

1 - The Project Fitness for Alzheimer (Fit4Alz)

The Fit4Alz project, coordinated by Instituto Politécnico de Viana do Castelo in Portugal (IPVC), lasted from march 2023 to June 2025. Considered as a multidisciplinary initiative, this project aimed to developing tools and guidelines for physical exercise practice in people with cognitive decline, such as Alzheimer's patients. The project combines physical and cognitive exercises to delay the symptoms of the disease.



Figure 1. School of Sports and Leisure of the Polytechnic Institute of Viana do Castelo (ESDL-IPVC)

This project was funded by the European Union with €400,000 and is composed of a consortium of 8 institutions (public and private) from 5 different countries. Involves Alzheimer's specialists, sports scientists, and neuroscientists, and aims to determine the impact of different physical training programs on the symptoms of the disease. In addition, a software was developed with engaging games, used as a complement to the training programs, as this software has been shown to have a better impact on cognitive development.

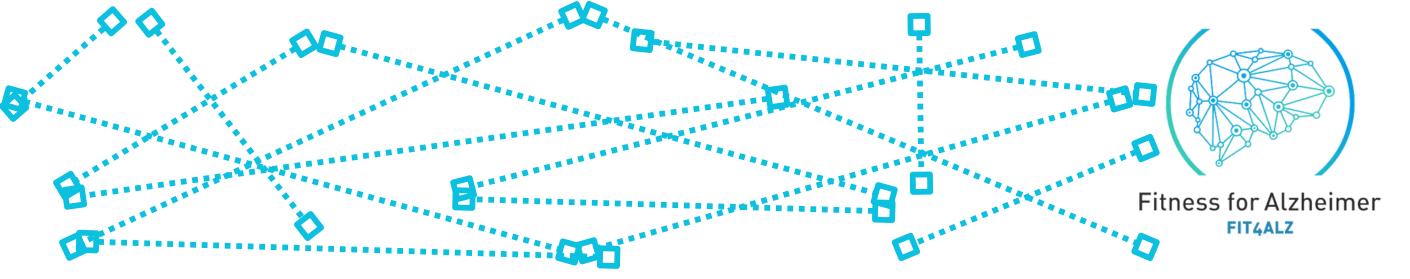
The study participants were elderly individuals with cognitive impairment, divided into four training/intervention groups: i) aerobic; ii) strength; iii) aerobic and cognitive; and iv) strength and cognitive. The results form the basis of this e-book, which serve as guidelines of intervention for elderly with cognitive decline. The project also includes disseminating the guidelines through professional training and publications



Specific objectives:

- 1. Develop new and valid software for cognitive training.
- 2. Analyze the impact of different training programs on individuals predisposed to AD.
- 3. Create guidelines and informative videos.
- 4. Conduct training to promote these guidelines.

The project could have a significant impact on preventing and improving the quality of life of Alzheimer's Disease patients and/or delaying symptoms, considering that there is no known cure for the disease.

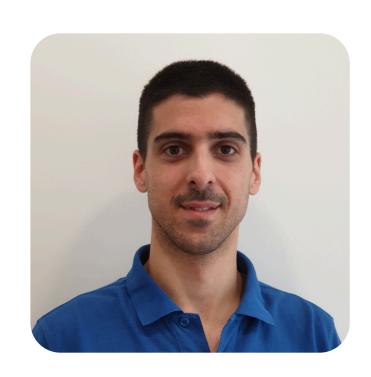






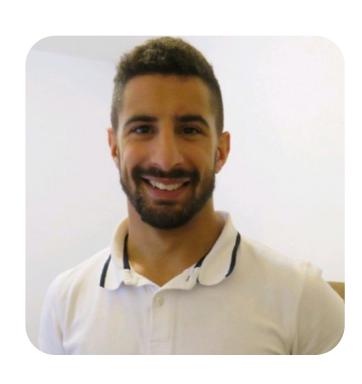
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She has a PhD in Sports Sciences and work as Assistant Professor in the School of Sports and Leisure in Melgaço, Portugal (ESDL-IPVC). Also, she is an integrated Researcher at CIDESD (Research Center in Sports Sciences, Health Sciences and Human Development).



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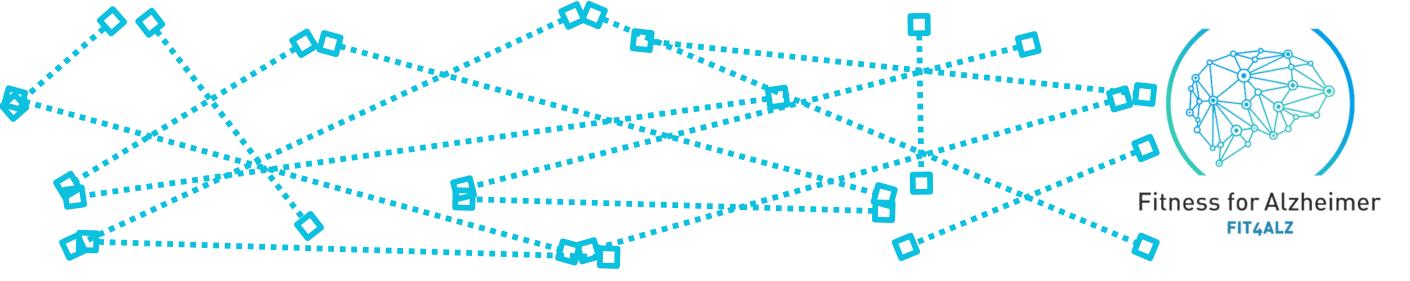
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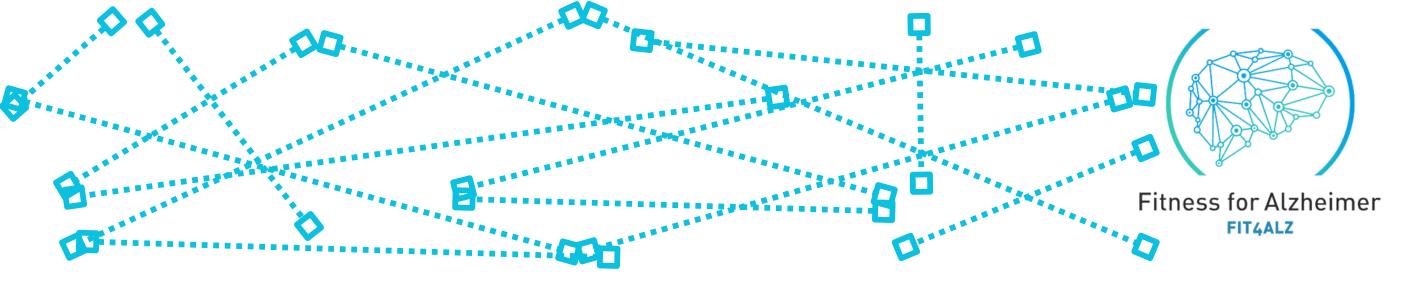
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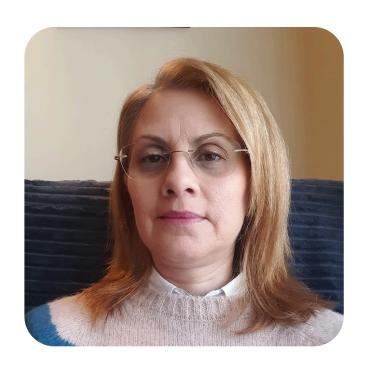


