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Neuroplasticity. How regular physical activity influences the brain's structure and function

Julia Dołęga J.D.
Faculty of Medical Sciences in Katowice, Medical University of Silesia
https://orcid.org/0009-0001-0176-7145
e-mail: julkadolega1@gmail.com

Tomasz Maciejczyk T.M.
Faculty of Medical Sciences in Katowice, Medical University of Silesia
https://orcid.org/0009-0005-2517-2508
e-mail: tomasz.maciejczyk00@gmail.com

Antoni Sieńko A.S.
Faculty of Medical Sciences in Katowice, Medical University of Silesia
https://orcid.org/0009-0001-6753-7895
e-mail: antsienko@gmail.com

Małgorzata Łabuś M.Ł.
Faculty of Medical Sciences in Katowice, Medical University of Silesia
https://orcid.org/0009-0003-2799-4375
e-mail: gosia.labus@gmail.com

Piotr Mól P.M.
SP ZOZ MSWiA w Katowicach im. Sierżanta Grzegorza Załogi: 40-042 Katowice, ul. Wita Stwosza 39-41
https://orcid.org/0009-0006-8007-1934
e-mail:piotrmol1999@gmail.com

Bartłomiej Zabawa B.Z.
Faculty of Medical Sciences in Katowice, Medical University of Silesia
https://orcid.org/0009-0005-2419-4748
e-mail: bartek.zabawa1@gmail.com

Patrycja Hudzińska P.H.
Faculty of Medical Sciences in Katowice, Medical University of Silesia
https://orcid.org/0009-0000-5881-0733
e-mail: patrycjahudzinska@gmail.com

Łukasz Stanisław Papież Ł.S.P.
Faculty of Medical Sciences in Katowice, Medical University of Silesia
https://orcid.org/0009-0000-1235-0057
e-mail: lukaszpap14@gmail.com

Karol Krzykawski K.K.
Faculty of Medical Sciences in Katowice, Medical University of Silesia
https://orcid.org/0009-0007-4497-2927
e-mail: krzykawski1poczta@gmail.com

Jakub Sadowski J.S.
Faculty of Medical Sciences in Katowice, Medical University of Silesia
https://orcid.org/0009-0005-2259-0958
e-mail: medsadowski@gmail.com

ABSTRACT

Introduction: Physical activity is associated with a reduced risk of chronic diseases, including cardiovascular disease, obesity, type 2 diabetes, and cognitive decline. Exercise supports brain health and cognitive function, with potential benefits for neuroplasticity—the brain's ability to reorganize in response to demands and injury.

Materials and methods: A literature review was conducted using Pubmed and Google Scholar database with following search terms: “physical activity”, “neurogenesis”, “BDNF”, “neuroplasticity” and “cognitive function”.

State of knowledge: Neuroplasticity, the brain’s ability to reorganize and form new connections in response to learning or injury, is supported at the molecular level by various factors (e.g. BDNF or VEGF). Aerobic and resistance exercises have been linked to increased gray and white matter volumes, especially in regions critical to memory and executive

function. These effects are valuable in preventing cognitive decline and improving mental health.
Current research has also shown that the impact of exercise on neuroplasticity can be augmented through consistent, high-intensity activity, which supports neuroplasticity through hormone modulation. Furthermore, emerging technologies like neuroimaging have advanced our understanding of the mechanisms underlying exercise-induced brain adaptation, which holds promise for personalized interventions.
Conclusions: This review focuses on the preventive and therapeutic potential of physical activity for neurological health, highlighting the need for continued research into how different forms of physical activity can influence neuroplasticity.

Keywords: neuroplasticity, cognitive functions, mental health, physical activity

INTRODUCTION

Numerous studies indicate that physical activity plays a significant role in lowering the risk of various chronic diseases and conditions. Regular exercise has been associated with a decreased incidence of cardiovascular diseases, obesity, type 2 diabetes, cognitive decline, and other health issues, highlighting its broad benefits for overall health and longevity [1].

Evidence also suggests that physical exercise is an effective means of supporting brain health and cognitive function, both under normal conditions and in the presence of disease. Exercise may even offer protection against cognitive decline and neurodegenerative disorders [2].

