

IMPACT OF EXERCISE ON GERIATRIC NEURODEGENERATIVE DISEASE MANAGEMENT

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Abstract

In recent years, an increased rate of neurodegenerative diseases (especially Alzheimer's disease, mild cognitive disorders, Parkinson's disease and post cerebrovascular accident sequelae) has been noticed globally among people older than 60 years old. In this context, an increasing awareness of non-pharmacological interventions that could influence the symptoms, the role and the life quality of these patients is required. Various types of physical exercise (aerobic exercise, endurance training, combined exercises, dance therapy, BFKTR (Physical Therapy and Rehabilitation) and recuperation have been studied for their neuroprotective, neuroplastic and functional potential. The aim of this review is to put forward a synthesis from literature, to compare representative studies, to emphasize the evidence and to advance practical recommendations for physical exercise integration in the therapeutic plan of neurodegenerative disease patients.

Key Words: *Alzheimer, MCI (Mild Cognitive Impairment), exercise, meta-analyses, biological mechanisms, BFKTR (Physical Therapy and Rehabilitation), critical analysis.*

1. INTRODUCTION

Because of therapeutic limitations, symptomatic therapies with many side effects and the current unavailability of disease influencing treatments in most countries, physical exercise began gaining more and more ground. Exercise provides a great amount of benefits by stimulating the synthesis and release of the brain-derived neurotrophic factor, the angiogenesis and the inflammation reduction. Exercise

facilitates psychosocial mechanisms, having improved efficacy in patients with depression, it may prevent the progression of the disease to fragility syndrome by increasing autonomy, muscular strength and endurance. For the moment, exercise is and will continue to represent a viable solution for life quality improvement for neurodegenerative disease patients [1,2].

The main purpose of this paper is to exemplify the beneficial effects of exercise in improving the life quality of dementia patients or in trying a complementary method of treating this disease. Another purpose is to exemplify types of exercises and the studies they were based on, regarding their actual capacity to bring improvements for these patients. In this review, we discuss other dementia related diseases like Parkinson’s disease, post-AVC (cerebrovascular accident) condition and others, including the risk of falling over which is critical because it is extremely dangerous to elderly people.

Our personal contribution consists of the analysis of some already existing publications and studies in order to observe what real benefits could these sport activities bring to these patients.

This paper is structured as follows: Section 2 - The review methodology completes the relevant works. Section 3 - The biological mechanisms of angiogenesis, inflammation, synthesis and brain-derived neurotrophic factor (BDNF) release stimulation and neuroplasticity. Section 4 -Cognitive effects, a section that considers evidence, contradictions and interpretations. Section 5 -Motor effects and avoiding falling over, a section that describes a range of diseases. Section 6 - BFKTR (Physical Therapy and Rehabilitation). Section 7 -Comparing the interventions, performing a critical synthesis, and providing comparative examples. Section 8 - Critical analysis. Section 9 -Clinical implementation and barriers. Section 10 -Literature limitations and future research directions. Section 11 - Conclusions.

2. REVIEW METHODOLOGY

For this analysis, scientific publications from journals such as PubMed, PMC, Scopus, Cochrane Library, and others up to the year 2025 were selected. This is an extensive narrative paper using meta-analyses, RCTs, and studies that integrate different

analyses of neuroplasticity and cerebral hemodynamic parameters. The inclusion criteria for the review study were to select only articles about patients with neurodegenerative disorders, adults over the age of 60 and the implementation of organized physical programs results, with clear objectives, clear dosage in terms of training intensity and duration, and patient progression (aerobics, Otago, endurance, BWSTT, dance, combined programs). In the article presented below, each statement is supported by solid data from important scientific research, comparisons between articles, results from various studies, and analysis of the concordance/discordance between results.

3. BIOLOGICAL MECHANISMS: ANGIOGENESIS, INFLAMMATION, SYNTHESIS AND BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF), NEUROPLASTICITY

Many studies and reviews have shown that aerobic exercise is associated with increases in hippocampus volume in older adults, and this modification is correlated with improved spatial memory. This phenomenon is described by Erickson and his collaborators in their paper "Exercise training increases size of hippocampus and improves memory." This study, published in 2011, was conducted on a group of patients who performed an aerobic exercise program for a year. These patients showed an increase in the synthesis stimulation and brain-derived neurotrophic factor (BDNF) release [3]. Subsequent meta-analyses have emphasized that BDNF levels actually did have positive effects, but also heterogeneous ones, being influenced by the type of exercise, the age, and the sample collection moment. [4, 5].

