

# Advanced technologies applied to physical exercise for dementia and Alzheimer's disease management: a narrative review

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## Abstract

The prevalence of Alzheimer's disease and other forms of dementia is increasing along with overall life expectancy, which poses a serious challenge to healthcare systems in general. Non-pharmacological therapies, such as physical activity, have gained popularity due to their potential to improve cognitive and motor function, particularly as the prevalence of dementia is predicted to increase with overall life expectancy. This narrative review aims to describe the issues affecting individuals with dementia and Alzheimer's disease in practicing physical activity, with a focus on strategies for promoting the latter such as the use of supportive technologies. Specifically, the central part of the review describes all the scientific studies to date that use technologies to promote and perform exercise in individuals with Alzheimer's disease and dementia. Our review describes that the technologies used to date are video sports games, virtual interfaces, inertial sensors, and virtual cycling experiences and these technologies have been demonstrated to have efficacy in balance, quality of life, physical performance, risk of falls, strength, and frailty assessment. However, there is little homogeneity in exercise protocols this suggests that technology can be a safe and effective tool for promoting an active lifestyle in patients with dementia, but further research is needed to maximize its usefulness and accessibility. Future studies could be devoted to investigating the specific characteristics in terms of frequency, intensity, time, and type that technology-assisted physical activity needs to have to be effective in individuals with Alzheimer's disease.

**Key words:** advanced technology; aging; Alzheimer's disease; cognitive impairment; dementia; growth factor; healthy lifestyle; neuroplasticity; physical activity; sports activities; technology

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## THE PROBLEM OF DEMENTIA AND STRATEGIES FOR TREATMENT AND PREVENTION

### Dementia: a wide degenerative condition

Over the past two centuries, global life expectancy has increased by about 2.5 years per decade. This is largely due to improved living conditions.<sup>1</sup> This rise has led to an increase in age-related diseases. These include cardiovascular diseases, cancer, and neurodegenerative diseases, including dementia.<sup>2</sup> Dementia affects millions. Its prevalence is increasing as the population ages. It is a major concern.<sup>3</sup> The symptoms of dementia vary according to its specific form and individual progression. It often starts with small signs of cognitive impairment. These signs include difficulties in memorization and problem-solving. As the disease progresses, behavioral changes occur.

These changes may include agitation, irritability,<sup>4</sup> and sometimes hallucinations.<sup>5</sup> Genetic, environmental, and neurobiological factors contribute to the multifaceted causes of dementia. Many forms share a common characteristic – abnormal protein accumulation in the brain. This disrupts nerve cell communication and causes cell death. It is further complicated by neurochemical dysfunction, neuroinflammation, and oxidative stress.<sup>6</sup> Dementia represents a wide range of neurodegenerative disorders. Each has unique characteristics and clinical manifestations. These include vascular dementia,<sup>7</sup> which results from cumulative cerebral ischemia and involves impaired blood flow to crucial areas of the brain, causing focal neuronal damage.<sup>8</sup> Lewy body dementia is characterized by abnormal accumulation of alpha-synuclein in brain

cells.<sup>9</sup> It is associated with a wide range of motor and cognitive symptoms that often overlap with those of Parkinson's disease.<sup>10, 11</sup> Huntington's disease is linked to a genetic mutation that causes excessive production and accumulation of a mutated version of the protein huntingtin. This leads to specific degeneration of striatal neurons and progressive loss of motor and cognitive function.<sup>12</sup> Frontotemporal dementia is less common. It causes the degeneration of the frontal and temporal regions of the brain. This leads to significant changes in behavior and personality.<sup>13</sup> Diagnosing dementia is challenging due to its diverse symptoms. It highlights the need for comprehensive understanding and international cooperation for effective management and support.

### **Alzheimer's disease: the most common pathology of dementia**

Alzheimer's disease (AD) is a progressive neurodegenerative disorder. It affects millions of individuals worldwide. It is among dementias. The devastating consequences on memory, cognitive function, and functional independence have sparked a growing interest in finding ways to prevent and intervene early. These strategies aim to delay or lessen symptoms, and protect cognitive health. The estimated prevalence of the disease in 2021 was 58 million. It is expected to exceed 88 million by 2050. Among these individuals with dementia, two-thirds have AD diagnosis.<sup>14</sup> The cause of this disease is complex. It is still the subject of extensive research. One of the main signs of AD is the presence of amyloid plaques in patients' brains. They consist of aggregates of a protein called beta-amyloid, which accumulates on the outside of nerve cells, forming insoluble deposits.<sup>15</sup> In addition to the plaques, there are also changes in nerve cell metabolism. There are also changes in how nutrients and chemicals essential for brain function are transported. Another relevant aspect in the pathophysiology of AD is chronic inflammation. The brain's immune system responds to the accumulation of amyloid plaques. It does this by producing inflammatory cytokines. These cytokines can damage nerve cells and promote progressive deterioration.<sup>16</sup> Moreover, the dysfunction of synapses plays a key role in the pathogenesis of AD. The connections between nerve cells, called synapses, transmit information in the brain. In AD, they deteriorate and are damaged by the process of amyloid plaque accumulation. This impairs the ability of the nerve cells to communicate. It contributes to the progressive loss of cognitive

function.<sup>17</sup> Consequently, motor functions also degenerate. Patients with AD manifest gait disorders, such as impaired stride length. This is found to be decreased in individuals with AD.<sup>18</sup> This phenomenon contributes for example to the increased incidence of falls in this category of patients. Other gait alterations include increased timing variability. It occurs during both gait initiation and walking at a constant speed. It is evident in the early stage of the disease.<sup>19</sup> Balance disorders are also present.<sup>20</sup>