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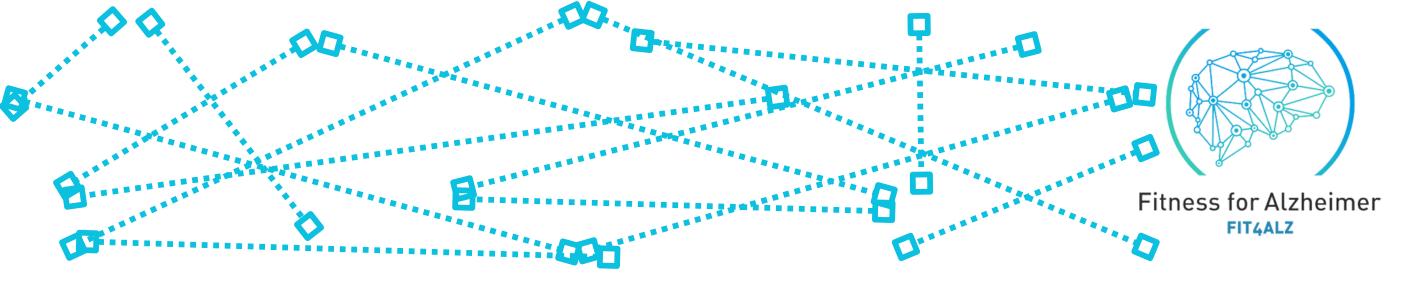
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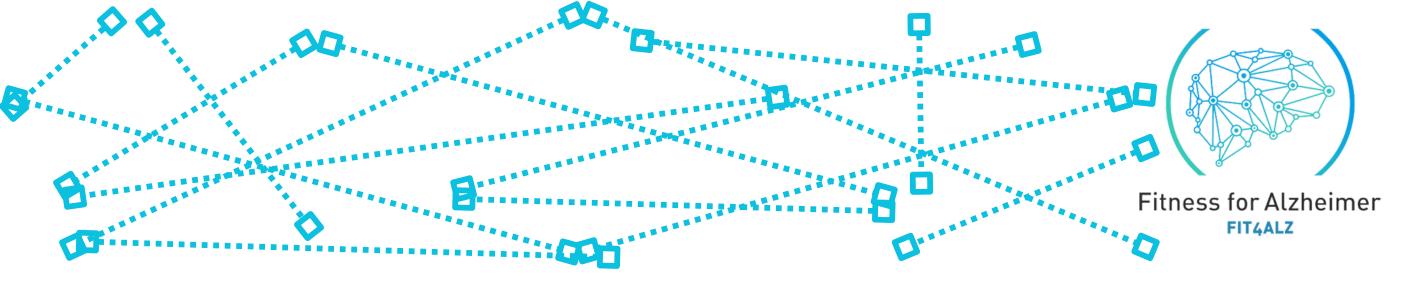
She holds a Master's degree in Clinical and Health Psychology and is responsible for the Northern Delegation of Alzheimer Portugal, where she works as a Clinical Psychologist. Additionally, she is in charge of the Caregiver Support Group, coordinates the Memo and Kelembra activities in schools, serves as a Trainer, and is the Coordinator of Café Memória Porto.



Marta Silva - Researcher

She is an Exercise Physiology and Health Promotion master student, at the School of Sport and Leisure of Melgaço of the Polytechnic Institute of Viana do Castelo. She has experience teaching Fitness classes, swimming lessons, personalized training, and she was also Physical Education teacher.









José Carvalho - Medical Assistant and Adviser

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The research team



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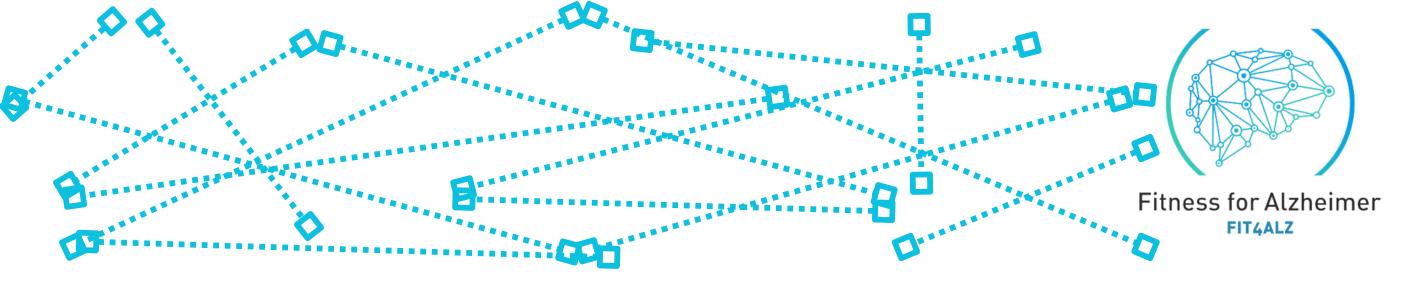
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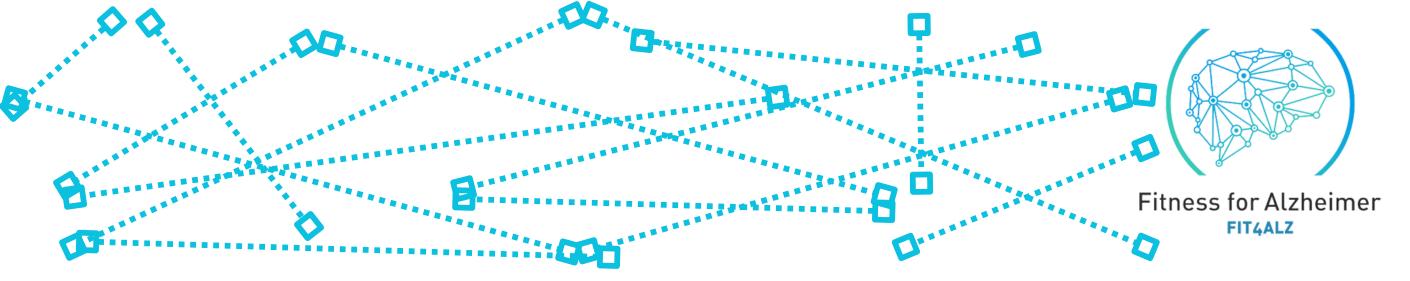
The research team





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The research team

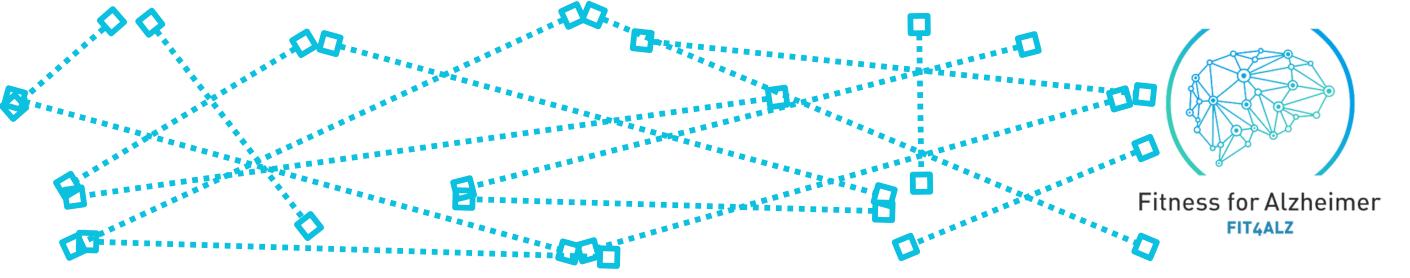




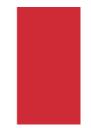


Spartaco Grieco - Project Manager

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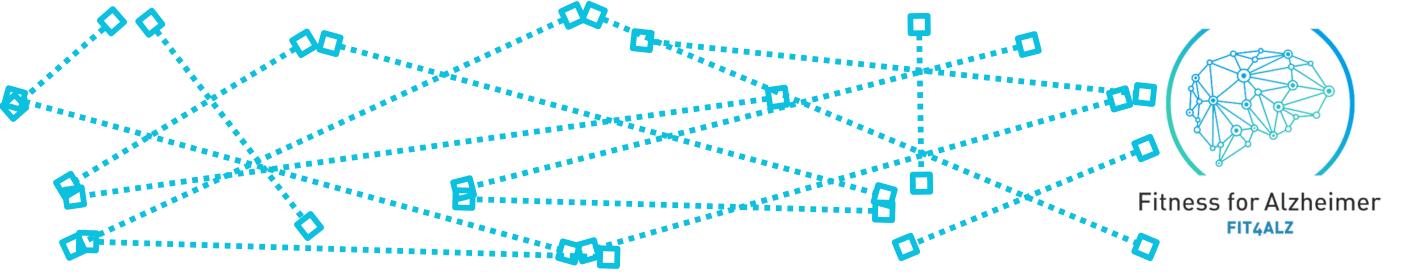
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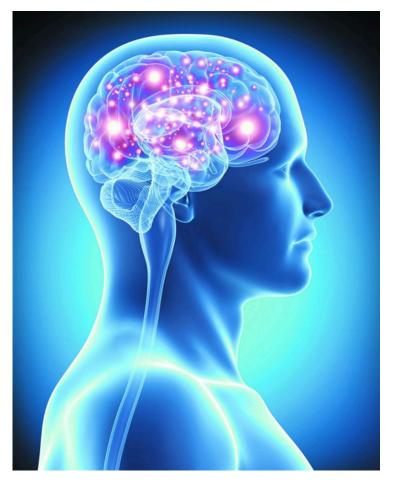
Tara Pavic- Researcher and Teacher

