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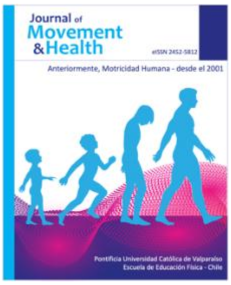

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Review

Neurobiological mechanisms, modalities, and clinical implications of exercise interventions for cognitive health in older adults: A narrative review

Mecanismos neurobiológicos, modalidades e implicaciones clínicas de las intervenciones de ejercicio para la salud cognitiva en adultos mayores: una revisión narrativa

Vergara Nieto, A✉[1,2]; Halabi Diaz, A[2,3,4]; Hernández Millán, M[2]; Sagredo, D[2]

Correspondence✉
MSc. Alvaro Vergara Nieto
Facultad de Ciencias de la Salud, Escuela de Nutrición y Dietética, UDD, Chile.
alvaro.vergara@udd.cl

Abstract
Objective: This narrative review synthesizes evidence from the last five years on the effects of physical exercise—categorized as aerobic, resistance, and multicomponent—on cognitive function in older adults, including those with MCI. **Results:** Meta-analyses and randomized controlled trials (RCTs) demonstrate that structured aerobic programs yield small-to-moderate improvements in episodic memory and processing speed, while resistance training enhances executive function and working memory. Multicomponent interventions outperform single-modality protocols, producing moderate gains in global cognition and verbal, visual memory, and executive domains in MCI populations. Mechanistically, exercise elevates neurotrophic factors, promotes hippocampal neurogenesis, improves cerebral perfusion, reduces inflammation and oxidative stress, and induces synaptic-plasticity–related epigenetic modifications, culminating in functional reorganization of brain networks. However, there are still research gaps to be addressed. Future research should employ standardized, multicenter trials with personalized exercise prescriptions, integrated biomarkers, and long-term follow-up, and explore multidisciplinary combinations with cognitive training and nutritional support. **Conclusion:** Collectively, these findings underscore physical exercise as a safe, accessible, and cost-effective strategy to preserve cognitive health and delay neurodegenerative progression in aging populations.

Key words: Cognitive Function; Cognition; Elderly; Exercise Therapy; Neurology; Neurobiology.

Resumen
Objetivo: Esta revisión narrativa sintetiza la evidencia de los últimos cinco años sobre los efectos del ejercicio físico (aeróbico, de resistencia y multicomponente) en la función cognitiva de los adultos mayores, incluidos aquellos con DCL. **Resultados:** Metaanálisis y ensayos controlados aleatorizados demuestran que los programas aeróbicos generan mejoras de leve a moderada en la memoria episódica y velocidad de procesamiento, mientras que el entrenamiento de resistencia potencia la función ejecutiva y la memoria de trabajo. Las intervenciones multicomponentes superan a los protocolos de modalidad única, produciendo ganancias moderadas en la cognición global y en los dominios de memoria verbal, memoria visual y funciones ejecutivas en poblaciones con DCL. El ejercicio eleva factores neurotróficos, promueve la neurogénesis hipocampal, mejora la perfusión cerebral, reduce la inflamación y el estrés oxidativo, e induce modificaciones epigenéticas relacionadas con la plasticidad sináptica, reorganizando redes cerebrales. Sin embargo, aún existen lagunas de investigación por abordar. Futuros estudios deberían ser multicéntricos estandarizados con prescripciones de ejercicio personalizadas, biomarcadores integrados y seguimiento a largo plazo, así como explorar combinaciones multidisciplinarias con entrenamiento cognitivo y apoyo nutricional. **Conclusión:** Estos hallazgos subrayan al ejercicio físico como una estrategia segura, accesible y rentable para preservar la salud cognitiva en adultos mayores.

Palabras clave: Función Cognitiva; Cognición; Adultos Mayores; Ejercicio Terapéutico; Neurología, Neurobiología.

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Highlights

- Physical exercise improves key cognitive functions (episodic memory, executive function, and processing speed) in older adults, including those with mild cognitive impairment (MCI).
- Multicomponent programs (aerobic + resistance) outperform single-modality protocols, producing moderate improvements in global cognition, verbal and visual memory, and executive domains.
- Cognitive benefits are explained by convergent neurobiological mechanisms, including increased BDNF and IGF-1 levels, enhanced cerebral perfusion, reduced inflammation and oxidative stress, and functional remodeling of brain networks.