However, the amyloid thesis is starting to lose credibility.<sup>21</sup> Recent studies are investigating the vascular hypothesis. It proposes that dementia is mainly vascular. The pulse's destructive effect on cerebral blood vessels causes it. Neurons are lost secondary to vascular rupture.<sup>22</sup> The vascular hypothesis claims that cognitive decline is caused by silent microhemorrhages. These microhemorrhages intensify with age due to the hardening of arterial trees. de la Torre<sup>23</sup> has developed the idea that hypoperfusion of cerebral capillaries is the key event in AD. Researchers have provided extensive experimental evidence that cerebral hypoperfusion can cause severe cognitive and memory loss. Another study suggests microhemorrhages are closely related to amyloid plaques. It claims they are located in the same pathology site.<sup>24</sup> They further state that microvascular deterioration begins early in the disease. Stabilizing the microcirculation may be clinically valuable for disease prevention and treatment.

### **Neuroplasticity: the brain's capacity of adaptation**

Until the 1960s, many scientists stated the adult nervous system was static. They thought it had a limited capacity for change.<sup>25</sup> Today, thanks to studies on both animals and humans, we know the adult human brain is continuously shaped by environmental influences.<sup>26</sup> The nervous system can reorganize in response to new demands and environments. This ability is known as "neuroplasticity."<sup>27</sup> Neuroplasticity can occur in various situations. Examples include acquiring new skills and repairing the nervous system after an injury.<sup>28</sup> The human brain is highly susceptible to the influences of the environment and the experiences we go through. This susceptibility leads to structural and functional changes, known as neural plasticity. However, as we age, the brain's ability to adapt and compensate diminishes. This leads to a decline in brain function. Neural plasticity declines, contributing to an overall reduction in cognitive abilities. This includes attention, memory, working memory, communication ability,<sup>29</sup> and motor function.<sup>30</sup> The concept of neuroplasticity has revolutionized the

understanding of the nervous system. It challenges the previous idea of a fixed and unchanging structure. The discovery of neuroplasticity highlighted the ability of the human brain to adapt and change in response to the environment and experience. Also, the acquisition of motor skills and their long-term preservation are strongly related to neuronal plasticity at the cortical and subcortical levels in the central nervous system. This system evolves and includes several interconnected and spatially distributed brain regions.<sup>31</sup>

### **The effectiveness of physical activity in improving subjects' living conditions**

A huge number of studies have demonstrated the significant benefits of adopting regular physical activity programs for both cognitive function and overall physical and mental function. Studies have consistently shown that exercise has a positive influence on cognitive processes,<sup>32</sup> including memory,<sup>33</sup> and attention.<sup>34-38</sup> For example, a review conducted by Erickson et al.<sup>38</sup> emphasized the strong correlation between physical activity and cognitive outcomes, highlighting the role of aerobic exercise in maximizing various aspects of cognition, such as attention skills, pointing out that Types influences the effect on attention task: Kelly et al. showed no effect of aerobic and resistance exercise on attention of healthy older adults but an effect of the Tai Chi practice on measures of attention in the same population.<sup>36</sup> However, if we consider the pathological elderly population exercise improves particularly domains of attention in people with schizophrenia<sup>35</sup> and in people post-stroke who improved performances in attention assessments<sup>37</sup> for example by significantly improving Addenbrooke's Cognitive Examination-Revised attention scores after aerobic exercise.<sup>34</sup>

In addition, Guure et al.<sup>39</sup> conducted a meta-analysis confirming the positive impact of physical activity on cognitive function, especially in older adults.

Physical activity has been shown to have a deep effect on general function and it was found that both resistance and aerobic training induce metabolic changes within the muscle by inducing molecular and cellular adaptations that regulate muscle hypertrophy.<sup>40</sup> Indeed, research conducted by Liu-Ambrose et al.<sup>41</sup> supports the effectiveness of resistance training in improving functional outcomes in older people. This randomized controlled trial provides evidence for the role of exercise in promoting independence and mitigating functional decline. Furthermore, another systematic review highlights the benefits of adapted

exercise programs for people with dementia, showing improvements in activities of daily living and physical performance.<sup>42</sup> Even today, unfortunately, there are no specific drugs targeted to treat AD and its various clinical manifestations. Hence, it is necessary to adopt more effective techniques to improve the quality of life and health outcomes of AD patients by integrating physical activity into therapy programs.<sup>43</sup> The evidence in the literature supports the effectiveness of physical activity in improving both cognitive and overall function. Practicing regular exercise programs affects cognitive well-being and also plays a crucial role in maintaining functional independence, significantly affecting overall quality of life.

### **The problem of adherence to physical activity programs and the key role of caregivers for individuals with Alzheimer's disease**

For these reasons, family caregivers play an essential role in supporting the health and well-being of older adults with dementia.<sup>44</sup> The presence of a motivated and knowing caregiver can positively influence patient adherence. Caregivers can provide emotional support, encouragement, and practical assistance in preparing and accompanying the patient to physical activity sessions. In addition, they can help monitor progress and identify any difficulties or challenges the patient might encounter during exercise.

Recent studies have highlighted the importance of caregivers' active involvement in physical activity programs. Lamotte et al.<sup>45</sup> recommended education and involvement of caregivers in intervention programs can improve the adherence and effectiveness of the interventions. In addition, caregivers' emotional support and understanding of the patient's needs and limitations can help create an environment that encourages participation and maintenance of physical activity over time. Active involvement and support of caregivers are critical to ensure the adherence and success of physical activity programs for people with AD. Education and support provided to caregivers can significantly improve the participation and benefits of physical activity for patients with these conditions. Dropout, or dropout rate, is a significant challenge in physical activity programs targeting individuals with AD. Many factors contribute to this complex and multifactorial phenomenon.

