

## REVIEW ARTICLE

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## Healing through movement: narrative review on exercise and neurological disorders

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### Abstract

**Background** Exercise has great potential for enhancing brain health and preventing or treating neurological conditions. Three molecular pathways have been identified: neuroprotection, neurotrophic factor increase, and neurotransmitter modulation.

**Methodology** We reviewed PubMed, Scopus, and Google Scholar according to PRISMA criteria. The inclusion criteria included studies with peer review providing molecular insights into the effects of exercise on brain function.

**Results** Through neurotrophic factors, neurotransmitter modulation, mitochondrial biogenesis, and neuroprotection, exercise benefits brain function. These modifications are correlated with better mood management, enhanced cognitive function, and the prevention of neurodegenerative diseases.

**Conclusion** The various benefits of exercise on neurological disorders and brain health are highlighted in this study, with particular attention to key molecular pathways. Exercise is a vital tool in the management of neurological health.

**Key words** exercise, neuroprotection, prisma guidelines, neuro modulation, synaptic plasticity

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## Introduction

Numerous beneficial impacts of physical exercise on the brain have been demonstrated, including enhanced neuroprotection, neuroplasticity, and improved cognitive performance [1, 2]. These impacts have been seen in both healthy persons and those with neurological diseases, from early infancy until old age [3]. Exercise affects brain function through molecular pathways that are being illuminated by recent research, although the mechanisms behind these effects remain unclear [4, 5].

The goal of this study is to present an overview of the current state of knowledge about the molecular mechanisms that explain exercise's positive effects on neurological diseases and brain function. Firstly, we will recap the benefits of physical activity for brain health and its possible effects on neurological conditions. After that, we will review a few of the molecular mechanisms that have been connected to mediating the impact of physical activity on the brain. To be more precise, we will discuss how exercise-induced modifications in brain function are influenced by substances such as neurotrophins, growth factors, and inflammatory cytokines.

## Background

For decades, Exercise has been acknowledged as a vital part of a healthy lifestyle, having advantages for managing weight, cardiovascular health, and overall health [6-8]. In recent times, studies have emphasized the significance of physical activity for neural functions in the brain, such as memory, learning, and emotional control [9-11]. These positive effects have been seen in both neurologically ill and neurologically healthy people, indicating that exercise may have a wide range of impacts on brain health as well as the prevention and management of neurological disorders.

Exercise may have a positive impact on neuroplasticity, the brain's capacity to adjust and change in response to experience [12]. Exercise has been shown to support the growth and branching of dendrites, the structures on neurons that receive inputs from another neuron, which is thought to underlie learning and memory processes, as well as to increase the production of new neurons in the hippocampus, a brain region crucial for learning and memory [13-15].

Exercise may also promote neuroprotection, the ability of the brain to resist damage and injury [3]. Exercise has been shown to protect against the loss of neurons and synapses in animal models of neurological disorders such as Alzheimer's disease and Parkinson's disease [16, 17]. Additionally, inflammation is a major cause of neurodegeneration and cognitive loss; exercise may help minimize this.

Recent studies have started to uncover potential molecular pathways that could mediate the benefits of exercise on the brain, even though the precise mechanism underlying these effects is still not entirely understood. These pathways comprise growth factors, inflammatory cytokines, and neurotrophins, among other substances. Comprehending these basic mechanisms could facilitate the identification of novel targets for therapies intended to enhance cognitive performance and prevent or treat neurological conditions. Furthermore, the significance of individual variations in the way each person responds to exercise is being increasingly acknowledged. To maximize brain function, tailored exercise interventions may be required, as some people may respond better to exercise than others. Future studies should focus on determining the molecular mechanisms that underlie individual variations in how the body responds to exercise.

## Methodology

### Objective

Using PRISMA criteria, a narrative review was conducted to thoroughly evaluate the positive effects of exercise on brain function and its implications for the prevention and treatment of neurological disorders (**Figure 1**).

### Search strategy

We conducted a thorough search of electronic databases, which included PubMed, Scopus, and Google Scholar, to find pertinent publications published between 2000 and 8th January 2023. Phrases like "brain function," "exercise," "neurological disorders," "synaptic plasticity," "neurotrophic factors," and associated phrases were utilized.

