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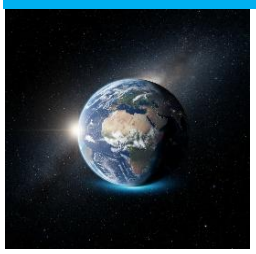

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The Role of Physical Activity in the Prevention and Progression of Alzheimer's Disease

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Abstract

Introduction and aim Alzheimer's disease (AD) poses a major public health challenge with limited pharmacological treatments, shifting focus to lifestyle interventions. This review analyzes the role of physical activity (PA) in preventing and modulating AD progression, focusing on cognitive function, brain structure, and molecular mechanisms.

Materials and methods A literature search was conducted in the PubMed database, focusing primarily on Randomized Controlled Trials (RCTs) and observational cohort studies concerning PA interventions in Mild Cognitive Impairment (MCI) and AD.

Summary: Evidence suggests PA significantly impacts clinical progression. In MCI, training may possibly delay conversion to dementia by 8-24 months, with neuroprotective effects sustaining post-intervention. Conversely, AD patients require continuous training to maintain benefits. Mechanisms involve "muscle-brain crosstalk" releasing neurotrophins (BDNF, IGF-1) and exerkines (irisin, cathepsin B, lactate), which promote neurogenesis and modulate neuroinflammation. Multimodal interventions (e.g., dance, Tai Chi) show superior cognitive outcomes compared to simple aerobic exercise. Efficacy is modulated by biological factors; APOE4 carriers and women may derive specific, distinct benefits from PA.

Conclusions PA is a crucial non-pharmacological strategy for AD. High-intensity and multimodal training offer the greatest therapeutic potential. Since efficacy varies by genetic profile and sex, personalized recommendations are essential. Implementation at the preclinical

stage is crucial for maximizing cognitive retention, yet introducing physical activity remains beneficial across all stages of AD.

Keywords Alzheimer's disease, physical activity, Mild Cognitive Impairment, BDNF, APOE4, neuroprotection.

Introduction

In the context of rapidly aging populations, dementia syndromes are becoming one of the main challenges for healthcare and social care systems. Systematic WHO data indicate that globally, 57 million people are living with dementia (as of 2021) and an additional 10 million patients are diagnosed with the condition annually. It is estimated that Alzheimer's disease (AD) accounts for 60-70% of these cases, making it the most common cause of dementia worldwide [1]. Alzheimer's disease is an age-related neurodegenerative condition whose primary causes and exact mechanisms of progression remain undetermined. The main pathological processes are characterized by the extracellular deposition of β-amyloid plaques (Aβ) in brain tissue and vessels, and the intracellular accumulation of neurofibrillary tangles of hyperphosphorylated—and therefore pathological—tau protein [2]. Amyloid-β, in both plaque and oligomer forms, impairs intersynaptic communication, leading to neuronal damage and death. Phospho-tau tangles (p-tau) disrupt neuronal architecture, impeding intracellular transport [3]. Other pathophysiological pathways considered by researchers as potentially initiating the disease process and modulating its course include neuroglial inflammation, reduced glucose metabolism, mitochondrial dysfunction, oxidative stress, and vascular changes [2].

The progression of AD is described as a time continuum, starting from the asymptomatic preclinical phase, through mild cognitive impairment (MCI) caused by AD, up to full-symptomatic Alzheimer's dementia. Researchers indicate that even in half of the people diagnosed with MCI may have an AD background [4]. Given systematic data indicating a two-fold increase in cases in Europe and a three-fold increase globally [5], the implementation of lifestyle interventions is gaining prominence. In 2020, The Lancet commission suggested that 40% of dementia cases are associated with modifiable risk factors for Alzheimer's disease, including physical inactivity [6]. Considering the limited pharmacological therapeutic options, preventive methods are becoming paramount in combating the annually increasing incidence of dementia syndromes.

The role of physical activity remains of interest to Alzheimer's disease researchers, not only due to improvements in cardio-respiratory fitness—which reduce cardiovascular risk, a factor closely linked to AD occurrence—but primarily due to how physical effort induces specific signaling pathways that mitigate the atrophy of key brain structures and promote neurogenesis, which translates clinically into improved cognitive function [7]. This paper aims to review the literature examining the relationship between physical activity and the prevention of AD onset as well as the modulation of its course, with a particular focus on cognitive function and the maintenance of the volume of key brain structures throughout the disease trajectory.