Hoffmann et al.<sup>46</sup> declared that the main causes of dropping out of the physical activity program were those related to musculoskeletal problems. Adherence to physical activity programs for people with AD is a

complex challenge. Numerous factors can influence participation in and compliance with such programs. First, severe cognitive impairment can make it difficult for individuals to understand and follow complex instructions, as well as to remember exercise routines.<sup>47</sup> This difficulty can increase the risk of frustration and dissatisfaction, making exercise routines more difficult to follow. Motor limitations, often present in patients with AD, are an additional obstacle. Problems such as muscle weakness, difficulty in coordination, and walking disorders<sup>19, 20</sup> can affect the ability to perform certain exercises or physical activities. These problems require specific adaptations and special attention to ensure that physical activity is safe and effective.

Behavioral alterations including agitation and apathy are widely present symptoms in individuals with dementia.<sup>48</sup> These may also be a significant barrier to adherence to physical activity programs. These symptoms could also be intensified by frustration or anxiety associated with physical activity, making it necessary to take a sensitive and adapted approach to encourage participation.

Environment and socialization play a crucial role in physical activity adherence. A safe, comfortable, and well-equipped environment and the presence of social support and encouragement from caregivers or health professionals can facilitate participation and promote a feeling of well-being.<sup>49</sup>

Thus, promoting physical activity adherence for people with AD requires a holistic approach that takes into account cognitive, motor, and behavioral challenges. Personalizing programs, providing an appropriate environment and offering meaningful social support, are the key to overcoming obstacles and promoting effective and rewarding participation.

### **What aspects of Alzheimer's disease can be improved with physical activity?**

Physical activity plays a crucial role in the management of AD, providing several significant benefits beyond the physical aspect. Recent studies have shown muscle and strength improvements in individuals who participate in regular exercise programs.<sup>50</sup> These help to maintain independence in activities of daily living and also slow the decline in muscle function associated with advancing age and the disease itself.

Physical activity plays a key role in increasing balance and motor coordination, fundamental aspects in preventing falls, which are a significant risk for individuals with AD.<sup>51</sup> Improving stability and safety in daily movements can greatly increase the quality of life

for those living with this condition.

In addition to physical improvement, physical activity promotes social interaction and group participation, providing opportunities for socialization and sharing experiences.<sup>52</sup> This is especially important considering that social isolation is often a challenge for individuals with AD.

From a psychological perspective, physical activity can help mitigate depression, a common symptom of this condition.<sup>49</sup> Exercise stimulates the production of endorphins and other well-being-related brain chemicals, thus helping to improve mood and overall mental health.

Therefore, physical activity plays a crucial multifactorial role in the management of AD. In addition to muscular and balance benefits, it promotes sociability, addresses depression, and facilitates participation in daily activities, contributing significantly to the well-being and quality of life of individuals affected by this disease.

### **The generic neuroprotective mechanisms of physical activity**

Different studies on humans and animals have highlighted the protective mechanisms of physical activity on brain function.

Exercise plays a crucial role in influencing adult neurogenesis through the action of various growth factors. Among these, brain-derived neurotrophic factor (BDNF), insulin-like growth factor 1 (IGF-1), and vascular endothelial growth factor (VEGF) are notably enhanced by physical activity in both humans and rodents. VEGF is notably enhanced by physical activity in both humans and rodents. This enhancement is linked to improved cognitive functions, including faster reaction times, better attention, and improved learning and memory capabilities.<sup>53</sup> Particularly noteworthy is VEGF, which is not only influenced by exercise but is also a pivotal factor for adult neurogenesis.<sup>54</sup> It has a dual role: angiogenic, promoting the formation of new blood vessels, and neurogenic, stimulating the growth of neurons in the hippocampus via various signaling pathways.<sup>55</sup> The activity of VEGF ties directly to hippocampal functions, impacting neurogenesis, neuronal plasticity, aspects of learning and memory; factors that are also promoted by physical exercise.<sup>56</sup> Additionally, BDNF, which is produced during exercise via the PGC-1 $\alpha$ /FNDC5 pathway, plays a vital role in the exercise-driven process of neurogenesis. It contributes significantly to synaptic plasticity and cognitive improvements, highlighting the multifaceted benefits

of physical exercise on brain functions.<sup>57</sup> Furthermore, IGF-1, is essential for maintaining brain plasticity and supporting adult neurogenesis, and physical exercise leads to a rapid increase in its circulating levels, which are crucial for both neurogenesis and cognitive processes.<sup>58</sup> Interestingly, the external administration of IGF-1 has been shown to restore neurogenesis and ameliorate cognitive deficits, further highlighting the interconnected roles of these growth factors and physical exercise for brain health and function.<sup>59</sup>

Exercise induces modulation of amyloid  $\beta$  turnover, inflammation, neurotrophin synthesis, and release.<sup>60</sup> In particular, the mechanism behind neurotrophin synthesis seems to be related to the already demonstrated increase of IGF-1 following a training period: insulin-like growth factor-I interfaces with the brain-derived neurotrophic factor system. The inactivation of insulin-like growth factor-I receptors, whose increase was induced by 5 days of aerobic exercise, inhibits the production of neurotrophic factor which is important for synaptic function, to mediate exercise-induced synaptic and cognitive plasticity.<sup>61</sup> In this way, structured and programmed exercise induces changes in the brain at the anatomical, cellular, and molecular levels by inducing a cascade of molecular processes that promote several positive physiological phenomena, neurogenesis, synaptogenesis, and the stimulation of neurotrophic factors that enhance learning, memory, and brain plasticity.<sup>62</sup>