Introduction

Population aging represents one of the foremost health challenges of the twenty-first century. It is estimated that by 2050 more than 20% of the global population will be over 60 years of age, with an increasing share exceeding 80 years.[1] This demographic shift is paralleled by a sustained rise in neurodegenerative disorders, among which mild cognitive impairment (MCI) and dementia constitute critical public-health concerns. MCI (defined by objective cognitive decline without significant interference in daily living activities) serves as a transitional state carrying a high risk of progression to dementia, particularly Alzheimer's disease.[2]

From a pathophysiological perspective, brain aging is marked by hippocampal atrophy, loss of functional synapses[3], heightened neuroinflammation, and disrupted activity in key neural networks such as the default-mode[4] and executive-control networks.[5] Concurrently, cerebral perfusion deteriorates, oxidative stress intensifies, and levels of neurotrophic factors, most notably brain-derived neurotrophic factor (BDNF), decline, collectively impairing synaptic plasticity and neurogenesis.[6,7] These changes disproportionately undermine episodic memory, executive functions, and processing speed; domains essential for maintaining functional independence in older adults.[8]

In light of the absence of curative pharmacological options for MCI and dementia, there is an urgent need for noninvasive, affordable interventions that preserve or enhance cognitive health in the elderly. Physical exercise has emerged as a promising neuroprotective strategy, demonstrating benefits across a range of cognitive domains as well as measurable improvements in brain structure and function. Properly executed exercise present a very favorable safety profile, moreover, it uniquely modulates multiple physiological systems at once—from improving cerebral blood flow to dampening inflammation and inducing beneficial epigenetic changes.[9,10]

This narrative review aims to synthesize and critically appraise the most recent (last 5 years) scientific evidence concerning the effects of physical exercise on general and specific cognitive functions in older adults. Details of the exercise intervention modalities most frequently studied (resistance training, cardio and concurrent) are given and the underlying neurological and biomolecular mechanisms elucidated. Finally, we will highlight key methodological limitations and pinpoint gaps in current knowledge to guide future research efforts.

Methods

This narrative review employed an integrative, systematic approach to synthesize clinical and experimental evidence on the effects of physical exercise on cognitive function in older adults. We included randomized controlled trials (RCTs), meta-analyses, systematic reviews, and open-label clinical studies published between January 2020 and May 2025.

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A comprehensive literature search was conducted in PubMed/MEDLINE, Scopus, Web of Science, Google Scholar, Embase, and the Cochrane Library. Search strategies combined controlled descriptors (MeSH) and free-text terms—for example: ("Physical activity" OR "Exercise" OR "Aerobic training" OR "Resistance training" OR "Combined exercise") AND ("Cognition" OR "Cognitive function" OR "Memory" OR "Executive function" OR "Brain plasticity") AND ("Older adults" OR "Aging" OR "Elderly" OR "Mild cognitive impairment" OR "Cognitive decline"). Keywords also included: physical exercise, executive function, episodic memory, neuroplasticity, MCI).

Inclusion criteria encompassed studies published in English or Spanish with full-text availability, enrolling participants aged ≥ 55 years who were cognitively healthy, had mild cognitive impairment (MCI) or were at high risk of developing MCI, implementing an exercise-only intervention (aerobic, resistance, or combined), and assessing at least one cognitive domain (e.g., memory, attention, executive function, global cognition). Trials reporting biomarkers, neuroimaging, or functional outcomes were eligible, as were systematic reviews and meta-analyses with pre-post or between-group evaluations. The 55 years old cutoff criteria was selected as newer evidence suggest that accelerated cognitive decline (and generalized biological decay) can be expected since the middle 50's.[11,12]

Exclusion criteria ruled out studies in pediatric, young-adult, or institutionalized populations; interventions combining exercise and pharmacology without an exercise-only arm; investigations lacking objective cognitive assessments; narrative reports, editorials, protocols, or abstracts without complete data; and studies with unjustified high risk of bias or poor methodological rigor.

Two reviewers independently screened titles, abstracts, and full-text articles, resolving discrepancies by consensus. Data included author, year, country, study design, exercise modality, intervention duration and intensity, participant characteristics, cognitive domains evaluated, and principal outcomes (effect sizes, biomarker changes).