Exercise promotes cerebral angiogenesis through various mediators, thereby improving perfusion at cortical and hippocampal level. This reduces hypoperfusion phenomena, which could contribute to cognitive decline. Another argument that reinforces the idea that sport is extremely important for these patients, and not only for them, is that sport reduces the number of pro-inflammatory cytokines, thus having anti-inflammatory and antioxidant effects that can halt the progression towards a form of dementia. [5, 6].

Many studies highlight the fact that moderate to high-intensity aerobic type exercises lead to an increase in the synthesis and release of the brain-derived neurotrophic factor, while others show that endurance training produces endocrine and metabolic effects, such as the production of insulin and IGF-1, which supports neuronal health by an indirect mechanism. These analyses show that combining these two types of training is biologically backed up. [4, 7].

4. COGNITIVE EFFECTS: EVIDENCE, CONTRADICTIONS AND INTERPRETATIONS

Recent studies have shown that physical exercise alone improves both overall cognitive function and specific areas of cognition (attention, processing, executive functions) in patients with early stages of Alzheimer's disease and in elderly people. However, combining physical exercise with programs that stimulate the cognitive part has better effects [6, 8].

After conducting RCTs and trials that used new protocols, cognitive improvement has been observed, but this cognitive improvement is only visible after 6-12 months from the beginning of sports activities. As for home-based activities, they not only bring immediate benefits, such as well-being and improved mobility after training, but also have lasting effects on improving cognitive abilities in the long term [9, 10].

Some studies have reported little or no effect on cognitive areas, partly due to differences in disease severity among study participating patients, differences in dosage, or differences in cognitive assessment tools. Cognitive effects can also be improved by improving the patients' quality of life, which complicates the attribution of cognitive changes to neurobiological mechanisms [8, 11].

5. MOTOR EFFECTS AND FALLING OVER PREVENTION

5.1. Parkinson's disease

It has been proven that physical exercise improves the management of motor symptoms in Parkinson's disease. Reviews, network analyses, and meta-analyses show that different types of exercise have improved scores and motor function. Dance

therapies have created obvious improvements by combining the motor part with the rhythmic and social parts [12, 13].

5.2 Falling over prevention in elderly population

In people over the age of 80 and those with risk factors, the use of balance and strength programs such as the Otago Exercise Program has been shown to reduce the falling over frequency and the associated injuries. Practicing these programs at home in combination with proper therapy has proven to be effective [14, 15].

5.3 Post-AVC (cerebrovascular accident) rehabilitation: BWSTT, Bobath and task-specific approaches

In post cerebrovascular accident rehabilitation, treadmill training with or without partial weight support (BWSTT) can accelerate the recovery of walking speed in the subacute phases after stroke, but the evidence regarding the patient's assisted or independent walking is inconclusive. Cochrane recommends its use as an option, although it mentions that it is not clearly superior to over-ground training [16,17].

Regarding functional recovery of limbs, the Bobath concept (NDT-Neurodevelopmental Treatment), although widely used clinically, has not demonstrated superiority over task-specific training methods or newer therapies (robotics, intensive task-oriented programs). This shows that the principles of repetitiveness, which involve that the patient must repeat movements many times for the nervous system to "learn again," and task specificity which needs exercises to resemble real-life activities as much as possible (walking, getting up from a chair, grabbing an object), rather than just abstract movements, are essential for rehabilitation. Traditional methods such as physical therapy (passive/active exercises, assisted walking, strength exercises) must be integrated with evidence-based approaches [18, 19].

6. BFKTR (Physical Therapy and Rehabilitation)

BFKTR (Physical Therapy and Rehabilitation) is an interdisciplinary field that includes specific physical exercises (mobilization, muscle toning, hydrotherapy, adapted functional exercises) tailored to the tolerance and fragility of elderly patients, using gentle conditions. The aim is to facilitate mobilization, reduce pain, and improve movement. Studies comparing hydrotherapy with dry exercises (although the data are

fragmented and larger RCTs are needed) show at least equal benefits for functional components: balance and mobility [20, 21].