In addition, progressive aerobic-based exercise on a cycling ergometer for 50 minutes for 8 weeks three times a week (10 minutes warm-up at 45%  $P_{max}$ , 30 minutes at 70%  $P_{max}$ , and 10 minutes cool-down at 45%  $P_{max}$ ) improved cerebral blood flow in older adult preventing cerebrovascular disease.<sup>63</sup> Small vessel disease, with the neurodegenerative processes, could cause dementia but physical activity decreases this possibility by reducing circulating sugar and fats by stimulating angiogenesis and improving cardiovascular function.

The practice of different types of physical activity carried out individually or in groups has shown long-term benefits from a cognitive point of view; It was shown that physical activity protracted over time can have favorable influences on brain plasticity and resilience to brain aging, actually opposing neurodegenerative phenomena: physically active individuals are less likely to develop dementia than inactive individuals, a period of 6 to 12 months of aerobic exercise is effective in achieving better cognitive scores by inducing an increase hippocampal

volumes and an attenuation of age-related gray matter volume loss just in the trained group.<sup>64</sup> who performed high physical activity significantly improved hippocampal gene expression more than low physical activity.<sup>65</sup> Promoting lifestyle changes in the pre-symptomatic and predementia stages could have the potential to delay at least one-third of dementia globally.<sup>66</sup> low level of physical activity is found to be associated with an increased risk of AD<sup>67</sup> and on the other hand long-term moderate to vigorous intensity physical activity improves cognitive outcomes in adults and the elderly.<sup>38</sup> Therefore, multimodal interventions that include active lifestyle adoption should be recommended for elderly populations because the link between physical and mental health has long been recognized: over the years, there have been several clinical trials testing the effects of a certain type of exercise on the cognitive performance of patients with different forms of dementia.<sup>68</sup> However, the heterogeneous nature of the interventions and the cognitive test and outcome severely limits the use of activity as a factor in preventing dementia. Several studies gave mixed results in terms of frequency, intensity, time, and type characteristics that the activity must have to be effective in producing the desired effects.<sup>69</sup> Thus, it is unclear what specific characteristics the exercise must have to be effective in a specific condition such as the subject with AD to improve physical performance.

Among the types of physical activity being considered for their effectiveness are new methods involving the use of technology to promote exercise by ensuring that the participant has immediate biofeedback such as those based on wearable sensors, virtual reality or gaming consoles, and many others. However, their effectiveness in promoting exercise that is effective for these individuals is being tested. The objective of this narrative review is therefore to discuss the effectiveness of specific exercise protocols, with particular reference to those involving the use of wearable technologies, applied to individuals with AD or dementia to identify the potentially most effective and most widely used protocol for improving motor skills and thus the quality of life of these individuals.

### Animal models

After clarifying the preventive role of physical exercise on brain aging and consequently, on dementia, it is good to refer to animal models to understand the physiological mechanisms through which exercise acts on cognition, neuroplasticity, and neurotrophic factors expression. Rats who performed 4 weeks of

aerobic exercise (running) showed an increased BDNF concentration in an exercise-time-dependent manner (over 4 weeks) from the first to the fourth week.<sup>70</sup> Mice who run progressively 1–5 km per night for three weeks improved memory tests and object recognition in contrast with sedentary mice: immobilization reduces cognitive function.<sup>71</sup> The same results have been found in the primates; monkeys who performed 1 hour running on a treadmill for 5 days a week, at 80% of maximal aerobic power for 5 months, had significantly better cognitive scores than sedentary animals.<sup>72</sup> Physical exercise has been shown to affect the hippocampus area in animal models, this brain region is directly involved in aging and, in diseases characterized by cognitive impairment.<sup>73</sup> In particular, the dendritic length, spine, and the neurogenesis of the dentate gyrus of the hippocampus area increase after continued exercise.<sup>74–78</sup> BDNF has been investigated *in vitro* too in animal models. It is demonstrated to be able in brain plasticity modulation by improving neurite outgrowth and synaptic function.<sup>79</sup> In addition, BDNF *in vitro* contributes to the survival of neurons affected by neurodegenerative conditions such as AD.<sup>80</sup> and BDNF concentrations increase after exercise.<sup>81–84</sup>

## NEW TECHNOLOGIES FOR PHYSICAL ACTIVITY MANAGEMENT

New technologies are revolutionizing the way physical activity is conceptualized, designed, and analyzed, offering innovative tools that could improve the experience and promote adherence. Below is a brief introductory explanation of the technologies most widely used in the context of physical activity.