Impact on Clinical Progression

Physical activity influences the clinical course of Alzheimer's disease. A crucial aspect for the proper analysis of the beneficial effects it brings in counteracting neurodegenerative processes and inhibiting cognitive deterioration is the assessment of the severity of cognitive dysfunction. Mild Cognitive Impairment (MCI) refers to a decline in cognitive function that surpasses typical age-related changes but does not interfere with daily activities. MCI affects between 3% and 22% of individuals aged 65 years and older [8]. Annually, 5% to 10% of those diagnosed with MCI progress to fully symptomatic Alzheimer's disease [9]. In light of current scientific evidence, it is justified to evaluate how physical activity influences cognitive functions in fully symptomatic AD and whether it can slow down or prevent conversion from the preclinical phase.

Interventions in patients with MCI

In the therapy of patients diagnosed with MCI, a key issue remains not only the immediate stimulation of cognitive functions but, above all, the durability of neuroprotective effects. Studies indicate that different training modalities offer distinct benefits in this regard. Uysal et al. demonstrated that a 12-week intervention combining aerobic training (treadmill) with stretching (3 sessions per week for 30 minutes, 50-75% MHR) yields measurable clinical benefits. Importantly, the intervention group achieved a score of 22.75 points on the Mini-Mental State Examination (MMSE), which constituted a statistically significant improvement not only in the baseline vs. post-intervention analysis (an increase from 20.92 points) but also a clear advantage over the control group, which concluded the study with an average score of 20.92 points. An additional benefit in this model was a significant reduction in depressive symptoms measured on the Hamilton scale [10].

In turn, data regarding long-term neuroprotection were provided by Broadhouse et al., who analyzed the impact of intense resistance training (approx. 80% MHR). In contrast to short-term effects, the improvement in ADAS-Cog scores persisted in a statistically significant manner at the one-year follow-up after the 24-week intervention. The mechanism responsible for this sustained effect is the preservation of hippocampal subiculum volume. This finding indicates that neuroplastic changes are initiated and maintained following training. From a clinical perspective, the intervention increased cognitive function by 1-2 points on the ADAS-Cog scale, which, according to the researchers' estimates, may delay symptom progression and conversion to Alzheimer's disease by 8 to 24 months. These results emphasize the significance of resistance training as a systematic activity [11].

Interventions in diagnosed Alzheimer's disease

Intervention priorities shift regarding patients with mild-to-moderate Alzheimer's disease. Inhibition of cognitive decline and alleviation of neuropsychiatric symptoms play a key role in discussing this group of patients. However, an analysis of available studies indicates that therapeutic efficacy is strictly correlated with training parameters. Simple interventions based on uniform aerobic exercise yield inconclusive results regarding global cognitive functions. Yu et al. employed a program based on moderate-intensity stationary cycling (60-minute sessions, 3 times per week, 70% MHR). Despite 6 months of work, this group did not achieve a statistically significant advantage on the ADAS-Cog scale compared with the control group performing stretching [12]. A similar tendency was noted by Angiolillo et al. in a study utilizing Nordic Walking (2 sessions per week for 6 months). Although the specificity of this effort translated into improvement in selected domains (executive functions, episodic memory), the intervention did not result in a significant increase in the global MMSE score [13].

Overcoming this barrier seems possible through enriching the training environment. Lok et al. demonstrated this by applying a combined model: exercises with music (3 times per week for 30 min) and brisk walking (2 times per week for 40 min). A program composed in this way resulted not merely in the inhibition of decline, but in a significant increase in MMSE scores relative to baseline (from 23.36 to 25.50 points), with a simultaneous reduction in depressive symptoms, as assessed using the Cornell Dementia Depression Scale [14].

Exercise intensity and the resulting oxygen uptake remain extremely important factors modulating the body's response. David et al. conducted a study involving patients with biomarker-confirmed AD pathology, using a comprehensive program comprising 60 minutes of combined aerobic and resistance training. The key observation concerned the nature of the

effort: vigorous-intensity activity, rather than moderate activity, most effectively built cognitive reserve (VO_2 max). The fundamental significance of this variable stems from the fact that it mediated not only the preservation of the volume of key structures (hippocampus, amygdala), but also, above all, a significant increase in Montreal Cognitive Assessment (MoCA) scores compared to baseline values. Interestingly, the greatest benefits were observed in patients with worse baseline status (low MoCA scores and VO_2 max), suggesting the potential for improvement even in an advanced stage [15].

