associated with lower risks of cognitive decline, dementia, and PD, even after adjustment for education, vascular risk factors, and baseline health status.⁵ Some analyses suggest a dose-response relationship, with greater benefits at moderate intensities and when activity is sustained across midlife and late life.

Randomized controlled trials provide more direct evidence of causal impacts on cognition and brain structure. A comprehensive systematic review and multilevel meta-analysis of exercise interventions in adults older than fifty years found that physical activities improved global cognitive functions, with particularly strong effects on executive function and memory. Aerobic training, resistance training, multicomponent programs, and Tai Chi were all beneficial when delivered at least at moderate intensity for around forty-five to sixty minutes per session.⁹

In people with mild cognitive impairments, both aerobic and resistance training have been shown to improve cognitive performance and, in some studies, to increase hippocampal volume and functional connectivity.³⁵ Additionally, exercise-based interventions improve gait speed, balance, and activities of daily living in PD, which are clinically meaningful outcomes even if they do not directly alter disease progression.

Multidomain prevention trials extend these findings by combining physical activities with dietary, cognitive, and vascular interventions. The FINGER study demonstrated that a two-year program including nutritional guidance, exercises, computer-based cognitive training, and intensive vascular risk management improved or maintained cognition compared with general health advice in older adults at elevated risk of dementia.⁹ Similar trials within the World Wide FINGERS initiative are ongoing in multiple countries and are beginning to explore neuroimaging and fluid biomarkers as endpoints, which will clarify whether multidomain lifestyle modification can slow the accumulation of AD pathology.⁹

Interactions With Diet, Sleep, Cognitive Training, and Social Engagement

Although this review focused on physical activities and abdominal breathing, it should be noted that their effects do not occur in isolation. Diet, sleep, cognitive activity, and social relationships interact with these interventions to shape brain ageing trajectories.

Mediterranean-style dietary patterns rich in fruits, vegetables, whole grains, olive oil, and fish are associated with lower risks of AD and slower cognitive declines in several cohorts.³⁶ The MIND diet, which combines the elements of Mediterranean and DASH dietary patterns and emphasizes leafy greens and berries, has been linked with reduced incidence of AD and slower cognitive declines even with moderate adherence.⁶ Physical activities and healthy diet are likely to act synergistically by converging on vascular, metabolic, and inflammatory pathways.

Structured cognitive training programs can enhance specific cognitive domains and may help maintain function in older adults and those with mild cognitive impairments.³⁷ When combined with exercise, cognitive training may benefit from increased neurotrophic support and improved cerebral perfusion induced by physical activities.

Sleep is emerging as a critical determinant of brain health, in part because the glymphatic system that clears metabolic waste products, including A β , is most active during slow-wave sleep. According to experimental research on mice, sleep substantially increases interstitial space and accelerates the clearance of metabolites from the brain.²⁸ Moreover, regular physical activities improve sleep quality and duration, and as noted above, abdominal breathing protocols can further promote parasympathetic dominance and sleep onset, thereby indirectly supporting glymphatic function and reducing neurotoxic protein accumulation.³⁸

Strong social networks and frequent social interaction are associated with lower risks of dementia and slower cognitive decline, even after controlling for other risk factors.³⁹ Group-based exercises, breathing classes, community programs and cognitively engaging activities can simultaneously increase physical activities, regulate breathing, and enhance social participation, thereby offering a pragmatic way to embed multiple protective factors into everyday life.

Practical Recommendations and Public Health Implications

Based on evidence, the World Health Organization recommends that adults perform at least one hundred fifty to three hundred minutes per week of moderate-intensity aerobic activities, or seventy-five to one hundred fifty minutes per week of vigorous-intensity activities, or an equivalent combination, together with muscle strengthening activities on at least two days per week.⁴⁰ These targets align well with doses of activity associated with cognitive and brain benefits in clinical trials.⁹

For individuals aiming specifically to support brain health and reduce neurodegenerative risk, practical guidance can emphasize the following points:

First, activities should be regular and sustained across midlife and later life. Even modest increases in movement among sedentary adults are associated with health benefits; however, greater gains are observed when people

progress toward or beyond current guidelines.

In addition, combining aerobic and resistance training is advisable. Aerobic activities (e.g., brisk walking, cycling, or swimming) improve cardiovascular and metabolic health and are strongly linked to hippocampal volume and memory, while resistance training supports muscle mass, functional capacity, and frontal lobe-based executive functions.³⁵

Further, multicomponent programs that integrate balance training, coordination tasks, and cognitively demanding movement (e.g., dance, Tai Chi, or adapted martial arts forms) may provide additional benefits for both cognition and fall prevention, especially in older adults.⁹

Moreover, simple breathing practices can be added at minimal cost and risk. Short daily sessions of slow abdominal breathing (e.g., five to fifteen minutes of paced breathing around six cycles per minute) can be integrated before or after physical exercises or used independently to regulate stress, improve sleep, and potentially influence the clearance of amyloid and tau-related metabolites.^{7,31,34}

Finally, physical activities and breathing practices should be framed as part of a broader non-pharmaceutical strategy that includes dietary optimization, sleep regulation, cognitive and social engagement, and rigorous management of vascular risk factors (e.g., hypertension, diabetes, and dyslipidemia).³⁹ Health systems and policymakers have a crucial role in enabling these behaviors by creating supportive environments, from safe walking and cycling infrastructure to community-based exercises and education programs, particularly in underserved regions where the burden of ND is rising fastest.³

Conclusion

NDs represent a growing global challenge, and drug-based treatments alone are unlikely to reverse current trends in incidence and disability. Converging epidemiological, clinical, and experimental data demonstrate that non-pharmaceutical interventions, with physical activities at their core and augmented by simple techniques (e.g., abdominal breathing), can substantially influence brain ageing trajectories. Regular physical activities and controlled breathing offer powerful, low risk means of reducing neurodegenerative risk and supporting cognitive resilience through improving cardiovascular and metabolic health, modulating immune and endocrine functions, enhancing neurotrophic support, promoting neurogenesis and synaptic plasticity, regulating stress physiology, and possibly augmenting glymphatic clearance.

Therefore, embedding evidence-based recommendations on physical activities, breathing practices, and other lifestyle factors into clinical practices, public health policies, and community designs is an essential complement to ongoing pharmacological innovations in the effort to prevent or delay ND while maintaining brain health across the lifespan.

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