### Wearable devices

Wearable devices, such as smartwatches or bracelets, offer continuous and non-invasive monitoring of a person's physiological parameters. They can record data such as heart rate, daily activity, number of steps, walking speed, fall detection, and physical activity recognition.<sup>85</sup> Wearable devices are also useful in measuring activity levels throughout the day, changes in the circadian rhythm, and changes in the sleep-wake cycle.<sup>86</sup> Also among the wearable devices recently found important use in motor rehabilitation have been wearable sensors, which can provide patients with instant visual, auditory, or vibrotactile biofeedback that is sensitive to the user's motor performance giving the possibility of having an interactive environment to facilitate motor learning because the sensors can accurately measure body movement and capture

any wrong movements to also promote postural reeducation.<sup>87</sup>

### Applications and software

Nowadays, the field of user-friendly and low-cost applications and software is constantly growing. There are applications and software specifically designed to provide customized exercise programs, progress monitoring, and exercise optimization tips.<sup>88</sup> These tools can be used to create exercise plans tailored to individual needs and skill levels. Apps are being developed that can recognize the personal characteristics of each subject such as a study that analyzed the posture and any postural alterations of individuals.<sup>89</sup> In addition, since coronavirus disease 2019 digital platforms have also been used to administer distance training protocols for the elderly population with neurodegenerative diseases demonstrating excellent results.<sup>90,91</sup>

### Virtual reality and augmented reality

Virtual reality (VR) and augmented reality are new technologies that allow the participant to control a virtual environment through the use of human senses like sight, touch, proprioception, and movement and therefore allow you to execute physical activity programs in immersive and engaging ways simulating the experience of real life while also significantly stimulating the central nervous system in terms of perception and response to different stimuli. VR technology allows participants to exercise in a limited space, thus reducing costs as it does not necessarily require the constant presence of trainers like more traditional workouts.<sup>92</sup>

VR technology has received attention as a new rehabilitation tool and the literature in this area has expanded in recent years. VR can provide patients with increased sensory stimulation, a more immersive environment, and real-time feedback during specific motor tasks reflecting motor learning and neuroplasticity.<sup>93</sup> In addition, it increases personal motivation and engagement by giving the ability to adjust the level of difficulty according to the patients' skill level. Due to its accessibility and safety, it can be used by patients at home without supervision for a short period.

### Exergame

Technology is increasingly taking hold in all areas of our lives even what was originally conceived as a gaming console, for the sole purpose of entertainment can be used to maintain an active lifestyle.<sup>94</sup> Exergaming derives from the union of the words exercise and

gaming and indicates video games that also allow for the practice of exercise by relying on technology that detects body movement or otherwise a physical reaction for “gaming” (e.g., getting points, winning a game, beating the opponent). This since 2006 has changed the way video games are viewed from being defined as a quintessential sedentary activity to a tool for promoting active living. Exergames are steadily increasing, thanks to the investments that large companies are making.<sup>95</sup>

In addition, the ability to stimulate psychomotor skills, hand-eye coordination, and three-dimensional control of the limbs in space have also made Video sports games useful for rehabilitation purposes. For example, the Nintendo is an exergaming-ready console. Indeed, Wii-Fit is a technology, included in the Nintendo console, designed to improve balance and fitness while providing enjoyment through different game training like yoga, strength training, aerobics, and balance games.<sup>96</sup> Active video game systems controlled through arm movements or by force plates are becoming increasingly popular. Since 2006, the Wii Fit console has been using VR with wireless controllers that allow interaction with the player through a motion-sensing system using three-dimensional accelerometer technology that detects changes in direction, speed, and acceleration of body segments. In addition, in the Wii Fit gaming console, a balance platform equipped with four strain gauge load sensors on each corner can be used to monitor the center of gravity and track weight-shifting movements.<sup>97</sup> By detecting these changes, the console can provide instant visual and auditory feedback to participants on the monitor through interactive games, so that the participant can make changes to his or her movements in real-time.<sup>98</sup> Although these gaming systems are growing in popularity and can be applied to improve health, few studies have tested their effectiveness on people with dementia or AD and this one could be very useful because it is easy to use at home, fun and challenging, and it can give you a chance to coincide physical training with cognitive training especially useful in this population.

## SEARCH STRATEGY AND SELECTION CRITERIA

In the central part of this narrative review, we analyzed articles from the most recent literature, providing a balanced and comprehensive overview of the most important discoveries on the types of technology-supported physical exercises most effective for improving quality of life and motor performance in individuals with dementia with special reference to AD. Subsequently,

the selected articles are summarized in **Table 1** by highlighting specific studies' characteristics “Author,” “Year,” “technology,” “Home-based,” “Frequency,” “Intensity,” “Session Time,” “Type,” “Outcomes” and “Results” to provide interested researchers with a detailed and schematic overview of all the recent studies on the use of technology for training in dementia and AD. Key words included “Alzheimer’s disease,” “wearable sensor-based exercise,” “exercise,” “sport,” “virtual reality,” “training,” “technologies,” “dementia,” “Wii-Fit,” and “exergaming.”

The searches were limited to studies published in English that included human studies related to technological supports of physical exercise, and dementia. Study designs included original articles and randomized controlled trials. We excluded narrative, systematic, and meta-analyses reviews. We performed the literature search from September 2023 to November 2023 on PubMed, Scopus, Web of Science, and Google Scholar, with no limitation on the publication date of the studies to be included. A summary of the literature selection process is expressed in **Figure 1**. The initial searches, after duplicate records were removed, revealed a total of 3656 articles, we have filtered these preliminary results by study designs, participants involved, or exercise protocols excluding those who did not have these characteristics adapted to the scope of the research.

Seven studies meet the eligibility criteria, and are considered appropriate for the central part of our narrative review. These 7 papers focused on the use of inertial sensors, video games, exergames, and VR (**Table 1**). The publication date range of the included studies was from 2012 to 2020. Of the seven papers included only one analyzed the effects of home-based training, and in another, it was not specified in the test. The other five papers adopted a type of training supervised by experts in specific settings. Two papers used the Wii Fit technology, one used video-sport games, one used virtual interface and inertial sensors, one used virtual cycling experience, one used exergames, and one used portable neuro-exergames. The frequency of weekly workouts ranged from 1 to 5 times a week, and the duration of the protocol was from 4 weeks to 3 months. Moreover, the duration of each session went from 20 minutes to 50 minutes. Regarding intensity, there was much heterogeneity among the studies. Five out of seven did not specify the intensity of the exercise, one study had set the intensity at 50 watts, and the other between 65% and 75% of the maximum heart rate.