Expert Sport Trainer and Researcher in MSV and former professional athlete in synchronized swimming for Croatian National Team

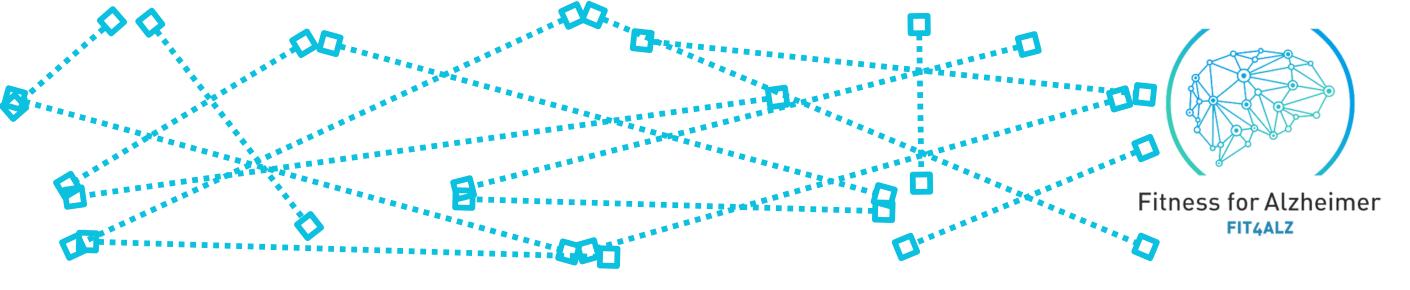




Alzheimer's disease (AD) is a progressive disorder characterized by the gradual deterioration of cognitive functions, such as memory, and executive functions [1]. Consequently, the ability to maintain sustained attention, verbal reasoning, solving problems, and do more than one task at a time significantly decreases [1]. This disease typically begins with some memory loss and confusion and increases to severe symptoms, such as disorientation, language problems, and the inability to perform the normal daily tasks [2]. Currently, there is no cure for Alzheimer's disease, and the available treatments focus on slowing the disease progression [3]. One of the strategies to slow the Alzheimer's disease progression is using cognitive training games to improve cognitive functions [4]. Although it was previously shown that such cognitive games can be effective in improving the cognitive function of the elderly without cognitive impairments [5], the same cannot be said about people with cognitive impairments [6].



AD is characterized by a progression from preclinical stages, where individuals exhibit no objective cognitive impairment, to mild cognitive impairment (MCI) and eventually dementia, marked by significant cognitive deficits and functional impairment [7,8]. Research frameworks, such as those proposed by the International Working Group (IWG) and the National Institute on Aging-Alzheimer's Association (NIA-AA), have delineated AD based on the presence of biomarkers such as the amyloid-beta, alongside clinical symptoms [9]. The NIA-AA's 2018 criteria further categorize AD into stages reflecting increasing severity [9].

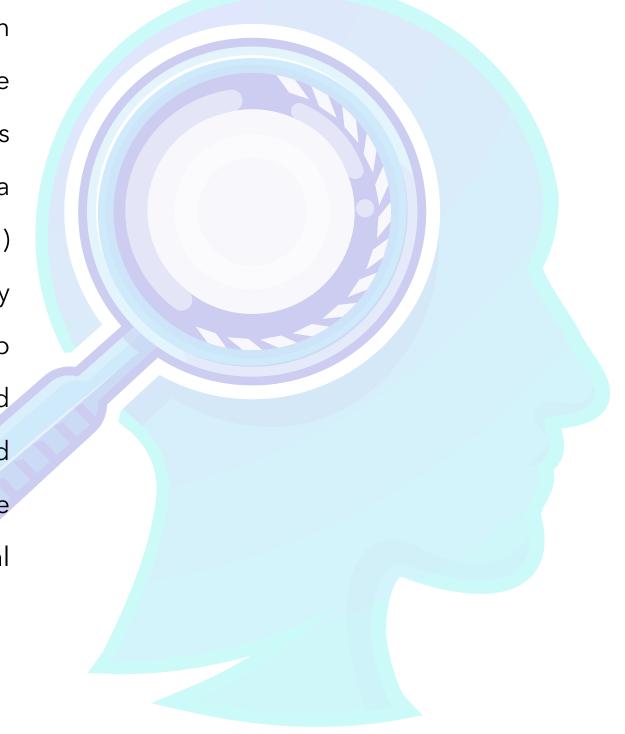


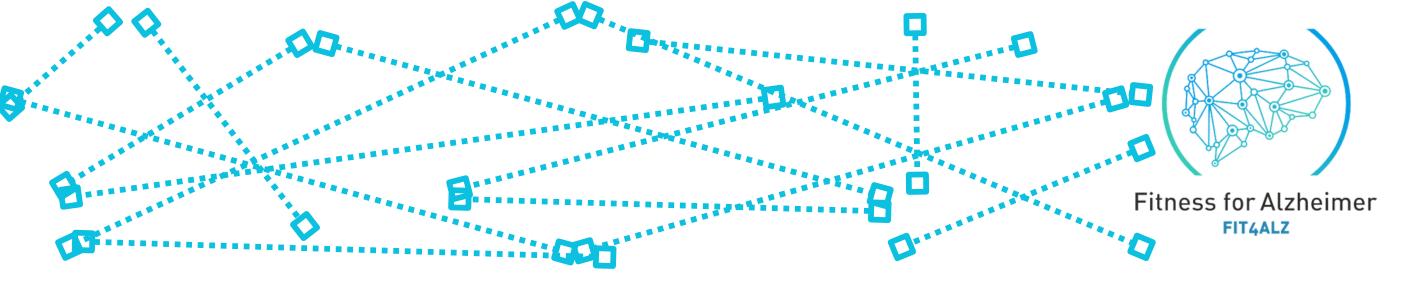
2.1. Diagnosis of AD

The early diagnosis of AD is of utmost importance for effective management and mitigation of its impact on patients. AD diagnosis has been made in the later stages after excluding other conditions, but the disease's progression begins years earlier with significant neuropathological changes such as amyloid-beta plaques and neurofibrillary tangles (NFTs) [10]. Advancements in diagnostic tools, particularly biomarkers, offer an opportunity for earlier detection [10]. Biomarkers, including those detectable through cerebrospinal fluid (CSF) analysis, magnetic resonance imaging, and positron emission tomography (PET) scans, can identify AD before clinical symptoms manifest [10].

These tools were endorsed by recent food and drug administration guidelines and the NIA-AA research framework, which support their use for diagnosing AD and monitoring disease progression [9]. Moreover, research using blood-based biomarkers holds promise for less invasive and more accessible diagnostic methods, potentially alleviating the current diagnostic difficulties.

The process of diagnosing AD early is both crucial and complex, particularly within the primary care framework where initial symptoms often first appear. It was previously proposed a diagnostic framework comprised of: (i) detect; (ii) assess; (iii) diagnose; and (iv) treat, as previously [11]. The detect domain is the first critical step which involves primary care providers and healthcare professionals recognizing the varied initial signs of AD [11]. These signs can include short-term memory lapses or psychological symptoms such as depression [12].