However, the difference in the durability of effects between AD and MCI must be emphasized, as vividly illustrated by the work of Fonte et al. The authors applied intense mixed training (3 sessions per week for 90 min) in both patient groups. In the post-intervention analysis, both MCI and AD patients showed a slowing of cognitive deterioration relative to controls. The dynamics of change only became apparent in the follow-up, three months after the intervention: while the effect was maintained in the MCI group, a significant decline was already evident in the AD group. This suggests that, unlike the preclinical phase, fully developed Alzheimer's disease requires uninterrupted, systematic physical activity to maintain the obtained benefits [16].

Neurobiological mechanisms

The role of BDNF and IGF-1

At the molecular level, physical activity exerts a multimodal influence on mechanisms related to the pathophysiology of Alzheimer's disease. Recent studies reveal an increasing number of factors that are part of exercise-induced signaling pathways influencing neuroplastic processes [17]. The literature describes a relationship termed "muscle-brain crosstalk," detailing substances that promote hippocampal neurogenesis and improve cognitive function [18].

Brain-Derived Neurotrophic Factor (BDNF) is a polypeptide growth factor that stimulates neurogenesis, neuronal growth and differentiation, and neuroregeneration, while also counteracting apoptosis. It exerts its effects through Tropomyosin receptor kinase B (TrkB) and p75NTR receptors. It modulates neuronal plasticity processes during learning and memory formation. BDNF is also present in the neuronal cytosol as a pro-neurotrophin (proBDNF), which exhibits similar physiological effects but has approximately 10-20 times weaker biological activity. This is of key importance in the context of proBDNF's higher affinity for p75NTR, which induces apoptotic processes in neuronal cells. Activation of the TrkB receptor triggers a signaling cascade that leads to the phosphorylation of GSK-3ß, thereby inactivating

it. In its active form, GSK-3ß has a pro-apoptotic effect, e.g., by phosphorylating the tau protein, and high levels of this kinase have been recorded in AD patients [19].

A central question for researchers remains how physical activity translates into neurobiological protection through the modulation of BDNF. The meta-analysis by Dinoff et al. provides a clear answer regarding acute aerobic exercise—demonstrating a significant increase in BDNF regardless of age, sex, or BMI—the impact of chronic exercise appears more complex [20]. In a study by Erickson et al. that covered a 6-month aerobic intervention, a simple increase in BDNF levels was not observed in the entire group. However, a key structural relationship was revealed: an increase in hippocampal volume (left and right) was observed exclusively in exercising individuals, and this increase significantly correlated with increased serum BDNF concentrations in these patients [21].

The protection of this specific structure is of fundamental importance, as Rao et al. indicates that the hippocampus undergoes neurodegeneration already at an early stage of the disease. It is essential for generating episodic memory (via the dentate gyrus) and transmitting the memory trace to the cerebral cortex for consolidation (via the CA3 region) [22]. Therefore, physical activity, by influencing BDNF levels, seems to directly counteract these adverse processes.

Like BDNF, a molecule closely linked to the modulation of GSK-3ß kinase activity in the context of AD pathophysiology, is insulin-like growth factor type 1 (IGF-1). A drastic decrease in IGF-1 receptors has been observed in the brains of individuals suffering from AD. This resistance induces increased GSK-3ß activity, leading to the hyperphosphorylation of tau protein [23]. Peripheral IGF-1 levels increase in response to physical exertion, although they do not necessarily reflect brain concentrations. The role of IGF-1 is also postulated as a mediator of the effects of physical activity on increased BDNF levels and improved cognitive function [24].

The Role of Exerkines

Recent studies focus on identifying factors and analyzing their metabolic pathways that, at the molecular level, mediate the effects of physical activity on the prevention and modulation of Alzheimer's disease. The key to understanding this relationship appears to lie in the role of substances termed exerkines, secreted by peripheral tissue cells. Some of them are able to cross the blood-brain barrier and stimulate the secretion of neuroprotective factors, including BDNF. The literature in this area remains largely limited to studies using animal models, yet these studies provide promising results [17].

The foundation of the muscle-brain communicative axis is irisin/FNDC5. It is a muscle-secreted molecule that not only regulates peripheral homeostasis, but also plays a mediating role in neuroprotection [25]. Studies on mouse AD models show that blocking its signaling pathway inhibits the beneficial effects of physical activity on neuroplasticity and memory retention [26], while an increase in its level correlates with the BDNF mobilization [27]. Importantly, from a clinical perspective, in humans, a decrease in irisin levels in cerebrospinal fluid (CSF) is characteristic of the "moderate-to-late AD" stage, in contrast to the MCI phase, suggesting its critical significance after conversion to the fully symptomatic form [26].