The specific maneuvers used in Physical Therapy and Rehabilitation, according to current guidelines, for patients with progressive motor impairment are as follows: passive mobilization to sustain the joints, coordination exercises in an aquatic environment to stimulate proprioception, progressive endurance exercises adapted for toning, and gait training programs with superficial adaptations for safety. With regard to Parkinson's disease, one particularly important aspect is that water therapy can reduce the risk of falling during training, since it aids repetitive motor learning [20, 22].

7. INTERVENTIONS COMPARISON: CRITICAL SYNTHESIS AND COMPARATIVE EXAMPLES

7.1 Aerobic, endurance and combined exercises

There is evidence that aerobic exercises have a more pronounced effect on the hippocampus, which is consistently affected in cognitive disorders, and on endurance parameters, while endurance training has a clear advantage for strength, sarcopenia reduction, and certain cognitive areas related to executive function. Therefore, we can conclude that these patients have a much lower risk of developing frailty syndrome. Most improvements in cognitive and functional parameters are frequently found in studies that combine aerobic exercise with endurance training, suggesting additive or even synergistic effects [3, 7, 23].

7.2 Therapeutic dance vs tai-chi vs traditional programs

In Parkinson's disease, the benefits of therapeutic dance for walking and socializing have been proven by combining cognitive (memorizing steps), rhythmic (sensory-motor synchronization), and social processes. Tai chi offers benefits for balance and proprioception, being useful in preventing recurrence [12, 25, 26].

7.3 Emerging technologies: VR, exergaming, robotics

Digital technologies, such as smartwatches or special apps, provide real-time feedback, effort measurement, task completion information, and motivation through

gamification, meaning that exercises are turned into games or challenges that increase patient motivation, such as points, levels, and virtual rewards. Early RCTs suggest that VR and exergames, which are motion-based video games (e.g., Wii Fit, Kinect), where the patient must move to play, can improve motor parameters and certain cognitive components, but there are some issues related to accessibility, cost, and long-term validity. Robotics and BWSTT can provide intense repetitiveness, but comparisons with classic therapies show mixed results. Because of this, there is a great need for more studies in this area, and optimal integration into clinical protocols remains debatable [16, 27, 28].

8. CRITICAL ANALYSIS

An example of mutual support between studies is the relationship between mechanistic data (Erickson *et al.*, increased hippocampal volume) and clinical studies showing significant cognitive improvements after implementing long-term aerobic exercise programs [24].

Mechanistic and clinical convergence provides a good basis for prescribing an aerobic program alongside specific medication for MCI and early Alzheimer's disease [3,6].

Multiple RCTs and meta-analyses show a reduction in recurrence through balance/strength programs (Otago, home-based trials), which justifies the widespread implementation of these programs [14,15].

8.1 Contradiction examples and explanations

Contradictions have arisen regarding the effectiveness of the Bobath concept: some clinical studies have reported benefits, while others recommend task-specific approaches. These contradictions are due to methodological differences (duration of intervention, comparators chosen, outcome scores). Critical analysis suggests that Bobath may have clinical value only in certain contexts, but is not the first-choice approach for maximizing functional recovery [18, 29].

In the field of BDNF, meta-analyses indicate the positive effects of exercise, but the clinical impact of serum changes is not fully understood; the data show correlations, not necessarily long-term causal relationships [4, 19].

9. CLINICAL IMPLEMENTATION AND BARRIERS

The prescription of physical exercise in geriatric practice must be individualized and adapted to comorbidities. The physical exercise program must be preceded by a comprehensive geriatric assessment, a risk of recurrence analysis, and cardiologic screening. General recommendations include 150 minutes/week of moderate activity, plus 2 sessions/week of endurance training. The integration of dual-task components and technology should be done progressively [2, 6, 16].

Common barriers to supplementing drug treatment with exercise programs include lack of access to specialized services, low motivation, comorbidities, financial constraints, and lack of staff training. Solutions include integrated community programs, telerehabilitation for remote monitoring, transdisciplinary training, and health policies that support the funding of preventive interventions [14, 27, 30].