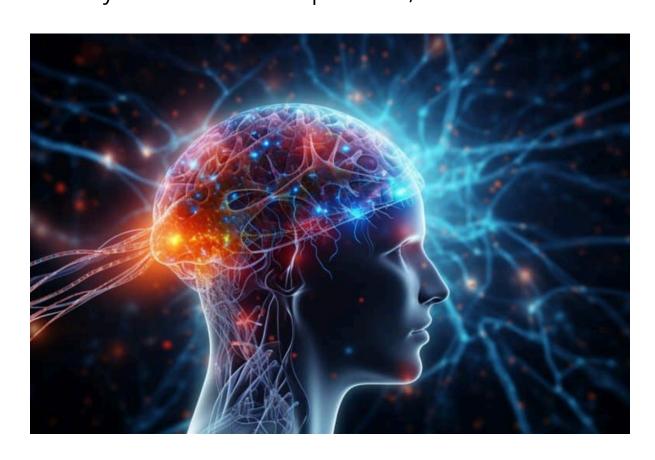
2.1. Diagnosis of AD

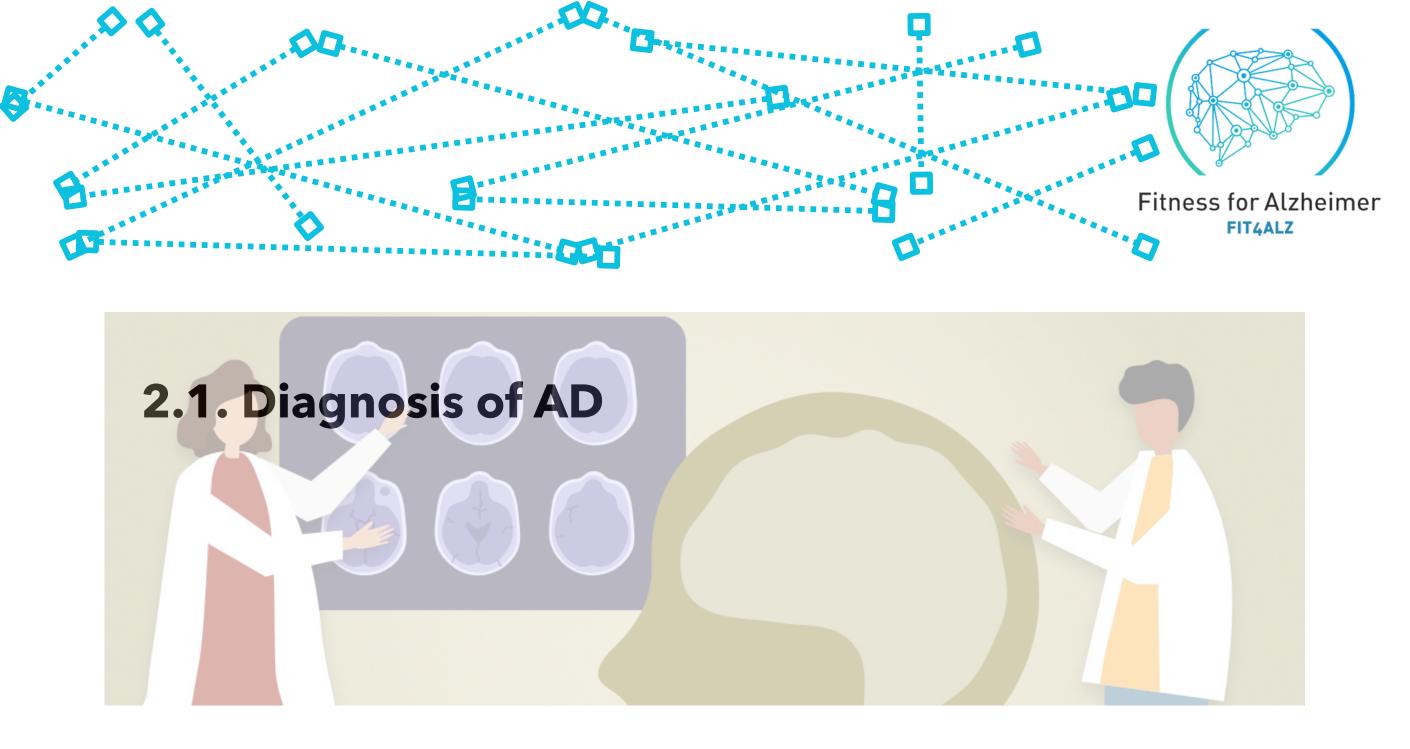
However, several issues can impede early detection. Patients might conceal their symptoms due to stigma, fear, or denial, while both family members and healthcare professionals might normalize these symptoms as part of the aging process [13,14]. This highlights the necessity for communicating with family members, who can provide feedback about the changes in daily functioning, behavior, and mood.

The assess domain involves primary care physicians conducting assessments of reversible causes of cognitive impairment [11]. It includes a detailed patient history, physical exams, and blood tests. Cognitive assessments such as the Montreal Cognitive Assessment (MoCA) are utilized to detect early signs of AD, while functional assessments evaluate the patient's ability to perform daily activities, signalling functional decline [15]. Behavioural assessment help differentiate AD from other psychiatric conditions [16]. If AD is still suspected, further specialist assessment might be necessary, employing MRI or PET scans to confirm the diagnosis of AD [16].

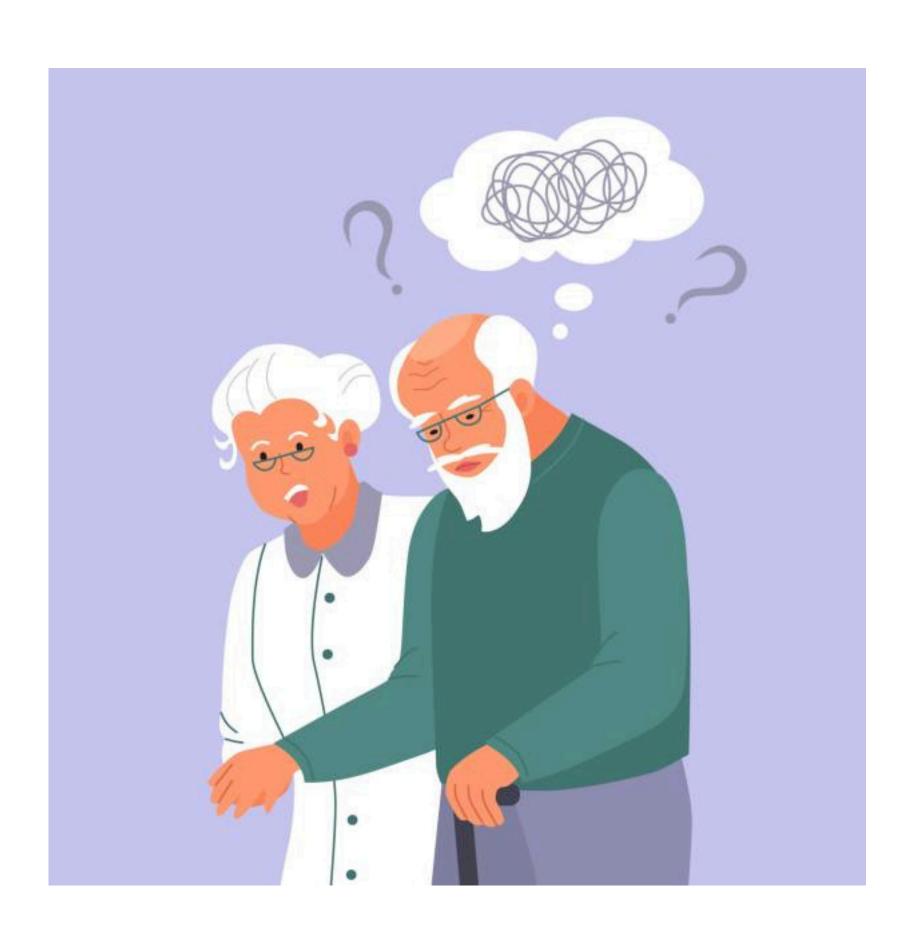
The diagnose domain involves analysing biomarkers to confirm suspected cases [11]. Through the PET scans, it is possible to visualize amyloid-beta plaques in the brain, providing evidence for AD when combined with clinical assessments, though their use can be limited by cost and accessibility [17]. Alternatively, CSF analysis through lumbar puncture that measures amyloid-beta, offers a direct reporting of AD [18]. However, this method is very invasive for the patients, and research is