**Table 1: Advanced technologies applied to physical exercise of dementia and Alzheimer's disease management**

Author	Year	Technology	Home-based	Frequency	Intensity	Session time	Type	Outcomes	Results
Padala et al. <sup>96</sup>	2012	Wii Fit	No	5/7x8 wk	NS	30 min	Strength training, yoga, and balance games	BBS, TT, TUG, ADL, IADL, and QOL-AD	BBS and TT improved
Uğur and Sertel <sup>103</sup>	2020	Wii Fit	NS	2/7x6 wk	NS	30 min	Balance and aerobic exercises	TT, balance test, 5TSTS, and gait speed	Improvement in all assessments in the exercise group but not in the control group
Yamaguchi et al. <sup>110</sup>	2011	Video-sports games	No	1/7x10 wk	NS	NS	Upper limbs (grab coins); Lower limbs (move their legs to music)	HDS-R, Kohs, and MOSES	HDS-R and Kohs Improved
Schwenk et al. <sup>99</sup>	2016	Virtual interface and inertial sensors	No	2/7x4 wk	NS	45 min	Sensor-based balance training program	CoM sway, gait speed and variability, and short-FES-I	CoM sway reduced. Short-FES-I improved
D'Cunha et al. <sup>101</sup>	2021	Virtual cycling experience	No	One occasion	50 watts light effort	25 min	Sit with their feet in the pedal exercisers' cycling at their own pace while viewing the screen	Mood questionnaire, PEAR, and EPWDS	Virtual cycling experience as an immersive and engaging alternative to usual activities
Karssemeijer et al. <sup>106</sup>	2019	Exergame training	No	3/7x12 wk	65% to 75% HR	30–50 min	Cognitive-aerobic bicycle training on a stationary bike connected to a video screen	EFIP, 6' Astrand cycle test; Ergometer test, TUG, 10MWT, 5TSTS, FICSIT-4, PASE, Katz index, SPPB	EFIP improved and TUG improvement trend
Anderson-Hanley et al. <sup>107</sup>	2018	Portable neuro-exergame	Yes	3–5/7x3 mon	HR range monitored but NS	20–40 min	iPACES: elliptical pedaler and a joystick to control the Memory Lane™ game installed on a tablet-laptop	Color Trails ratio, Digit Span ratio, Stroop ratio, Word recall, ADAS delayed, BDNF, cortisol, DHEA-S, IGF-1	Stroop A/C and ADAS improved. Adults, with MCI, may benefit from interactive physical and cognitive exercise

Note: 10MWT: Ten-Meter Walk Test; 5TSTS: five-time Sit-to-Stand Test; ADAS: Alzheimer's Disease Assessment Scale; ADL: daily living; BBS: Berg Balance Scale; BDNF: brain-derived neurotrophic factor; DHEAS: dehydroepiandrosterone sulfate; EFIP: Evaluative Frailty Index for Physical activity; EFIP: The Evaluative Frailty Index for Physical activity; EPWDS: Engagement of a Person with Dementia Scale; FICSIT-4: Frailty and Injuries: Cooperative Studies of Intervention Techniques; HDS-R: Hasegawa's Dementia Scale-revised; IADL: instrumental activities of daily living; IGF-1: insulin-like growth factor; Kohs: Kohs block-design tests; MOSES: Multidimensional Observation Scale of Elderly Subjects; NS: not specified; PASE: Physical Activity Scale for the Elderly; PEAR: Person-Environment Apathy Rating Scale; QOL-AD: Quality of Life-AD; Short-FES-I: Short Falls Efficacy Scale International; SPPB: Short Physical Performance Battery Test; TT: Tinetti Test; TUG: Timed Up and Go.