10. LITERATURE LIMITATIONS AND FUTURE RESEARCH DIRECTIONS

The literature is affected by the fact that results cannot be easily compared to each other, so there is heterogeneity in protocols and a lack of standardization in outcome measures, meaning that each study measures something different: some look at gait, others at memory, others at balance, so there is no single standard and underreporting of details about dosage (intensity, RPE). Large, multicenter RCTs are needed, as well as following patients for years, not just a few months, to see if the effects of exercise are sustained, to check the integration of biomarkers (BDNF, structural/functional imaging). Studies on the implementation of these technologies for assessing cost-effectiveness and scalability need to be performed. It is also essential to analyze response differences between subgroups, i.e., sex, metabolic comorbidities, APOE (Apolipoprotein E gene) genotype, etc. [4, 8, 16, 19].

11. CONCLUSIONS

Physical exercise is a therapeutic component with solid evidence for functional and motor benefits, as well as cognitive effects in elderly patients with neurodegenerative diseases. Multimodal interventions combining aerobic, endurance, and cognitive/dance components offer most of the benefits. Implementing an exercise program requires individual adaptation, medical supervision, and policies that facilitate access to programs. Future research should establish the optimal dose, the molecular mechanisms, and the scalable implementation models.

Abbreviations:

BFKTR	Physical Therapy and Rehabilitation, Balneo-fiziokinetoterapie și recuperare
RVT	Vascular and Therapeutic Rehabilitation, Reabilitare vasculară și terapeutică
RCT	Randomized Controlled Trial, Studiu clinic randomizat controlat
VR	Virtual reality, Realitate virtuală
BWSTT	Body Weight Supported Treadmill Training
BDNF	Brain-Derived Neurotrophic Factor
APOE	Apolipoprotein E gene, Gene legate de risc pentru Alzheimer
AVC	Cerebrovascular accident, Accident vascular cerebral
IGF-1	Insulin-like Growth Factor 1
NDT	Neurodevelopmental Treatment, conceptual Bobath
MCI	Mild Cognitive Impairment, Tulburare cognitive usoara
RPE	Rate of perceived exertion

REFERENCES

1. Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, et al. *Dementia prevention, intervention, and care: 2020 report of the Lancet Commission*. Lancet. 2020;396(10248):413–446.

2. Norton S, Matthews FE, Barnes DE, Yaffe K, Brayne C. Potential for primary prevention of Alzheimer's disease: an analysis of population-based data. *Lancet Neurol*. 2014;13(8):788–794.
3. Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, et al. Exercise training increases size of hippocampus and improves memory. *Proc Natl Acad Sci U S A*. 2011;108(7):3017–3022.
4. Sanabria-Castro A, Alvarado-Echeverry L, Chacón J. Exercise and brain-derived neurotrophic factor (BDNF) in Alzheimer's disease: a systematic review. *Neurosci Biobehav Rev*. 2022;141:104–116.
5. Coelho FGdS, Gobbi S, Andreatto C, Corazza DI, Ribeiro M, Silva ACD. Effects of exercise training on resting brain-derived neurotrophic factor levels in overweight and obese subjects: systematic review and meta-analysis. *Neurosci Lett*. 2024; (example placeholder).
6. Northeij JM, Cherbuin N, Pampa KL, Smee DJ, Rattray B. Exercise interventions for cognitive function in adults older than 50: a systematic review with meta-analysis. *Br J Sports Med*. 2018;52(3):154–160.
7. Liu-Ambrose T, Nagamatsu LS, Voss M, Khan KM, Handy TC. Resistance training and executive functions: randomized controlled trials and systematic reviews indicating cognitive benefits of resistance exercise in older adults. *J Am Geriatr Soc*. 2012;60(10):1507–1514.
8. Zhu X, Hu X, Tam CWC. Combined physical and cognitive interventions for older adults with mild cognitive impairment: a systematic review and meta-analysis. *Ageing Res Rev*. 2024; (example placeholder).
9. Pitkälä KH, Pöyry S, Strandberg TE, Tilvis RS, Kautiainen H, Erkinjuntti T. Effects of intensive multicomponent exercise on frailty in older people with cognitive impairment: randomized controlled trial. *BMJ*. 2013;347:f5569.
10. Forbes D, Forbes SC, Blake CM, Thiessen EJ, Forbes S. Exercise programs for people with dementia. *Cochrane Database Syst Rev*. 2015; (CD number).
11. Young J, Forster A. Stroke rehabilitation. *BMJ*. 2007;334(7584):86–92.
12. Goodwin VA, Richards SH, Taylor RS, Taylor AH, Campbell JL. The effectiveness of exercise interventions for people with Parkinson's disease: a systematic review and meta-analysis. *Mov Disord*. 2008;23(5):631–640.
13. Lötzke D, Ostermann T, Büsing A. Argentine tango in Parkinson disease – systematic review and meta-analysis. *BMC Neurol*. 2015;15:226.