Owing to the review's integrative aim, findings are organized by exercise modality (aerobic, resistance, combined), summarizing cognitive effects alongside implicated biomarkers and molecular pathways (Table 1). Although no new meta-analysis was performed, quantitative results from prior meta-analyses were incorporated to bolster the robustness of our narrative synthesis.

Results and discussion

Table 1. Characteristics of representative studies included in this narrative review.

Authors	Intervention	Intensity / Duration	Frequency	Cognitive Assessment Tools	Main Cognitive Outcomes	Biomarkers
Aghjayan et al. (2022)	Aerobic	Moderate (≥3900 min total)	≥3 times/week	Episodic memory, processing speed	Improved memory and processing speed	↑BDNF, ↑ VEGF, ↑ IGF-1
Yuan et al. (2022)	Dance (aerobic)	Variable	2–4 times/week	MMSE, verbal/visual memory tests	Improved memory and hippocampal volume	Not specified
Gholami et al. (2025)	Resistance training	40–80% 1RM	2–3 times/week	Executive function, working memory	Improved executive function and working memory	↑ BDNF

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Vints et al. (2024)	Resistance training	50–70% 1RM, 12 weeks	3 times/week	Stroop, MoCA	Improved inhibitory control	↑IGF-1, ↓ IL-6
Liu et al. (2025)	Multicomponent	Mixed; 12–24 weeks	≥3 times/week	MMSE, MoCA, memory tasks	Improved global cognition and memory	↑BDNF, ↑ IGF-1
Luo et al. (2024)	Multicomponent	Not specified	Not specified	Global cognition assessments	Cognitive improvement	↑BDNF, ↓inflammation
Thaiyanto et al. (2021)	Multicomponent	Not specified	Not specified	Cognition and fall-risk tests	Improved cognition and reduced fall risk	Not reported
Montero-Odasso et al. (2023)	Exercise + cognitive + Vit D	Not specified	Not specified	Executive function tasks	Improved executive function	Not reported
Noguchi-Shinohara et al. (2025)	Exercise + nutrition	Not specified	Not specified	Memory assessments	Improved memory	↑ IGF-1
Leung et al. (2024)	Combined (aerobic + resistance)	Varied	Not specified	Global cognition tests	Improved cognitive function	↑ BDNF, ↑ IGF-1, ↓inflammation
Zhang et al. (2025)	Dance (multimodal)	Variable	Not specified	Cognition, mobility, balance	Improved cognition and mobility	Not specified
Oberlin et al. (2022)	Various (review)	Various	Various	Multiple cognitive domains	General cognitive benefits reported	Not specified
Wang et al. (2024)	Aerobic / resistance	Not specified	Not specified	N/A	↑TAC, ↓ MDA	Oxidative stress
Paiva-Prudente et al. (2023)	Physical exercise (various)	Not specified	Not specified	Not specified	↑Cerebral blood flow velocity	Not specified

↑ indicates improvement or increase; ↓ indicated decrease. 1 RM indicated 1 Repetition Max, a measure of maximal effort in resistance training; MMSE, Minimal Mental State Examination; MoCA, Montreal Cognitive Assessment; BDNF, Brain-derived neurotrophic factor; VEGF, Vascular Endothelial Growth Factor; IGF-1, Insulin-like Growth Factor 1; IL-6, Interleukin-6; MDA, Malondialdehyde; TAC, Total Antioxidant Capacity.

Types of Exercises and Cognitive Effects

Aerobic Exercise: Recent evidence indicates that aerobic exercise enhances episodic memory and processing speed in older adults. In a meta-analysis of 36 randomized controlled trials (RCTs) involving dementia-free participants aged ≥55 years, Aghjayan et al. (2022) reported a significant effect size (Hedges' $g = 0.28$), with the greatest improvements seen in individuals who accumulated ≥3.900 total intervention minutes of moderate-intensity activity performed at least in three sessions per week during the intervention.[13] Some ludic forms of exercise outside of traditional gym setups are also effective. Several meta-analysis on dance therapy for older adults with MCI, yielded increases in hippocampal volume, episodic memory and overall cognitive performance.[14,15] From a mechanistic perspective, aerobic exercise boosts cerebral blood flow, stimulates neurogenesis, and elevates neurotrophic factors—BDNF, VEGF, and IGF-1—thereby enhancing synaptic plasticity and gray-matter volume in regions

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critical for memory.[2,13] The summary of aerobic training variables, as well as expected outcomes can be found in Figure 1, in the middle section.