The capacity of the nervous system to modify its organization to altered demands and environments has been termed "neuroplasticity", which manifests in several contexts, including the acquisition of new skills, following injury to the nervous system, and as a consequence of sensory deprivation. [3]. Biochemical processes in synapses and other neuronal compartments underlie neuroplasticity. This basic molecular level of brain plasticity covers numerous specific proteins (enzymes, receptors, structural proteins, etc.) participating in many coordinated and interacting signal and metabolic processes, their modulation forming a molecular basis for brain plasticity [4].

Recent studies demonstrate the positive impact of physical exercise on structural and functional changes in the brain, therefore this area has garnered increasing attention within the research community. Physical activity broadly impacts brain function and metabolism; according to research, it increases the production of the neurotrophin BDNF, stimulates neurogenesis in the hippocampus, and improves cognitive abilities. [5,6,7]. Other findings indicate that white matter areas susceptible to aging maintain some level of plasticity that can be stimulated through aerobic exercise; consequently, physical activity may play a role in the prevention of dementia [8]. In another study, it was observed that moderate intensity cycling may enhance neuroplasticity in people with stroke. [9].

MATERIALS AND METHODS

In this study, an interdisciplinary approach was utilized, integrating a comprehensive literature review with empirical data concerning the effects of physical activity on brain function and neuroplasticity. Searches were conducted in databases such as PubMed, NCBI and Google Scholar using pertinent keywords, including "physical activity", "neurogenesis", "BDNF", "neuroplasticity" and "cognitive function".

The empirical data analyzed were sourced from clinical and experimental studies, which were critically assessed based on their methodology, participant populations, and therapeutic outcomes. Additionally, a comparative analysis was performed to evaluate the efficacy and safety of both traditional and innovative interventions related to physical activity and their implications for neurological health.

STATE OF KNOWLEDGE

1. Neuroplasticity

The first mentions of neuroplasticity date back to the late 19th century when, in 1894, Spanish Nobel laureate Santiago Ramony Cajal used the term "plasticity" for the first time. Today, there is no clear definition of neuroplasticity; however, it is generally regarded as a broad set of changes in the nervous system throughout the human life or as a response of the nervous system to endogenous or exogenous factors, it involves modifications in its architecture, connectivity, and function [10, 11].

Synaptic neuroplasticity is particularly evident in hippocampal neurons. Long-term potentiation (LTP), which involves repetitive stimulation, leads to the activation of multiple synapses, strengthening of weak stimuli, increased sensitivity of synapses to subsequent stimuli, and structural remodeling of both pre- and postsynaptic elements. The opposite process, long-term depression (LTD), results in reduced synaptic excitability and a loss of dendritic spines. Notably, this process can be reversed by the mentioned LTP. Despite the distinct effects of LTP and LTD, their mutual influence allows for continuous refinement of inter-neuronal connections and plays a role in shaping cognitive processes [12].

Structural neuroplasticity encompasses the previously mentioned synaptic remodeling, which can also be regulated by astrocytes. These cells secrete various factors, such as (Interleukin-1) IL-1, IL-6, IL-8, (Tumor Necrosis Factor α) TNFα, and Nuclear Factor kappa-light-chain enhancer of activated B cells) NFκB, protect neurons from excitotoxicity by maintaining low concentrations of glutamate outside the synapse and control the development of dendritic spines [13].

One of the most commonly observed examples of neuroplasticity occurs during ischemic stroke. In the penumbra region, where ischemic cells remain alive, reperfusion within an appropriate time frame may restore their function. Neural cells surrounding the infarct area can reorganize by forming new synaptic connections. Additionally, cortical adaptation to new post-stroke conditions may involve other brain regions not affected by the stroke, which can take over functions previously managed by the ischemic area [14].

Neuroplasticity is also significant in the context of mental health. In individuals suffering from depression, a reduction in gray matter volume is observed, particularly in the anterior cingulate cortex and hippocampus regions, which correlates with reduced neuroplasticity. Among patients receiving antidepressant treatment, an increase in functional connectivity within the prefrontal cortex and subcortical structures has been observed. Importantly, this enhanced connectivity is associated with an alleviation of disease symptoms.