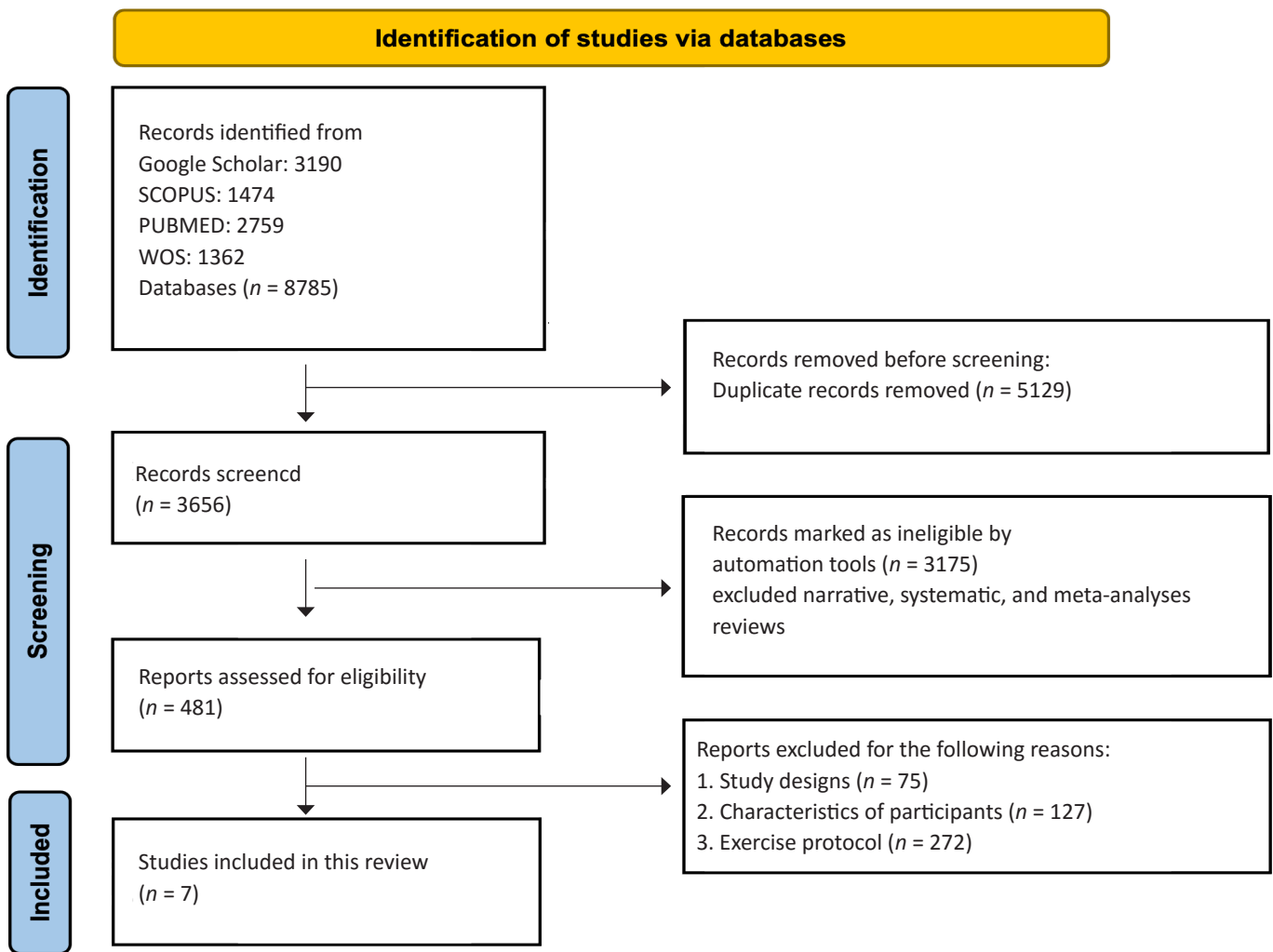


Figure 1: Study selection process.

The outcomes assessed in the studies could be clustered in balance, quality of life, physical performance, risk of falls, strength, and frailty assessment, performed through questionnaires and standardized tests. The results showed different improvements in the different studies but in all the variables mentioned (**Table 1**).

In this review, we aim to shed light on the types of training supported by innovative technologies for individuals with cognitive decline.

The pilot study by Schwenk et al.<sup>99</sup> explored the feasibility, user experience, and effects of a novel sensory balance training program in individuals with mild cognitive impairment. The study included a total of 22 participants, including 12 in the intervention group and 10 in the control group. The study's equipment, which consists of five inertial sensors, an interactive virtual user interface, and a 24-inch computer screen, was created especially for monitoring and enhancing balance control. Several variables were measured

in the study, including center of mass swing area, walking speed and variability measured with wearable sensors, fear of Falling assessed using the Short Falls Efficacy Scale International, and Cognitive performance assessed using the Montreal Cognitive Assessment and Trail Making A and B tests. Wearable sensors are included in a balancing training program for older persons in this study to provide real-time feedback on their exercise-related mobility performance. Balance turns out to be a fundamental component of activities of daily living, especially in the elderly; in a systematic review by Lesinski et al.,<sup>100</sup> balance-focused exercise programs were evaluated on healthy elderly subjects and it emerged that structured and individualized exercises were able to improve balance control, while also improving performance in activities of daily living. In agreement with these studies, the balance training program proposed by Schwenk et al.<sup>99</sup> is effective in reducing Center of Mass sway, reducing fear of falling, and improving eyes-closed balance and gait speed in

terms of pre-post change in the intervention group compared with the control.

Regarding virtual reality, a pilot study by D’Cunha et al.<sup>101</sup> explored the potential benefits of using new technologies to combat social isolation and sedentary behaviors in nursing homes for the elderly. Virtual group cycling is the technology used in this study. The study’s findings imply that virtual group cycling activities may benefit patients’ psychological well-being and socialization in addition to improving their physical and mental health by enhancing their muscle strength, flexibility, and coordination. Furthermore, the research indicates that virtual group cycling activities could be a useful tool to address social isolation and sedentary behavior in this patient population. Regarding the effect of technologies including VR on individuals with dementia, one study used a VR method on people with dementia in which subjects reported increased pleasure and alertness and decreased apathy during the session.<sup>102</sup> Similarly, the study included in our review<sup>101</sup> also indicates that virtual group cycling activities could be a useful tool to address social isolation and sedentary behavior in this patient population.

On the other hand, Uğur et al.<sup>103</sup> investigated the effect of VR applications on balance and gait speed in individuals with AD. Thirty-two people with mild to moderate AD were included in the study. They assessed walking speed, balance, and fall risk. The technology used was the Nintendo Wii. The results showed that the exercise group had lower scores than the control group and that the Tinetti scale score decreased in the control group and increased in the exercise group so there was an improvement in all assessments in the exercise group but not in the control group.

Padala et al.<sup>96</sup> used the same technology as the Nintendo Wii to improve walking and balance in people with mild AD. The study included 22 subjects, 11 were placed in the Wii-Fit group and 11 in the walking group. They took the Tinetti Test, the Berg Balance Scale, and the Timed Up and Go Test. They also measured functional ability, quality of life, and cognition.