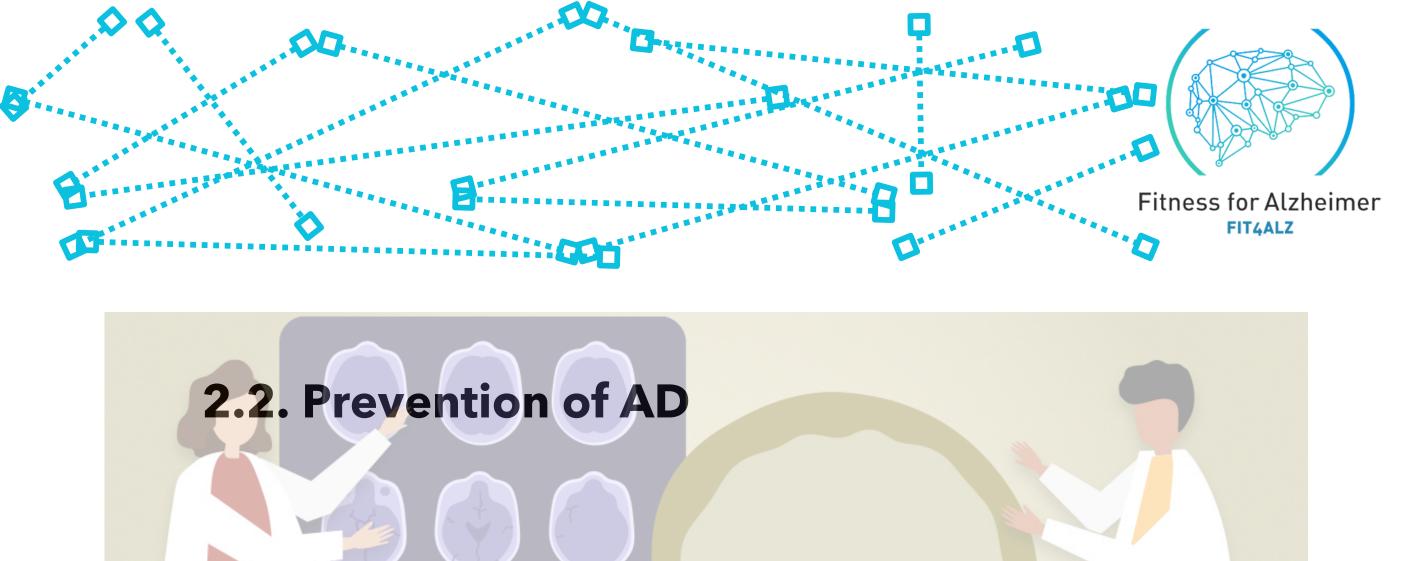
now examining less invasive diagnostics with blood-based biomarkers showing potential, where initial AD screening could be more routinely integrated into primary care assessments by improving early detection [10,19].





In the treatment domain, clinicians focus on AD management, focusing on both pharmacological and non-pharmacological approaches [11]. It is expected to provide emotional support and ensure regular follow-ups (every 6-12 months) to monitor AD progression using cognitive and functional assessments, and adjusting treatments based on observed changes [20]. Non-pharmacological strategies such diet, physical exercise, and cognitive training can improve cognitive function and quality of life [21]. Pharmacological interventions may be prescribed to temporarily alleviate symptoms, offering short-term benefits in cognition and daily functioning without altering the disease course [11].





A previous study identified as modifiable risk factors for the AD, the diabetes, hypertension, obesity, physical inactivity, depression, smoking, and low educational attainment [22]. That study suggested that up to 49.4% of AD cases might be attributable to these risk factors if they were independent [22]. However, after accounting for the interdependence among these risk factors, this was adjusted down to 28.2% [22]. That is, nearly a third of AD cases could potentially be prevented or delayed through effective interventions. The study proposed that a 10% reduction per decade in the prevalence of each risk factor could decrease AD prevalence by 8.3% by 2050 [22]. This fact shows the relevance of the long-term benefits of implementing preventive strategies/interventions to retard AD occurrence

and/or its progression.

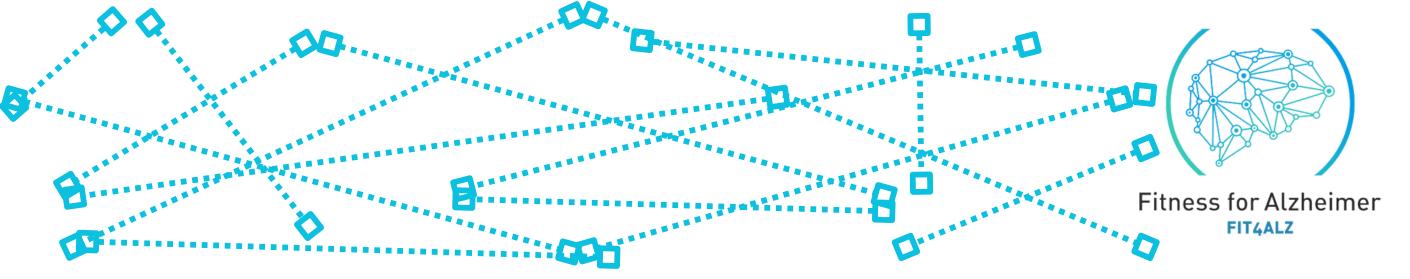


Implementing physical exercise interventions is crucial for preventing AD given its significant impact on reducing one of the previously mentioned modifiable risk factors (i.e., the physical inactivity) [23]. Research indicates that physical inactivity is highly attributable to AD cases, reinforcing that regular physical activity is a key preventive measure [24]. As physical exercise interventions can be programmed to different age groups and health conditions, its implementation could lead to a notable decrease in AD prevalence [25]. Physical exercise interventions not only promote a greater physical fitness level, but also may improve cognitive performance and overall mental well-being [26]. The upcoming section will focus on how physical exercise impacts the AD.

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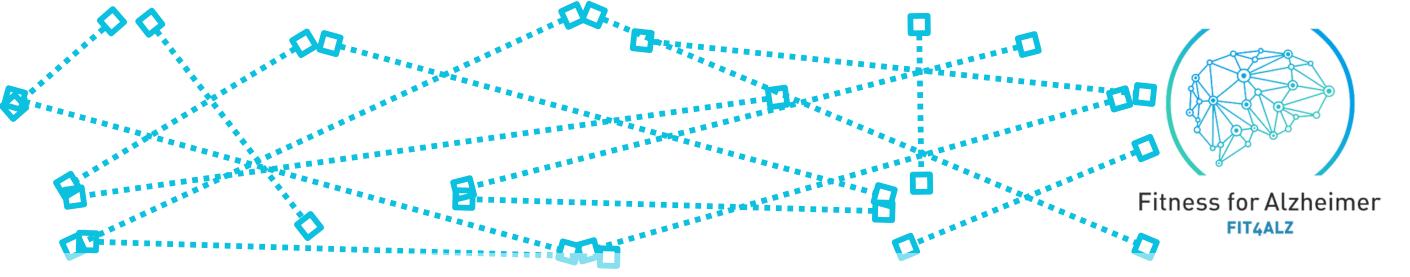


3. The influence of Physical Exercise on Alzheimer's disease

As the prevalence of AD continues to rise globally, it has become a pressing public health challenge, especially in aging populations. Although pharmacological treatments for AD exist, they primarily address symptoms and fail to halt or reverse the disease's progression, emphasizing the need for preventive and complementary strategies.

Physical exercise has emerged as a promising non-pharmacological intervention for delaying the onset and progression of AD. Evidence suggests that regular physical activity influences neuroplasticity, reduces systemic inflammation, enhances cardiovascular health, and promotes cognitive resilience, which are factors implicated in the pathophysiology of AD [1]. Furthermore, epidemiological studies demonstrated that higher physical activity levels correlate with a reduced risk of developing AD. Exercise programs, including aerobic, resistance, and multimodal activities, have shown potential in mitigating cognitive decline and improving executive functions and memory in individuals at risk or in the early stages of AD [2,3].

The potential benefits of physical exercise in preventing and managing Alzheimer's disease are supported by a growing body of evidence spanning cellular, clinical, and epidemiological studies [4,5]. Regular exercise influences brain activity through different mechanisms, many of which directly counteract the pathophysiological symptoms of AD, such as amyloid-beta accumulation, tau hyperphosphorylation, and neuroinflammation [6].