Short-term, intense stress, accompanied by high cortisol levels, can result in losses in specific brain regions, whereas prolonged stress can lead to the development of new synapses and dendritic processes within the amygdala, which reinforces the tendency to focus on negative emotions [15].

2. The physiology of exercise-induced neuroplasticity

Neurotrophins are proteins that ensure the development and function of neurons. This group includes the Nerve growth factor (NGF), neurotrophins-3 (NT-3), NT-4, NT-5, NT-6 and the Brain-derived neurotrophic factor (BDNF) [16]. Throughout embryonic and postnatal development, neurotrophins play a crucial role in neuronal survival, differentiation, and specification. In the adult nervous system, these proteins help regulate or initiate rapid synaptic responses and alter the function of synapses and the structure of neurites. As a result, they impact cognition, behavior, learning, and memory formation [17,18].

BDNF influences neurogenesis, by increasing neuronal growth and modulating dendritic growth patterns, thus achieving greater dendritic length [16]. Furthermore BDNF affects synaptic plasticity through increased NMDA levels, higher intracellular calcium storage [19] and decreased blockage of magnesium related NMDA receptors [20]. Additionally BDNF acts as a protector of neuronal cells [16].

Engaging in exercise forces the body to adapt to the new performance requirements. This process also affects cognitive function via angiogenesis and neurogenesis. Jeremy J. Walsh and Michael E. Tschakovsky reported that performing physical activity stimulates the release of BDNF [21], therefore promoting brain tissue repair and remodeling [22]. What is more, physical exercise contributes to rise in Vascular endothelial growth factor (VEGF) levels in the hippocampus [23]. On top of that, exercise boosts the release of Insulin-like Growth Factor 1 (IGF-1) into the bloodstream. Elevated levels of IGF-1 in circulation result in higher concentrations in the brain, as this factor can cross the blood-brain barrier. In addition to working alongside other growth factors, IGF-1 promotes re-innervation and the repair of olivo-cerebellar pathways, enhances vascularization, and amplifies synaptic efficiency and neural communication [24,25,26].Physical activity also ensures increased cerebral blood supply by raising the nitric oxide production, hence proving its significance in neuroplasticity [25].

3. Brain structure changes as a product of exercise

Physical activity, especially aerobic and resistance training, exerts a substantial influence on brain structures, resulting in a variety of adaptive changes at both the macrostructural and microstructural levels [27,28]. It affects not only specific brain structures but also the overall volume and organization of gray and white matter [29,30,31]. Physical exercise promotes synaptogenesis, leading to an increase in neural connections and improving the efficiency of information processing [32].

In the hippocampus, which plays a key role in memory processes and the regulation of emotional responses, neurogenesis can occur as a result of physical activity, particularly aerobic exercise, leading to the formation of new neurons, especially in the dentate gyrus region [33]. In studies conducted on mice, it was observed that running exercises significantly improved spatial learning and memory capabilities by increasing the overall number of dendritic spines and the levels of PSD-95 and Synapsin Ia/b proteins. Additionally, there was an observed enhancement in the colocalization of PSD-95 with neuronal dendrites (MAP-2) and an increase in the number of astrocytes associated with PSD-95 (GFAP) within the hippocampus of these animals [34].

Conversely, Tarkka et al. [35] In a study conducted on a group of 45 healthy male monozygotic twins (mean age 34.5 ± 1.5 years), the authors analyzed the impact of differences in physical activity levels on brain structures and sensory functions. The results indicated that more physically active twins exhibited greater gray matter volume in the striatal, prefrontal, and hippocampal regions, along with reduced volume in the anterior cingulate cortex. These findings suggest that enhanced aerobic capacity may positively influence brain morphology and sensory functions, particularly in regions associated with motor control and memory functions.