Nowadays, the benefits that training brings to balance and consequently to activities of daily living are well known. This study is consistent with previous studies in older adults who confirm the improvement in balance and gait through this type of technology.<sup>104, 105</sup>

The results state that the use of Wii-Fit brought significant improvements in balance and gait, effects similar to those reported by subjects who participated in the rigorously supervised walking program.

Two of the seven articles<sup>106, 107</sup> included in our review focused on exergame technology. Exergaming is a technology-based activity that calls for physical reaction or movement of the body. This type of activity has been credited with dispelling the myth that video games are only for sedentary people and encouraging active living. Karssemeijer et al.<sup>106</sup> conducted a randomized controlled trial demonstrating that exergaming can reduce frailty and improve physical and cognitive function in individuals with dementia. The study analyzed a total of 115 people divided into three groups: the exergame group, the active control group, and the aerobic exercise group. The study included measures for several variables. The TOPICS-MDS Frailty Index was used to measure frailty at baseline. The Timed Up and Go Test and the Ten-Meter Walk Test were used to measure mobility. The 6-minute Åstrand Cycle Ergometer test was used to measure physical fitness. The Five-Times Sit-to-Stand Test evaluated lower extremity strength and endurance. Subsequently, two other measurements were taken, post-intervention at 12 weeks and follow-up at 24 weeks. According to the authors’ findings, exergaming is a practical and creative kind of exercise that has received positive subjective feedback from dementia patients. In actuality, the exergaming group adhered to the protocol more closely than the aerobic group did. Furthermore, it was demonstrated that exergame training was useful in lowering the individuals’ fragility. The authors’ findings seem to be consistent with a previous systematic review’s results,<sup>108</sup> which show that exercise improves sit-to-stand, step length, balance, mobility, and walking endurance in individuals with mild cognitive impairment or dementia. Also, compared to other people with normal cognition, patients with dementia are less likely to engage in regular exercise; therefore, an exercise regimen using exergames may be able to address this issue.

The second study adopting exergames as a training method for subjects with cognitive decline, which we decided to include in this review, is by Anderson-Hanley et al.<sup>107</sup> This was the only study we included that analyzed a home-based protocol. This study investigated the effects of an interactive physical and cognitive exercise program called Interactive Cognitive Exercise iPACes™ on individuals with mild cognitive impairment and their caregivers. In particular, the study assessed how this exercise and cognitive program affected verbal memory, executive functions, and salivary biomarkers like BDNF, cortisol, dehydroepiandrosterone, and IGF-1, and 31 participants were included in the study.

An iPad with a pedaling device attached was used to run the protocol. The program featured interactive cognitive games and pedaling exercises that required the use of joysticks and touch screens. It also featured a real-time feedback system that tracked the heart rate and pedaling speed of each participant. Based on the data that showed the Alzheimer's Disease Assessment Scale and the Stroop Test A/C did indeed improve. Thus, the results indicate that a 3-month training plan consisting of regular exercise and interactive cognitive exercise was feasible and can have a positive impact by increasing executive functions and verbal memory. Consistent with the results of this study, it has emerged from the literature that exercise in the elderly with AD or related dementia improves executive function.<sup>109</sup>

Only one of the seven studies included in our review deals with the technology of video sports games.<sup>110</sup> The study focuses on using sports video games to help senior people with dementia recover; in fact, the authors suggest a rehabilitation strategy focusing on encouraging patients to get better through social engagement. The technology employed in this study takes advantage of games that demand timing and exact three-dimensional control of limbs in space, as well as psychomotor skills like hand-eye coordination. The study was conducted on nine subjects with mild to moderate dementia. Results of the study indicate that participants' overall cognitive performance, visuospatial and constructive function, and some behavioral traits such as irritability and social withdrawal improved significantly.

## CONCLUSIONS AND DIRECTIONS FOR FUTURE RESEARCH

The importance and support that technology can provide in the dissemination of an active lifestyle in all age groups is evident and well-established.

However, there is a paucity of scientific evidence and original articles testing such tools in individuals with dementia and AD. To our knowledge, there are seven original articles published between 2012 and 2020 that specifically used video-sports games, virtual interfaces, inertial sensors, and virtual cycling experiences; of these, only one study detected the home-based setting with these technologies for the training; the training frequency tested to date included 1 to 5 sessions per week for 3–12 weeks, with imprecise (and often unspecified) information about the intensities used in each session. Instead, the duration of each session in various studies ranged from 20 to 50 minutes. Exergame consoles appear to be

the most widely used and effective tools because they are easy to use and fun for participants who are then stimulated to keep training. Although our narrative review concludes that technology is a reliable and risk-free tool for promoting motor activity practice even in individuals with dementia and AD, it is evident that there is little homogeneous data in the standardization of training protocols in terms of single session duration, intervention period, and training intensity. In addition, to make technology an effective contributor to lifestyle change in the elderly with dementia or AD, it would be important to make the subject autonomous in training by testing more Homebase training with these tools and recognizing the importance of intensity monitoring during training. So, future studies should provide for homogeneity in the protocols administered, with the possibility of making subjects autonomous by standardizing workouts to be done at home.

### Author contributions

Data interpretation, manuscript design, writing—original draft, data extraction: MS. Methodology, manuscript design, writing—original draft, data extraction: AA. Critical review, revision, manuscript design, and conceptualization: GM. All authors have read and agreed to the published version of the manuscript.

### Conflicts of interest

None declared.

### Data availability statement

Not applicable.

### Open access statement

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