Exercise-dependent Cathepsin B (CTSB) acts via a parallel pathway. In study on mouse models subjected to aerobic exercise, not only was an increase in protein concentration observed, but also a statistically significant increase in CTSB gene expression, which correlated with increased BDNF levels. These results find confirmation in human cohort: after a 4-month intervention (treadmill running), the rise in plasma CTSB showed a positive correlation with the improvement of cognitive functions, specifically regarding the visuospatial memory trace [28].

A significant link between metabolic and structural pathways is lactate. As a product of anaerobic metabolism, it promotes the SIRT1/PGC-1α pathway, stimulating irisin secretion and increasing BDNF levels [27,29]. Simultaneously, it plays a key role in the VEGF secretion cascade, inducing angiogenesis via the HCAR1 receptor, which constitutes a fundamental neuroprotective mechanism [30].

VEGF itself thus demonstrates a dual action: vascular and neurogenerative [18]. In response to high-intensity interval training, a significant increase in VEGF in the hippocampus and cerebral cortex, as well as a densification of the vascular network, were noted in mice [30]. This is reflected in the metabolic parameters of the human brain: Tubi et al. demonstrated that higher CSF VEGF levels correlate with increased glucose metabolism in critical regions regarding AD pathophysiology (temporal and parietal cortex, posterior cingulate gyrus) in patients with amyloid pathology. This group also achieved better results in executive function tests, confirming the translation of molecular mechanisms into the observed clinical effect [31].

Neuroinflammation and Clearance of Pathological Proteins

Exerkines and neurotrophins triggered by physical exercise act in an autocrine or paracrine manner, inducing a neuroprotective effect [18, 21]. In light of recent studies, hemodynamic mechanisms related to interstitial fluid transport in the central nervous system (CNS), as well as the modulation of the microglial immunological profile mediated by physical activity, also

significantly inhibit neuropathological processes. In transgenic mice, a 6-week running intervention improved cognitive function scores and decreased beta-amyloid deposits by enhancing clearance of interstitial fluid in the CNS [32].

Physical activity also influences the conversion of microglia from a pro-inflammatory (M1) to a protective/anti-inflammatory profile (M2), although the validity of this classification in humans remains a subject of debate. Mee-Inta et al. highlight the pro-inflammatory influence of molecules such as TNF-alpha and IL-1β, as well as the anti-inflammatory character of IL-4 and IL-6, the latter of which stimulates the secretion of the anti-inflammatory IL-10 and the IL-1 receptor antagonist (IL-1Ra). Moreover, lower IL-6 concentrations are observed in individuals diagnosed with AD [33].

A study on transgenic mice subjected to a resistance training intervention resulted in a general reduction in microglial density, suggesting the suppression of chronic inflammation. In the hippocampus of mice from the experimental group, an increase in anti-inflammatory cytokines IL-10 and IL-4 was observed, with a concurrent reduction in TNF-alpha and IL-1β. After the intervention, beta-amyloid plaque volume was reduced in a statistically significant manner [34].

Study on human cohort conducted by Casaletto et al. aligns with findings from animal models. The American-Canadian team demonstrated that higher physical activity was associated with a lower proportion of activated (inflammatory) microglia, particularly in regions linked to AD pathophysiology (inferior temporal gyrus, ventromedial caudate nucleus). The greatest benefits in this regard were derived by patients with advanced AD [35].

Factors Modifying the Efficacy of Physical Activity

Widely recognized and well-documented predictive factors for Alzheimer's disease include both sex and the polymorphism in the gene encoding apolipoprotein E (APOE). According to data, women present a higher probability of developing Alzheimer's disease. The presence of the APOE epsilon 4 allele in patients is one of the key risk factors for a higher incidence of Alzheimer's disease [36].

A meta-analysis of twenty prospective cohort studies indicates a more than two-fold higher probability of developing the disease in APOE4 allele carriers compared to individuals with other variants, and an 86% higher possibility of conversion from Mild Cognitive Impairment (MCI) to fully symptomatic Alzheimer's disease [37]. The literature also indicates a prevalence rate of 91% and a mean age of diagnosis at 68 years for homozygous carriers of the epsilon 4 variant, compared to 47% and 76 years for heterozygotes, and 20% and 84 years for individuals free from this variant, suggesting an earlier age of onset for this patient population [38].