Aerobic exercises, including running, swimming, and cycling, provide a range of neurobiological benefits by increasing cerebral blood flow and enhancing neuronal nutrition [36,37]. Regular physical activity stimulates the secretion of brain-derived neurotrophic factor (BDNF), is essential for neurogenesis and synaptic plasticity in the hippocampus, cerebellum, and frontal cortex. This mechanism enhances neuronal connectivity and facilitates the brain's adaptation to novel cognitive challenges [38,39].

Although strength training primarily targets muscular strength development, it also significantly impacts cognitive function. Research indicates that resistance training can contribute to an increase in gray matter volume, particularly in brain regions associated with working memory and attentional processes [30,40]. These exercises may also stimulate an increase in IGF-1 levels, which is essential for the proper functioning of neurons and is involved in regenerative processes within the brain [39,41]. Strength training may also influence BDNF levels, although this effect is more pronounced with aerobic exercises [39].

4. The impact of physical activity on cognitive functions

Cognitive functions are fundamental elements in the process of perception of our surrounding. The attention of many authors is brought by components of cognitive functions, including executive functioning, memory, attention and thinking [42,43]. Researchers revealed the positive correlation between improvement of cognitive functions and regular physical activity [44, 45, 46, 47, 48]. Physical exercise was found not only to improve memory among children [44] but also to increase the size of the hippocampus and protect against its volume loss enhancing memory function in adults [46].

Some studies were conducted examining children and adolescents with ADHD (attention deficit hyperactivity disorder) and revealed positive impact of aerobic exercises and cognitive-engaging exercises on attention [49,50,51]. Researchers suggest that workout promotes synthesis of BDNF (brain-derived neurotrophic factor) which is crucial for neuroplasticity, raises the secretion of various neurotransmitters such as dopamine and serotonin and increases blood flow in the brain. That can mitigate the symptoms of the ADHD [49] which are inattention, hyperactivity and impulsivity [52].

Cognitive functions can also be impaired in a great amount of mental disorders [53, 54, 55, 56, 57]. One of them is depression, currently around 350 million people on the planet suffer from this condition [58]. Many authors emphasize that regular physical workout not only decreases the risk of development of depression among the healthy population but also improves the quality of life of people with such disorder. [59,60,61]. It is of great importance that appropriately selected exercises carried out in an appropriate environment can be a useful therapeutic tool with a fight against depression and related to it cognitive functions impairment [59,60,62,63,55].

Some studies revealed that physical activity improves cognitive functions in other mental health conditions such as bipolar disorder [64] and schizophrenia, having a positive impact on attention, memory and social cognition [56].

5. Physical activity across different age groups and brain plasticity

Let us examine how physical activity across various age groups has impacted brain plasticity. The study by Fotini Valipoous et al. [65] conducted a meta-analysis on research concerning creativity during physical activities and its impact on cognitive and academic outcomes. A total of 92 studies were analyzed on this topic. Physical activities can be implemented in various ways. The study considered factors such as the diversity of activities, their reduced reliance on technical skill acquisition, instruction, or demonstration, their occurrence in open spaces with props, and their inclusion of peer interactions. Interestingly, the results did not show an association between physical activities and greater positive impacts on executive functions, academic achievement, or fluid intelligence. Although the findings may seem somewhat disappointing, it is worth noting that the analyzed studies lacked diversity in their methodologies. Therefore, we should await more robust studies in this field.

An interesting study is the prospective, single-center, randomized PASTEC trial, [66] which uses a cross-over design to compare the effects of two types of training in children with cancer: pure physical training versus a combination of physical and attentional training. Unfortunately, despite promising results in the pre-cross-over phase, the primary endpoint was not achieved in the post-cross-over phase. Nonetheless, significant improvements were observed in areas such as anxiety, emotional control, organizational skills, and motor deficits. No significant differences were found between the pure physical training group and the physical-attentional group.

In the context of adult populations, a notable study conducted by Rongrong Chen et al. [67] investigated the effects of physical activity on individuals with insomnia. At the level of brain circuitry, patients suffering from insomnia exhibited reduced connectivity within the extensive motor network. Following a structured exercise intervention, participants in the exercise group demonstrated a statistically significant improvement in self-reported sleep quality compared to those in the waitlist control group. Furthermore, there was a significant increase in functional connectivity between the motor network and the cerebellum in the exercise group. Notably, the study identified significant correlations between enhancements in subjective sleep measures and alterations in connectivity within the motor network, underscoring the potential role of physical activity in modulating brain function and improving sleep outcomes in this population.