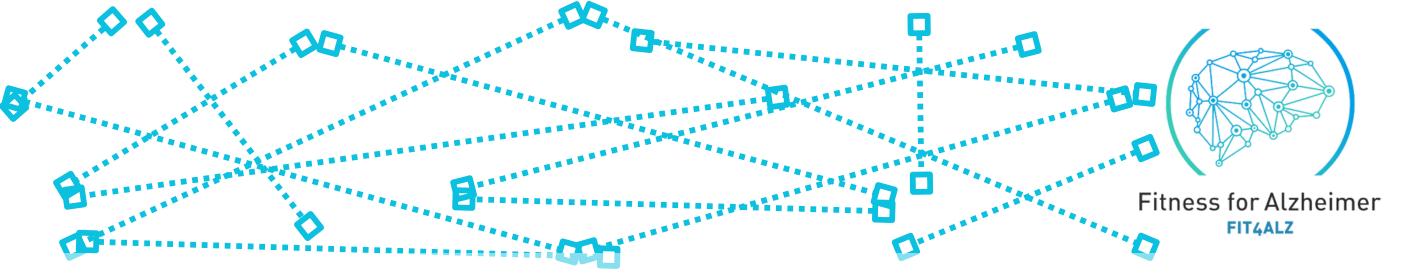


3.1. Neurobiological responses to exercise

Exercise induces neuroplasticity and neurogenesis, primarily by upregulating neurotrophic factors such as the brain-derived neurotrophic factor (BDNF) [7]. BDNF supports neuronal survival, synaptic plasticity, and cognitive functions, particularly in the hippocampus, a region severely affected by AD [8]. Studies in animal models have shown that aerobic exercise enhances hippocampal BDNF levels, resulting in improved memory performance [9,10]. Additionally, exercise modulates oxidative stress and reduces neuroinflammation, which are major contributors to neuronal damage in AD [11,12].

Exercise also improves cerebral blood flow (CBF) by improving endothelial function and promoting angiogenesis, potentially mitigating the vascular contributions to cognitive impairment [13,14]. Increased CBF ensures adequate delivery of oxygen and nutrients to the brain, supporting metabolic demands and reducing the buildup of amyloid-beta [15].





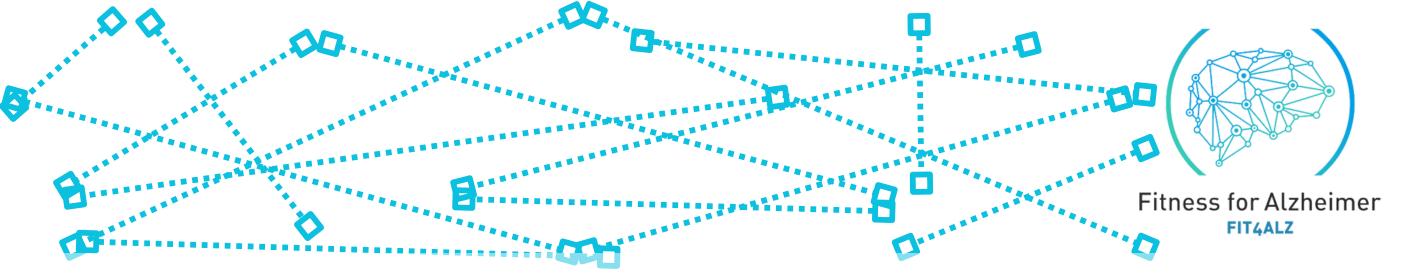
3.2. Cognitive and Clinical Outcomes

being in older adults [19,20].

Clinical trials have consistently demonstrated the cognitive benefits of exercise for individuals with mild cognitive impairment (MCI) or early AD [16-18]. Aerobic exercises, such as walking, cycling, and swimming, have been linked to improvements in attention, executive function, and memory [18]. Resistance training may complement these effects by enhancing global cognitive function and promoting musculoskeletal health, which supports overall well-

Furthermore, multimodal exercise programs that combine physical and cognitive activities have shown additive effects on cognition, suggesting that synergistic interventions could maximize benefits [21,22]. For example, Tai Chi and dance, which integrate physical movement with coordination and rhythm, have demonstrated efficacy in improving cognitive function and mood while reducing fall risks in older adults with AD [23,24].





3.3. Future challenges

Despite the promising evidence, several challenges remain in establishing physical exercise as a standard intervention for AD. One limitation is the heterogeneity in exercise protocols across studies, including differences in intensity, frequency, and duration, making it difficult to determine the optimal exercise prescription [25,26]. Moreover, adherence to exercise programs can be challenging for individuals with advanced AD due to motor and cognitive impairments, necessitating supervised interventions [27]. Another issue is the reliance on self-reported physical activity data in observational studies, which can introduce bias and limit the accuracy of findings [28]. Future research should prioritize objective measures of physical activity, such as wearable devices, to validate the dose-response relationship between exercise and cognitive health [25,29].

Integrating physical exercise as a public health strategy for AD prevention offers a cost-effective and accessible approach to reducing the burden of dementia. Community-based exercise programs can target at-risk populations, including older adults with sedentary lifestyles, obesity, or vascular risk factors. Additionally, promoting physical activity as a lifelong habit through education initiatives may ensure long-term benefits. Also, innovative interventions, such as virtual reality exercise platforms and smartphone and web-based applications, may ensure better engagement and accessibility for older adults, including those in residential care settings [25].



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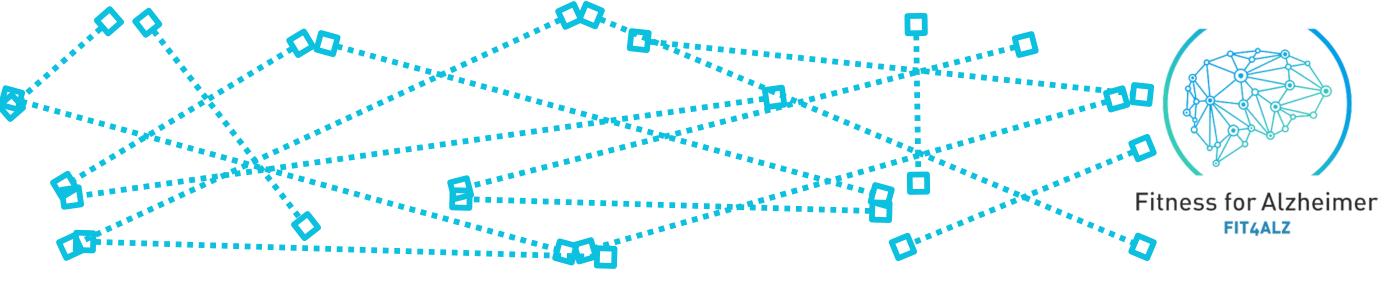
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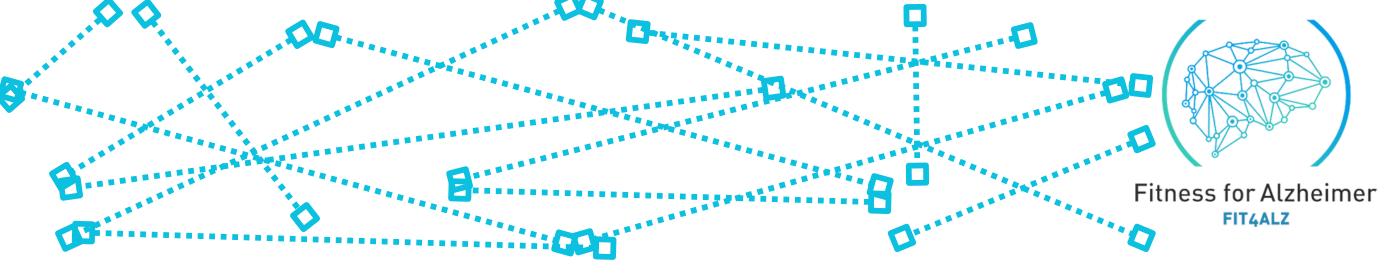




The project began with the development of a scoping review [1], which analysed validated applications and software used in scientific studies aimed at stimulating cognition in older adults with cognitive decline. The review included 34 studies and revealed a wide variety of intervention protocols. It was observed that combining physical fitness and cognitive assessments could provide a more comprehensive understanding of the interventions' impact. Moreover, the effectiveness of cognitive training applications requires further investigation, considering individual differences and real-world outcomes.