However, the extent to which these predictive factors influence the protective mechanisms provided by physical activity in the prevention and modulation of Alzheimer's disease progression remains under investigation. Results of a study conducted by a Spanish-American team demonstrated that APOE4 allele carriage moderates the impact of regular exercise on the prevention of Alzheimer's disease onset. Cognitively unimpaired patients who carried the APOE4 allele and were less physically active (<1845 MET-minutes/week) constituted a significantly more vulnerable group regarding the onset of Alzheimer's disease due to increased β-amyloid deposition, compared to non-carriers [39].

In a study of an analogous cohort, this conclusion was confirmed following acute physical exertion. Moreover, the group of patients with the APOE4 burden exercising at high intensity (robust increased flow in the middle cerebral artery) achieved higher scores in cognitive tests (Stroop test), despite increased β-amyloid burden, compared to both the "APOE4 carrier + low-intensity exercise" group and the "APOE4 non-carrier + high-intensity exercise" group. The above results demonstrate the key neuroprotective role of physical activity. An efficient cerebral vascular response may increase the brain's resistance to the chronic, neurotoxic effect of β-amyloid deposition. The APOE4 genotype appears as a crucial modulator that can intensify the negative effect of low physical activity or amplify the positive impact in patients engaging in moderate to intense exercise [40]. Although the APOE4 genotype appears to be a fundamental modulator of the interaction between physical activity and pathophysiology, recent studies demonstrate that women with two copies of the APOE4 allele experience a significantly faster age-related decline in cognitive function than men with the same genotype [41]. In the heterozygous state, a higher level of neurodegeneration was observed in them, even at the same level of β-amyloid in CSF [42].

In light of these results, it is justified to state that women may be the primary beneficiaries of the positive impact of physical activity on the prevention of Alzheimer's disease. This is confirmed by the Wang Y study, which demonstrated the preventive character of regular moderate-to-vigorous physical activity (MVPA) when performed for 300 minutes per week or more. However, upon stratification by sex, this effect remained statistically significant exclusively for women, becoming more pronounced when exceeding 600 minutes per week [43].

Physical activity provides a universal benefit. Analysis of the study conducted by Gonneaud et al. showed that higher activity levels preserve gray matter volume and increase glucose metabolism in the cingulate gyrus in both genders. However, the patient's sex determines the biological pathways of these protective mechanisms. This dimorphism in women manifests in

their brain hemodynamic response: increased perfusion in the precuneus/posterior cingulate gyrus region was observed exclusively in women, allowing them to maintain cognitive proficiency despite potential pathological changes [44,45].

In men, the mechanism appears to be more directly targeted at pathology (lower amyloid burden values retained statistical significance exclusively in this group), and particular emphasis should be placed on maintaining good physical condition. Male patients with low mobility were characterized by a much more rapid decline in cognitive functions compared to an analogous group of women, who underwent slower deterioration [44,45].

Type and Dose of Training

Both aerobic and resistance training effectively inhibit cognitive deterioration. In light of recent studies, new directions are emerging regarding the type of physical activity, especially those simultaneously combining physical effort with concentration and pattern memorization. Mind-body exercises are a type of activity that combines precise movement with breathing techniques and emphasizes mindfulness during execution [46]. Researchers demonstrate not only their positive impact on cognitive function preservation but also their superiority over classical moderate-intensity aerobic training, which will be presented later in this chapter.

In studies of patients diagnosed with amnestic mild cognitive impairment (aMCI), the release of neuroprotective mediators and the modulation of cognitive functions were analyzed under the influence of aerobic and resistance exercises, and in a control group whose lifestyle did not change [47] or was modified by low-intensity effort [48]. In both intervention groups, reaction time shortened (Flanker Test); however, aerobic training was associated with a statistically significant increase in the release of BDNF, IGF-1, and potentially VEGF ($p=0.050$), whereas resistance training resulted only in the mobilization of IGF-1[47]. In a 16-week observation, the effect of cognitive function stimulation was maintained; however, in the aerobic exercise group, IGF-1 release lost significance, and in the resistance group, it approached statistical significance ($p=0.052$) [48].