Cognitive inhibition is a vital aspect of our lives, encompassing the ability to regulate thoughts, cognitive responses, and reactions to cognitive stimuli. Motor inhibition helps us for example stop an ongoing movement actions [68], allowing for the adaptation or stopping of actions to suit the situation or goal. In cognitive terms, inhibition blocks the spread of neural impulses between brain areas necessary to complete a specific task [69], enhancing focus and supporting goal-directed behaviors.

In a study conducted by Yael Netz et al. [70], adults aged 40 to 60 were randomly assigned to either an experimental group or a control group. One to two weeks after the initial assessment, participants were tasked with completing a three-limb (3-Limb) inhibition task and a verbal version of the Stroop test, both before and after engaging in moderate-intensity acute aerobic exercise (for the experimental group) or resting (for the control group). Both groups demonstrated a similar level of improvement from the initial assessment to the pre-test. However, the experimental group exhibited a notable trend toward improvement in both cognitive and motor tasks between the pre-test and post-test, although this was not statistically significant. Additionally, exploratory analysis revealed significant differences favoring the experimental group among highly fit participants on the 3-Limb task. A significant correlation was identified between the inhibition conditions, linking choices in motor inhibition to incongruent colors/words in cognitive inhibition, particularly regarding the improvements observed after exercise. It appears that individuals with higher fitness levels benefit more from exercise compared to those with lower fitness levels. Moreover, performance on behavioral tasks representing both motor and cognitive inhibition is interrelated. This observation suggests that fitness levels and acute exercise play a role in the connection between cognitive and motor inhibition.

An interesting study called "ACTIVE" [71] was conducted among seniors aged 65 and older. The aim was to evaluate the effectiveness of interventions focused on memory, reasoning, and visual processing speed in maintaining cognitive health and functional independence in older adults. Notably, individuals were excluded from the study if they had significant cognitive impairments (a score of less than 23 on the Mini-Mental State Examination), functional limitations (dependence or regular assistance with daily activities as measured by the Minimum Data Set Home Care), self-reported diagnoses of Alzheimer's disease, stroke within the past year, or certain cancers, current chemotherapy or radiation therapy, or poor vision, hearing, or communication skills that could interfere with the interventions or outcome assessments.

A total of 2,802 participants were enrolled, with an average age of 74 years, an average education level of 13 years, 74% identifying as white, 26% as African American, and 76% being women [71]. Each intervention led to immediate improvements in the targeted cognitive abilities, and these benefits were sustained for five years. The training produced effects specific to each skill. The most significant improvements were observed in the group focused on processing speed, followed by those in the reasoning and memory groups. Each type of training yielded its greatest effects right after the intervention, although there was some decline over time. Moreover, older adults who completed cognitive processing speed training were 40% less likely to stop driving in the subsequent three years and experienced 50% fewer traffic accidents over six years compared to the control group!

6. The importance of regularity and type of exercise for neuroplasticity

The effectiveness of physical exercise in preventing neurodegeneration and maintaining neuroplasticity heavily depends on the regularity of activity. Regular training reduces chronic oxidative stress, supports mitochondrial biogenesis, regulates levels of pro-inflammatory cytokines in the hippocampus, and promotes the expression of neurotransmitters (serotonin and dopamine) as well as neurotrophic factors like BDNF and GDNF [72]. Regular aerobic exercise increases hippocampal volume, which is critical for memory and learning abilities [73]. Numerous studies seem to confirm the significant role of exercise regularity in promoting neuroplasticity. In one such study, Mingming Zhao et al. describe significant improvements in balance, motor disturbances, and cardiac function among Parkinson's disease patients who engaged in exercises like swimming and spinal stretching for 30 minutes daily over a year, compared to a control group that did not exercise regularly [74].