Strength/Resistance Training: Resistance training, performed at 40–80% of one-repetition maximum (1RM) two to three times weekly, also improves executive function, attention, and working memory. Gholami et al. (2025) synthesized data from 11 RCTs to show significant increases in circulating BDNF (mean difference 0.73 ng/ml) alongside reductions in depressive symptoms.[6] In another 12-week RCT (three sessions/week at 50–70 % 1RM) targeting adults at high risk for MCI, improvements in inhibitory control correlated positively with IGF-1 and IL-6 levels.[16] A 2025 meta-analysis in *Sports Medicine – Open* concluded that moderate-to-high-intensity resistance training enhances executive and visuospatial functions, accompanied by increases in IGF-1 and prefrontal perfusion.[2] From a structural point of view, resistance exercise preserves white-matter integrity and attenuates brain atrophy with accentuated effects on the hippocampus, effects linked to elevated BDNF, IGF-1, and irisin.[6,17] The summary of resistance training variables, as well as expected outcomes can be found in Figure 1, in the left section.

Combined/Multicomponent Interventions: Protocols combining aerobic, resistance, and balance/flexibility exercises outperform single-modality programs. In a review and meta-analysis of 13 RCTs (n = 1,776), Liu et al. (2025) found a moderate effect on global cognition (standardized mean difference, SMD = 0.31), with largest gains in verbal and visual memory as well as executive function among individuals with MCI.[8] These multicomponent interventions typically involved ≥3 sessions per week over 12–24 weeks, each lasting ≤40 minutes.[8] Luo et al. (2024) confirmed these benefits in frail older adults with cognitive impairment, highlighting the synergy of combining resistance and aerobic training.[18] Furthermore, there is direct evidence supporting strong reductions in frailty and improvements in cognitive measurements for older women.[19] In general, concurrent (multicomponent) exercise protocols appear to be much more effective than isolated approaches.[20] Moreover, dual-task approaches (exercise plus concurrent cognitive challenges) produced additional improvements in executive function and were found effective for delaying onset of MCI and dementia.[21] At the molecular level, multicomponent exercise maximizes elevations in BDNF and IGF-1, promotes neurogenesis, enhances cerebral perfusion, strengthens synaptic plasticity, and reduces inflammatory and oxidative-stress markers.[18] The summary of multicomponent training variables, as well as expected outcomes can be found in Figure 1, in the right section.

Most Benefited Cognitive Areas: Executive functions are consistently enhanced across all exercise modalities.[2] Episodic and working memory also improve following structured aerobic training (≥3.900 total minutes) or combined interventions with nutritional support in individuals with MCI, highlighting the efficacy of exercise intervention.[22] Findings for processing speed and attention are more variable: some studies report no significant change, while others document moderate gains after resistance training.[2] Baseline cognitive status further shapes these outcomes. Cognitively healthy older adults tend to experience broader gains, especially in immediate memory and global cognition, whereas those with MCI derive smaller yet clinically meaningful benefits.[23] Liu et al. (2025) observed comparable improvements in executive function and memory among healthy and MCI groups, noting that resistance and aerobic protocols preserved hippocampal and precuneus integrity and elevated BDNF and irisin even with just two moderate-to-high-intensity sessions per week.[8] In adults with obesity or metabolic syndrome, combined aerobic plus resistance training increases IGF-1 and BDNF, enhances cerebral perfusion, and reduces inflammation—mechanisms linked to cognitive improvement.[24] A summary of cognitive outcomes expected for each case can be found in Figure 1.

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Neurobiological and Molecular Mechanisms

The cognitive benefits of physical exercise in older adults arise from a coordinated interplay among neurotrophic, vascular, anti-inflammatory, antioxidant, and synaptic-plasticity processes.