Thus, the effect on cognitive functions is significant in both physical activity models; however, at the molecular level, they act via distinct pathways. Between aerobic and resistance efforts, a combination of both seems most appropriate, ensuring a various approach to attenuating cognitive function loss.

An alternative to classical physical exertion remains multimodal training, encompassing aerobic, neuromotor, cognitive, and social domains. A study conducted by Chen et al. evaluated whether a Mind-Body exercise, such as Tai Chi Chuan, shows superiority compared with

traditional aerobic training. A cohort of 328 patients with mild cognitive impairment and type 2 diabetes were randomized into three parallel groups: Tai Chi Chuan exercises, moderate-intensity walking, and a control group whose lifestyle did not change. In the intervention groups, the scope of physical effort was defined as three training sessions per week, each lasting 60 minutes, for a period of six months. Analysis of the results of the cognitive function test battery performed 12 weeks after the end of the intervention showed a statistically significant point difference favoring Tai Chi over both the control and the fitness walking groups (24.67 versus 23.84 in the walking group and 22.77 in the control group) on the Montreal Cognitive Assessment scale. Moreover, Mind-Body training improved immediate and delayed memory (Wechsler Memory Quotient), shifting ability (Trail-Making-Test part B), and processing speed (Digit Symbol Substitution Test) compared with the control group, whereas classic aerobic training demonstrated superiority only in inhibiting cognitive deterioration. The absolute difference between intervention groups may not appear impressive; however, the Tai Chi Chuan group's advantage of 1.90 points over the control and 0.84 points over the fitness walking group constitutes a promising effect, considering that individuals with MCI lose an average of 0.52 points on the MoCA annually [49].

The multimodal approach also showed efficacy through choreography training.

In individuals attending one-hour dance classes twice a week, a greater beneficial effect on cognitive functions was observed than in a group practicing classic aerobic-resistance training with dual-task elements (e.g., fitness walking and repeating city names). Dance is a complex sensory-cognitive training requiring the acquisition of new motor skills. The dance group achieved significantly greater improvement in the storage and retrieval of memory traces (Wechsler Memory Scale-Third Edition: Verbal Recognition Memory) than the second intervention group (aerobic-resistance). The ability to recall from visual memory and consolidation (Repeatable Battery for the Assessment of Neuropsychological Status: Visual Delayed Recall) increased following each type of intervention, yet only by approximately 27% in the aerobic-resistance group, versus approximately 40% in the dance group [50].

The positive impact of implementing a cognitive and/or social component into classic aerobic-resistance training seems indisputable. It promotes various types of memory, its consolidation, and supports information processing abilities. Promising results from extensive studies by researchers worldwide should provide an impetus for creating diversified training plans that activate protective mechanisms through multiple pathways.

Conclusions

Physical activity constitutes a key, non-pharmacological strategy modifying the course of Alzheimer's disease. In the MCI phase, it may possibly delay conversion to the fully symptomatic form of the disease by as much as 8 to 24 months, and neuroprotective effects persist even after the cessation of regular physical effort. Conversely, in diagnosed AD, systematic training appears to be a necessary condition for maintaining the efficacy of inhibiting cognitive deterioration. Recent studies indicate the superiority of high-intensity multimodal training. The concurrent engagement of the motor and cognitive spheres yields significantly better effects than simple interventions. However, the current evidence base has limitations. Many studies are conducted on small samples or with short follow-up periods, limiting the ability to assess long-term intervention effects. In addition, differences in PA protocols and participant characteristics make direct comparison and synthesis of results challenging. The efficacy of physical effort is also mediated by individual factors, such as sex or the carriage of the APOE4 gene allele. Despite the well-established positive influence of physical activity among populations of AD patients and individuals at risk for this condition, particularly positive effects are observed among individuals carrying the APOE4 variant; furthermore, there are indications of sexual dimorphism in the scope of protective mechanisms induced by physical effort.

Disclosure

Authors' Contributions

Conceptualization was done by Jakub Kaźmierczyk; methodology by Jakub Kaźmierczyk and Michał Popczyk; software by Jakub Jopek, checking by Aleksandra Marciszewska; formal analysis by Hanna Tymchenko; investigation by Agnieszka Piechowicz; resources by Agnieszka Przybyłowska; data curation by Martyna Świątecka; writing-rough preparation by Ewa Buczkowska; writing-review and editing by Aleksandra Marciszewska; visualization by Jakub Kaźmierczyk and Hanna Tymchenko; supervision by Natalia Popczyk; project administration by Ewa Buczkowska.

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