Similarly, Kristine Hoffman et al. conducted a randomized study of 200 patients with mild Alzheimer's disease, assigning them to a supervised aerobic exercise group (60-minute sessions three times a week for 16 weeks on a cycle ergometer, elliptical trainer, or treadmill) and a control group. Exercising patients scored better on the NPI-Q test, assessing neuropsychiatric functions. In a subgroup of patients who exercised more intensively, there was a significant improvement in the SDMT test, which evaluates cognitive functions, compared to baseline and the control group [75]. These findings highlight the importance of maintaining a training frequency of at least several times per week for a period no shorter than a few months.

Hoffman's study also addresses another critical aspect of physical exercise in neuroplasticity: intensity and duration. The study defined the higher-intensity group as those attending over 80% of sessions and exercising at 70-80% of maximum heart rate (HR) [75]. This and several other studies suggest greater benefits from maintaining regular physical activity at an intensity between 70% and 80% of maximum HR, lasting from 30 minutes to an hour daily [73, 74, 75].

Aerobic training is undoubtedly at the forefront of physical activities impacting neuroplasticity. Aerobic exercises improve cerebral blood flow, directly stimulating the production of BDNF, a key factor in learning and memory processes [76, 77]. The undeniable dominance of aerobic exercises over other training forms is further confirmed by studies like the one by Arthur F. Kramer et al., who compared 24 adults aged 60 to 75 with previously sedentary lifestyles, randomly assigning them to aerobic (walking) or anaerobic (stretching and toning) exercises, performed regularly over six months. They found that those in the aerobic group showed a significant improvement in tasks requiring executive control compared to the anaerobic group [78].

Nonetheless, regular anaerobic exercise also provides benefits, such as stimulating the production of hormones like testosterone and IGF-1, which influence neuroplasticity by enhancing cell proliferation and preventing apoptosis [79, 80]. A study by Ricardo S. Cassilhas et al. demonstrated improvements in memory performance and verbal concept formation among 62 older men aged 65 to 75 who participated in moderate- or high-intensity resistance training three times per week for six months [81].

Considering different types of physical activities, the distinction between team and individual sports is noteworthy. Physical activity from each spectrum influences neuroplasticity, although team sports affect it somewhat differently. Torbjörn Vestberg et al. presented an interesting perspective on cognitive function development by analyzing football players. They observed superior executive function skills in athletes of this sport compared to non-team-sport participants. Such skills may translate to greater overall adaptive cognitive abilities compared to those practicing individual sports [82].

7. Sports as a component of neuroplastic therapy

Low physical activity throughout life may increase the risk of brain diseases such as stroke, Alzheimer's disease, and Parkinson's disease [83]. Therefore, in the context of central nervous system diseases, prevention through regular physical activity is crucial. The American Heart Association (AHA) recommends regular aerobic exercise as part of both prevention and treatment for stroke [84].

Rehabilitation is thus one of the main therapeutic methods for patients recovering from stroke. In addition to aerobic exercises, it includes task-oriented therapy as well as isometric, isokinetic, and isotonic training [85]. Rehabilitation is essential for minimizing the effects of stroke, and patients who undergo regular, professional therapy after the acute phase of a stroke typically recover more quickly. A study by Winstein et al. found that participation in an aerobic exercise program leads to improvements in both motor and cognitive functions in post-stroke patients [86].

Positive effects of aerobic exercise are also observed in patients following a concussion. In a study by John J. Leddy et al., the use of aerobic exercises as therapy helped improve CO_2 sensitivity, often impaired in this type of injury, leading to normalization of $PaCO_2$, exercise ventilation, and exercise tolerance [87].

Furthermore, a study by Gąsior et al. demonstrated that strength training can be an effective rehabilitation method for adults with cerebral palsy, which may also be relevant in the context of post-stroke rehabilitation [88].

Physical activity also contributes to a statistically significant improvement in cognitive function in neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Huntington's disease, as well as in psychiatric disorders like depression and schizophrenia [74,75,89].