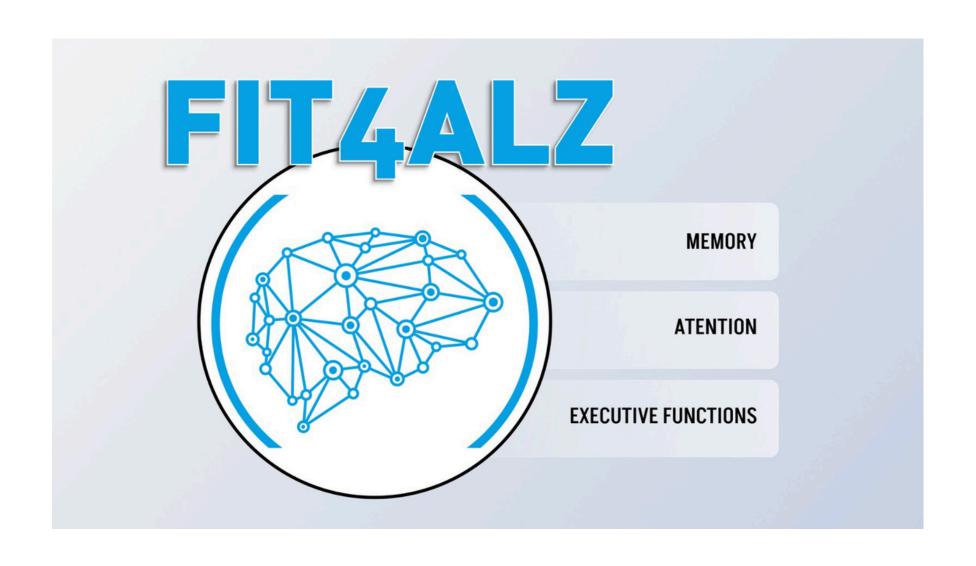
In parallel, the research team analysed the applications and software mentioned in the reviewed studies and added other free tools not previously cited. This analysis showed that the most common games for older adults with cognitive decline focused on three main cognitive functions: memory (64%), attention (59%), and executive functions (59%). Language (41%), orientation (27%), praxis (18%), and gnosis (14%) appeared less frequently, while cognitive functions such as social cognition and visuospatial skills were not represented.

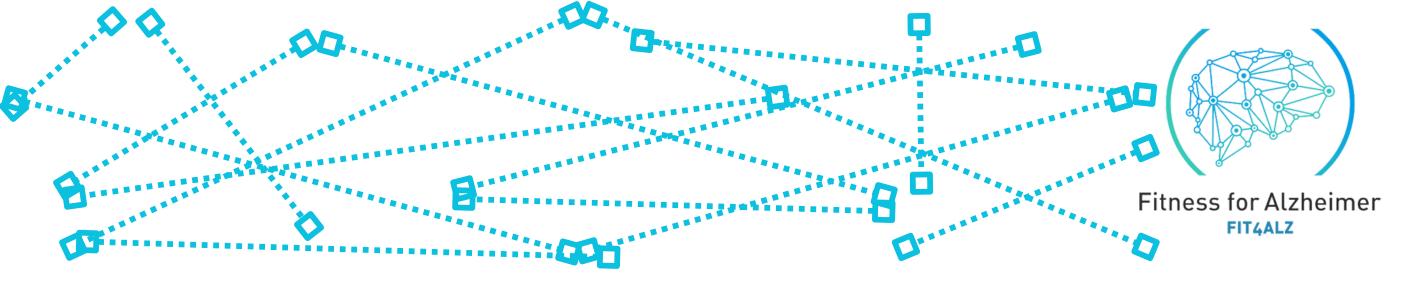


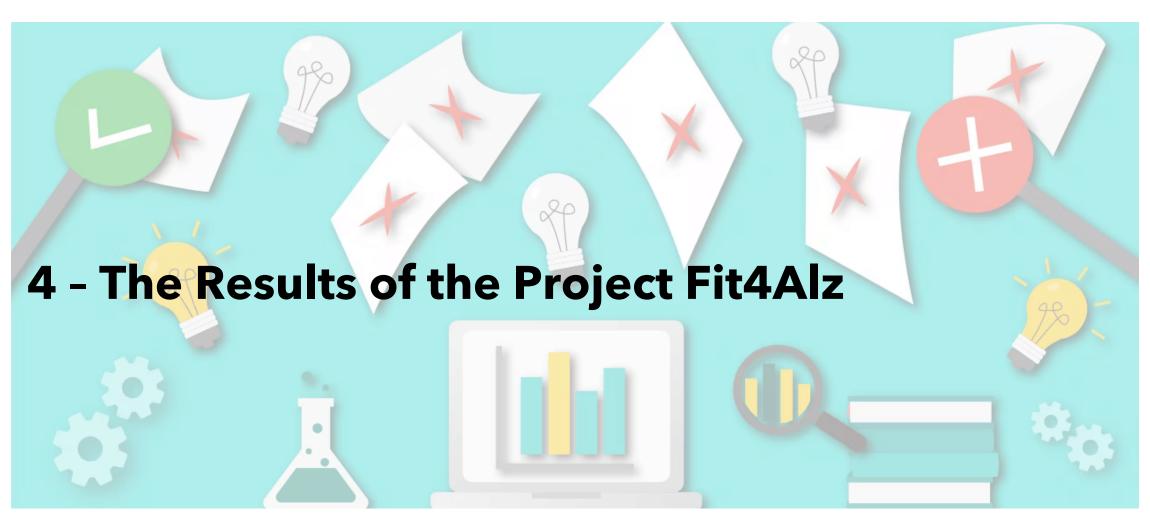




Based on these findings, the software developed for the project focused on the three most relevant cognitive functions: memory, attention, and executive functions. Six games were created – two for each function: for memory, the games "Matching Pairs" and "Repeat the Sequence"; for attention, "Find the Differences" and "Face to Face"; and for executive functions, "Stroop" and "Tap or Avoid." Each game includes five levels of complexity, based on response time and number of correct answers. This software was later used in the intervention phases and could be find in the project site (https://fit4alz.wixsite.com/fit4alz). In the physical exercise interventions, it was not possible to identify a specific methodology that led to superior cognitive improvements, as all experimental interventions resulted in cognitive gains. In fact, the second experimental study (currently under review for publication), which included a control group, confirmed what the first study [2] had already suggested: physical exercise has a positive impact on both cognition and physical fitness, as all groups improved – except for the control group, which maintained its baseline levels (despite a tendency toward cognitive decline).







One surprising finding was that the inclusion or absence of cognitive training had no impact on outcomes. Two possible explanations may account for this: 1) despite efforts to design games using everyday scenarios and problem-solving situations, these activities may not have a direct transfer to real-life cognitive abilities; 2) improving cognitive functions may require more than 12 weeks of stimulation.

This project reinforces the **benefits of physical exercise in promoting healthy aging**, emphasizing that the most important factor is engaging in physical activity – at least at a moderate intensity – regardless of whether the methodology focuses on resistance training or aerobic exercise.

All information about the project and its outcomes are exposed in our:

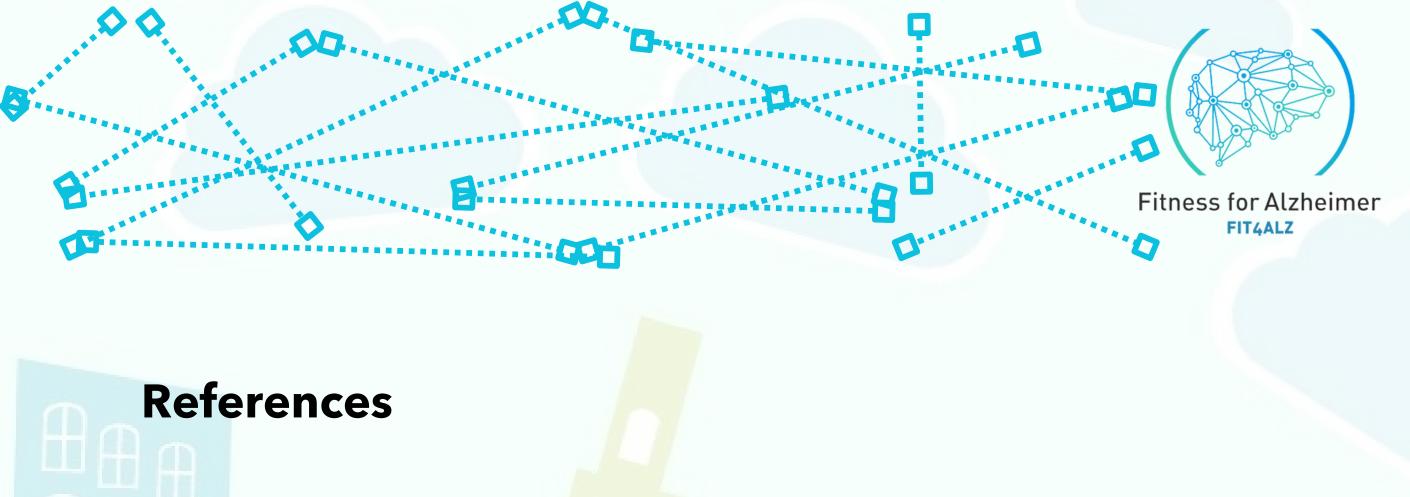
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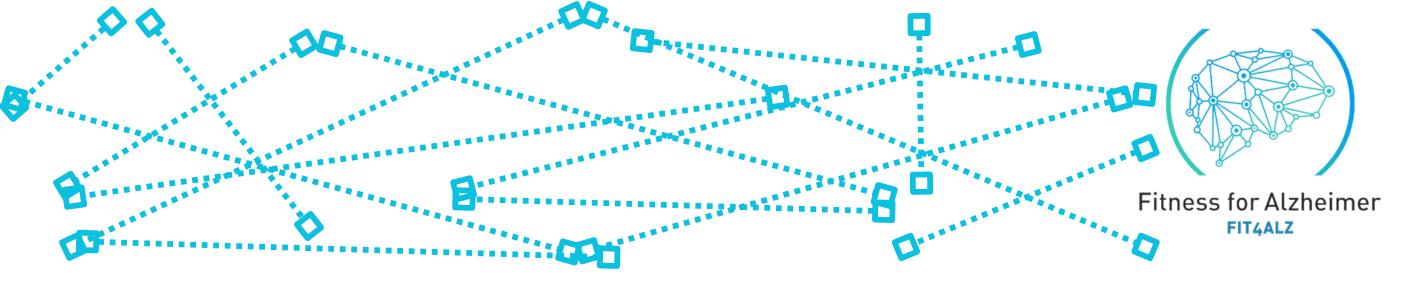
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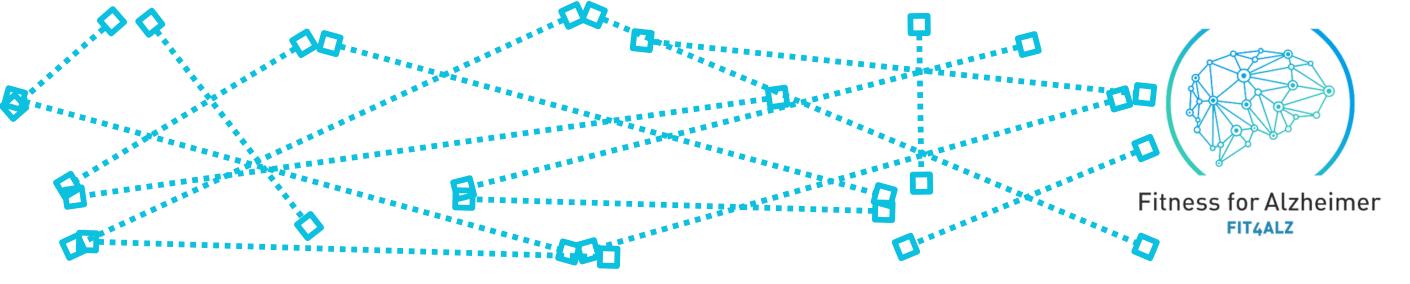


5 - Proposal for Physical Exercise Prescription for People with Dementia

Based on the results of the project, the main recommendation is that individuals engage in physical activities they find enjoyable. Research consistently shows that motivation plays a crucial role in maintaining long-term adherence to physical exercise. According to Self-Determination Theory (SDT), supporting autonomy and fulfilling basic psychological needs are essential for fostering autonomous motivation [1]. This type of motivation has been linked to healthier food choices and sustained participation in vigorous physical activity over time [2].

Considering factors such as frequency, volume, and intensity, individuals may choose to focus on aerobic exercise, strength training, or a combination of both. Notably, both approaches have demonstrated benefits for physical and cognitive health, although slight differences were observed in specific physical outcomes. While aerobic training appears to be more effective in improving cardiovascular capacity and functional mobility, strength training stands out in enhancing muscle strength and agility.

Exercise guidelines for older adults highlight the importance of a comprehensive fitness program that incorporates aerobic, resistance, balance, and flexibility training. International standards – such as those from the ACSM, AHA, WHO, and national bodies like those in Austria – recommend at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity aerobic activity per week, ideally divided into sessions of no less than 10 minutes [3–5]. Strength training should be performed twice a week, targeting major muscle groups with multiple exercises and repetitions. While exercise cannot halt the aging process, it significantly reduces the negative effects of a sedentary lifestyle and contributes to a longer, healthier life.



5 - Proposal for Physical Exercise Prescription for People with Dementia

With this in mind, our research team developed and implemented two distinct exercise methodologies, both of which showed promising results in delaying cognitive decline. The characteristics of each are detailed in Tables 1 and 2 below. We recommend a minimum frequency of three sessions per week and strongly emphasize the importance of exercise intensity. Of course, all activities should be carried out under the supervision of a qualified instructor who can tailor both the exercises and their intensity to individual needs.

Table 1. Description of plan A and B of aerobic training sessions.

| Plan A | Time | Phase | Exercise | Methodology | Intensity | HR |
|--------|--------|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|-----------|------------|
| | 5' | Warm-up | Single-joint and multi-joint exercises that allow for the gradual increase of body temperature. If possible, activities that individuals enjoy and promote group participation. | Continuous | 5/6 RPE | 60% |
| | 42-44' | Fundamental | Two times: 1. Jumping jacks 3. Walk out 9. High knee 10. Lunge 4. Kipping 8. Plank knee | 6 x 2' 1' rest between each repetition 4-6' walk between sets | 7/8 RPE | 75- 85% |
| | 3' | Cool down | Walking or some low activity | Continuous | 3/4 RPE | 40% |
| Plan B | Time | Phase | Exercise | Methodology | Intensity | HR |
| | 5' | Warm-up | Single-joint and multi-joint exercises that allow for the gradual increase of body temperature. If possible, activities that individuals enjoy and promote group participation. | Continuous | 5/6 RPE | 60% |
| | 42-44' | Fundamental | Two times: 2. Burpees 6. Squat 7. Lunge with kick 11. Butt kicks 5. Running 12. Step up and down | 6 x 2' 1' rest between each repetition 4-6' walk between sets | 7/8 RPE | 75- 85% |
| | 3' | Cool down | Walking or some low activity | Continuous | 3/4 RPE | 40% |

5 - Proposal for Physical Exercise Prescription for People with Dementia

Table 2. Description of the strength training plan.

| Weeks 1 to 12 | Time | Phase | Exercise | Methodology | Intensity | HR |
|---------------|--------|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|--------|
| | 5' | Warm-up | Single-joint and multi-joint exercises that allow for the gradual increase of body temperature. If possible, activities that individuals enjoy and promote group participation. | Continuous | 5/6 RPE | 60% |
| | 42-44' | Fundamental | Two blocks of tri-sets 1st block: 1 hip-dominant exercise 1 anti-core exercise 1 upper pull exercise 2nd block: 1 knee-dominant exercise 1 anti-core exercise 1 upper push exercise | Hip- and knee-dominant exercises 1st week: 2x5 reps 2nd week: 2x8 reps 3rd week: 2x10 reps 4th week: 3x8 reps 5th week: 3x10 reps Weeks 6-8: 3x12 reps Weeks 9-12: 3x15 reps Anti-core holds 1st week: 2x10s 2nd week: 2x20s 3rd week: 2x25s Weeks 4-12: 3x30s | 4/5 RIR | 75-85% |
| | 3' | Cool down | Walking or some low activity | Continuous | 3/4 RPE | 40% |



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