Neurotrophic Factors: Brain-derived neurotrophic factor (BDNF) has been extensively investigated in aging populations. Aerobic, resistance, and combined exercise programs consistently elevate plasma BDNF levels, as confirmed by a recent meta-analysis showing increases regardless of training modality, detectable both peripherally and centrally.[6] Moreover, long-term interventions (>6 months) elicit BDNF rises that correlate with hippocampal volumetric gains, supporting the hypothesis that exercise-induced BDNF promotes hippocampal neurogenesis and neuronal survival.[6,7]

Vascular Adaptations: Improved cerebral perfusion is another key mechanism. In a 12-month RCT of moderate-to-vigorous aerobic exercise, global cerebral blood flow increased and arterial stiffness decreased, measured in both the middle cerebral artery and carotid arteries.[9,25] Enhanced hippocampal perfusion subsequently optimizes oxygen and glucose delivery, which is associated with better memory and learning outcomes.[9,25]

Anti-inflammatory and Antioxidant Effects: Exercise also downregulates proinflammatory and oxidative-stress markers. A systematic review found that regular training in older adults reduces circulating IL-6, TNF-α, and C-reactive protein.[10] Complementary meta-analytic data demonstrate increases in total antioxidant capacity alongside reductions in malondialdehyde (MDA), a marker of lipid peroxidation.[26] Together, these changes mitigate inflammation- and oxidation-driven synaptic dysfunction.

Myokines and Intracellular Signaling: At a finer molecular level, combined exercise protocols augment muscle-derived factors such as irisin and IGF-1.[27] These "exerkines" activate TrkB, PI3K/Akt, and MAPK/ERK pathways, fostering synaptic plasticity and the formation of new synapses.[6,7] Exercise also induces epigenetic modifications (demethylation of BDNF and vascular endothelial growth factor (VEGF-A)[28] promoters and downregulation of repressive enzymes like DNA-methyltransferases (DNMTs)[29] and histone deacetylases (HDACs)[30], thereby facilitating transcription of neuroplasticity-related genes.[7]

Functional Network Reorganization: Functional neuroimaging studies reveal exercise-induced network remodeling. In an fMRI RCT, 6–12 weeks of training increased connectivity within the default-mode network (DMN), the salience network, and between these networks and the executive-control network—changes that correlated with cognitive improvements.[5] This reorganization, together with elevated BDNF and IGF-1, confirms activation of neuroplastic pathways and optimization of frontoparietal–hippocampal circuits.[2,5]

In summary, exercise promotes cognition in older adults through a multifaceted neurobiological framework: upregulation of neurotrophic factors and "exerkines", enhanced cerebral vascular health, reduced inflammation and oxidative stress, and functional reconfiguration of brain networks via synaptic plasticity and epigenetic remodeling. This integrated understanding provides a robust foundation for designing clinical exercise interventions aimed at preserving cognitive function during aging.

Limitations of Current Evidence and Perspectives for Future Research

Although recent studies confirm the potential of physical exercise to beneficially modulate cognition in older adults, the body of evidence still faces several limitations that impede uniform interpretation and systematic clinical application. One major weakness is the high methodological heterogeneity across trials—in exercise modality, intensity, frequency, and duration, as well as in the choice of cognitive assessment tools—making it difficult to establish precise dose–response relationships for specific populations.[2,8]

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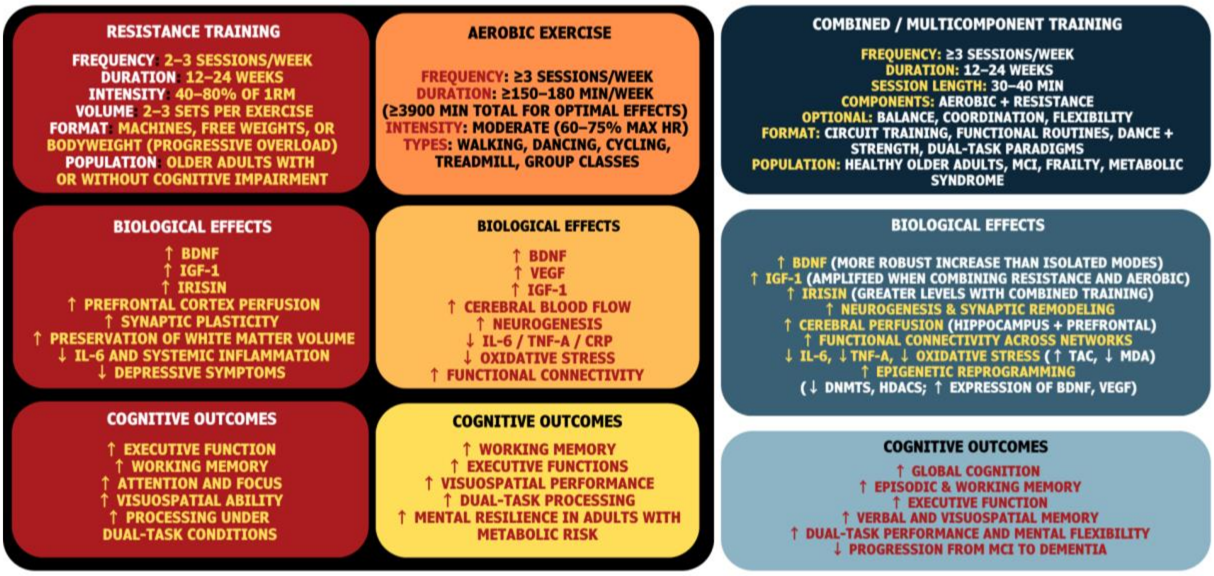
Moreover, there is a paucity of long-term randomized controlled trials: most interventions last only 8–24 weeks. This restricts our understanding of the durability of cognitive gains over time and the role of exercise in preventing conversion from MCI to dementia. Likewise, few studies concurrently evaluate clinical, cognitive, molecular, and structural outcomes, which prevents drawing robust causal links between exercise-induced biological mechanisms and observed cognitive changes.[6,10]