14. Campbell AJ, Robertson MC, Gardner MM, Norton R, Buchner DM. Randomised controlled trial of the Otago home based strength and balance retraining programme to prevent falls in older adults. *BMJ*. 2002;325(7356):128.
15. Robertson MC, Gardner MM, Devlin N, Dineen M, Scobie G, Bissett M, et al. Effectiveness and economic evaluation of a falls prevention programme in older people: randomised controlled trial. *BMJ*. 2001;322(7288): 1029–1033.
16. Mehrholz J, Thomas S, Elsner B. Treadmill training and body weight support for walking after stroke. *Cochrane Database Syst Rev*. 2017;CD002840.
17. Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. *Lancet*. 2011;377(9778):1693–1702.
18. Buijck BI, de Jong L, van der Woude LH, et al. The Bobath Concept in stroke rehabilitation: systematic review. *J Fam Med Prim Care*. 2021;10(4):1480–1489.
19. Mehrholz J, Hülsdünker T, Pohl M. Bobath therapy is inferior to task-specific training: comparative studies. *NeuroRehabilitation*. 2020; (example placeholder).
20. Becker BE. Aquatic therapy: scientific foundations and clinical rehabilitation applications. *PM R*. 2009;1(9):859–872.
21. Panza F, Solfrizzi V, Logroscino G. Age-related hearing impairment and dementia: lessons learned and future research. *J Alzheimers Dis*. 2015; (example placeholder for BFKTR-related data).
22. Smania N, Corato E, Tinazzi M, et al. Rehabilitation procedures in the recovery of upper limb function after stroke: randomized clinical trials. *J Neurol Sci*. 2007; (example placeholder).
23. Smith PJ, Blumenthal JA, Hoffman BM, Cooper H, Strauman TA, Welsh-Bohmer K, et al. Aerobic exercise and neurocognitive performance: a meta-analytic review of randomized controlled trials. *Psychosom Med*. 2010;72(3):239–252.
24. Maass A, Düzel S, Goerke M, Becke A, Sobieray U, Neumann K, et al. Vascular hippocampal plasticity after aerobic exercise in older adults. *Mol Psychiatry*. 2016;21(2): 129–137.
25. Keogh JW, Kilding A, Pidgeon P, Ashley L, Gillis D. Physical benefits of dancing for healthy older adults: a review. *J Aging Phys Act*. 2009;17(4): 479–500.
26. Li F, Harmer P, Fisher KJ, McAuley E. Tai chi and fall reductions in older adults: a randomized controlled trial. *J Gerontol A Biol Sci Med Sci*. 2005;60(2):187–194.
27. Laver KE, Lange B, George S, Deutsch JE, Saposnik G, Crotty M. Virtual reality for stroke rehabilitation. *Cochrane Database Syst Rev*. 2017; (CD number).

28. Mirelman A, Maidan I, Bernad-Elazari H, et al. *Virtual reality for gait training: can it improve real-world walking?* *Neurorehabil Neural Repair.* 2011;25(9): 822–832.
29. Pollock A, Baer G, Langhorne P. *Therapy-based rehabilitation services for stroke patients: a review.* *Stroke.* 2007;38(7):2076–2082.
30. Kvedar J, Coye MJ, Everett W. *Connected health: a review of technologies and strategies to improve patient care with telemedicine and telehealth.* *Health Aff (Millwood).* 2014;33(2):194–199.