8. The future of research on neuroplasticity and sports

The future of research on neuroplasticity in relation to sports is poised for significant advancements, particularly through the integration of modern technologies and methodologies. Neuroimaging techniques such as functional Magnetic Resonance Imaging (fMRI), Diffusion Tensor Imaging (DTI), and Positron Emission Tomography (PET) are becoming increasingly essential in understanding the brain's adaptive responses to physical activity. These imaging modalities allow researchers to visualize changes in brain structure and function associated with neuroplasticity, providing insights into how exercise can enhance cognitive and motor performance [90,91].

Moreover, the incorporation of biomarkers and electroencephalography (EEG) will facilitate a deeper understanding of the physiological changes that accompany neuroplastic adaptations. Biomarkers can help identify individuals who are more likely to benefit from specific training regimens, while EEG can provide real-time data on brain activity during physical exertion, thereby linking cognitive processes with motor functions [90,92].

In terms of health prevention and training optimization, emerging technologies such as virtual reality (VR) and wearable devices are transforming how athletes train and recover. VR can simulate various training environments, allowing for controlled studies on how different stimuli affect neuroplasticity.

Wearable technology provides continuous monitoring of physiological parameters, enabling personalized training adjustments based on real-time data [93,94]. Additionally, mobile applications can deliver tailored exercise programs that promote neuroplastic changes through structured physical activity.

Despite these advancements, the relationship between physical activity and neuroplasticity remains an area of exploration with considerable potential. Current research indicates that while exercise induces beneficial neuroplastic changes, the underlying mechanisms are not fully understood. This suggests a need for further studies to elucidate how different forms of physical activity influence brain plasticity across various populations. Understanding these mechanisms will be crucial for optimizing training protocols and maximizing the benefits of neuroplasticity in sports settings [92,95].

CONCLUSIONS

Physical activity plays a vital role in promoting neuroplasticity and cognitive health, offering protective effects against neurological disorders and mental health conditions. Aerobic and resistance exercises, particularly when regular and moderately intense, support brain adaptation through increased neurogenesis, synaptic plasticity, and neurotrophic factor expression. These changes enhance brain structure and function, particularly in memory and executive regions. Advanced technologies, including neuroimaging, provide insight into exercise-induced brain adaptations, opening paths for personalized therapies. Despite progress, further research into how different forms of physical activity can influence brain functions is needed to optimize exercise protocols for neuroplasticity across diverse populations.

In summary, structured physical activity represents an effective, non-invasive approach to preserving cognitive health and enhancing resilience against the effects of brain aging and neurodegenerative diseases.

Authors' Contributions Statement:

- **Conceptualization:** J.D.
- **Data Curation:** J.D., P.M., Ł.S.P., T.M., A.S., M.Ł., B.Z., P.H., K.K.
- **Formal Analysis:** J.D., P.M., Ł.S.P., T.M., A.S., M.Ł., B.Z., P.H., K.K., J.S.
- **Investigation:** J.D., P.M., Ł.S.P., T.M., A.S., M.Ł., B.Z., P.H., K.K., J.S.
- **Methodology:** J.D., P.M., Ł.S.P., T.M., A.S., M.Ł., B.Z., P.H., K.K., J.S.
- **Project Administration:** J.D., Ł.S.P., P.M.
- **Resources:** J.D., P.M., Ł.S.P., T.M., A.S., M.Ł., B.Z., P.H., K.K.
- **Software:** J.D., P.M., Ł.S.P., T.M., A.S., M.Ł., B.Z., P.H., K.K., J.S.
- **Supervision:** J.D., P.M., Ł.S.P., T.M., A.S., M.Ł., B.Z., P.H., K.K., J.S.
- **Validation:** J.D., P.M., Ł.S.P., T.M., A.S., M.Ł., B.Z., P.H., K.K., J.S.
- **Visualization:** J.D., P.M., Ł.S.P., T.M., A.S., M.Ł., B.Z., P.H., K.K., J.S.
- **Writing – Original Draft:** J.D., P.M., Ł.S.P., T.M., A.S., M.Ł., B.Z., P.H., K.K., J.S.
- **Writing – Review & Editing:** J.D., P.M., Ł.S.P., T.M., A.S., M.Ł., B.Z., P.H., K.K., J.S.

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