Regarding participant characteristics, older adults with common comorbidities (diabetes, obesity, or cardiovascular disease) are underrepresented, despite the fact that these conditions influence both cognitive function and exercise responsiveness. Additionally, the majority of trials focus on cognitively healthy seniors or those with MCI, leaving a knowledge gap about the effectiveness of exercise in more advanced stages of cognitive decline and dementia.

Figure 1. Training the aging brain. Illustrating how exercise rewires cognition, while summarizing the main results of this narrative review.



↑ indicates improvement or increase, ↓ indicated decrease. 1 RM indicated 1 Repetition Max, a measure of maximal effort in resistance training; BDNF, Brain-derived neurotrophic factor; VEGF, Vascular Endothelial Growth Factor; IGF-1, Insulin-like Growth Factor 1; IL-6, Interleukin-6; TNF-A, Tumor Necrosis Factor Alpha. CRP, C-Reactive Protein; DNMTS, DNA Methyltransferases; HDACS, Histone Deacetylases; MDA, Malondialdehyde; MCI, Mild Cognitive Impairment.

Future Directions

To keep exploring the promising potential of different exercise protocols, as well as to better understand the key variables related to the responses in cognitive capacity, the following aspects are understood as critical for future studies.

- *Standardized multicenter trials:* Develop large-scale RCTs using harmonized, well-defined exercise protocols that integrate physiological, neuropsychological, and functional-neuroimaging measures.
- *Personalized exercise prescriptions:* Tailor interventions by accounting for age, baseline cognitive status, polypharmacy, nutritional condition, and habitual activity levels.
- *Multidisciplinary approaches:* Combine physical exercise with cognitive training, nutritional support, or psychosocial interventions to amplify and broaden cognitive benefits, ultimately fostering more comprehensive strategies for healthy aging.

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- *Meta-analysis and systematic reviews:* Should focus on improving the understanding of specific neurologic outcomes, as well as covering specific subgroups of the elderly population.

Conclusions

Over the past decade, a robust and growing body of evidence has demonstrated that physical exercise is both an effective and safe intervention for preserving and enhancing cognitive function in older adults. From a biomolecular and mechanistic perspective, these cognitive gains rest on a complex neurobiological framework: from reductions in inflammatory and oxidative-stress markers to improved brain perfusion. Despite these promising findings, significant methodological gaps remain; gaps that need to be filled consequently to achieve better understanding and individualization potential of exercise for MCI. Taken together, concurrent exercise emerges as an accessible, cost-effective strategy for promoting healthy cognitive aging, with the potential to yield substantial public-health benefits worldwide in the coming decades.

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Affiliations
[1] Departamento de I+D+i, CatchPredict SpA, Avenida Ramón Picarte 780, Valdivia 5090000, Chile.
[2] Departamento de Investigación y Desarrollo, Good Research and Science (GRS), Avenida Ramón Picarte 780, Valdivia 5090000, Chile.
[3] Departamento de Ciencias Químicas, Facultad de Ciencias Exactas, Universidad Andrés Bello, Avenida Republica 275, Santiago 8370146, Chile.
[4] Facultad de Ciencias de la Salud, Escuela de Nutrición y Dietética, Universidad del Desarrollo, Ainavillo 456, Concepción 4070001, Chile.

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