### Inclusion criteria

Studies on the impact of exercise on brain function and neurological diseases. Research papers that are published in journals with peer review. Research presents molecular perspectives on the modifications in brain function brought about by exercise. Papers composed in the English language.

### Exclusion criteria

Reviews, opinion pieces, and non-research publications. Studies that lack adequate mechanistic or molecular details. Full-text versions of the articles are not accessible.

### Study selection

The title and abstract are reviewed independently by two reviewers to ensure relevancy. Final inclusion was determined by evaluating full-text articles that satisfied the inclusion criteria.

### Data extraction

Using a standardized form, data were gathered on research parameters, participant demographics, exercise interventions, detected molecular changes, neurological outcomes, and pertinent findings.

### Quality assessment

By using the proper tools, the methodological quality of the included studies was evaluated, considering variables including research design, methodology, and bias.

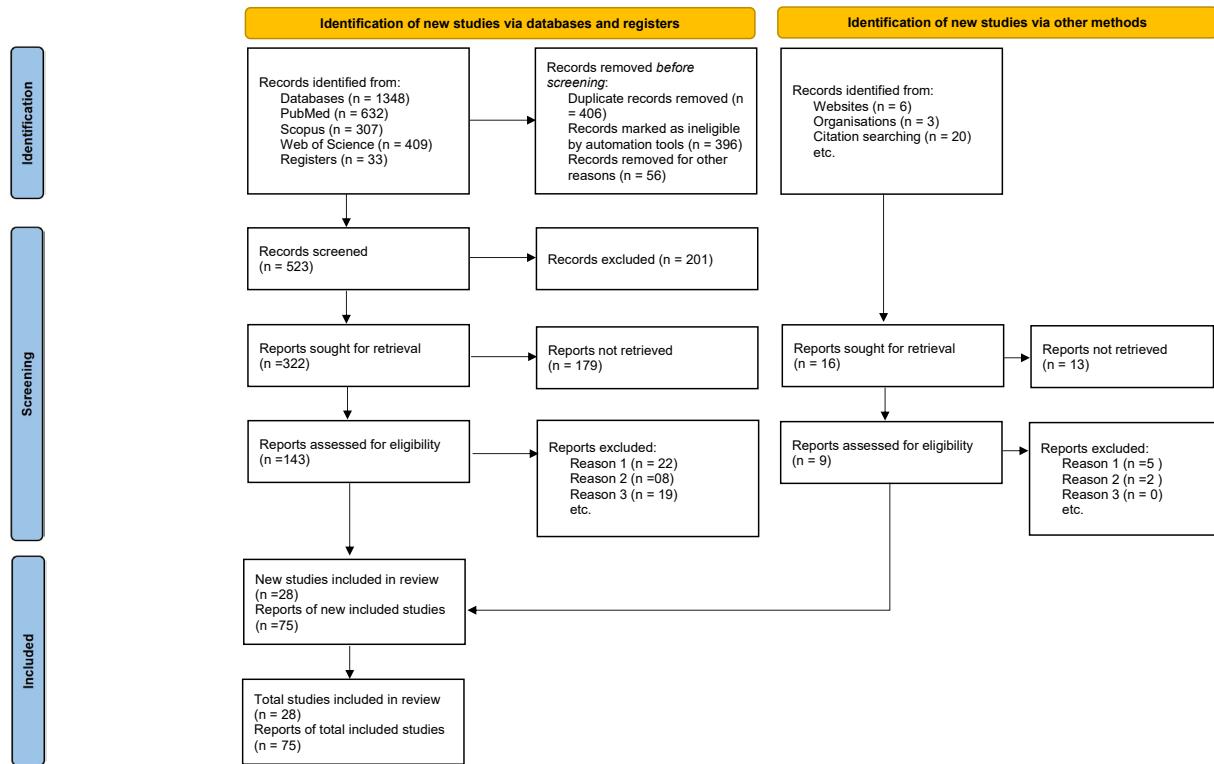
### Data synthesis

A narrative synthesis was carried out to provide an overview of the molecular pathways that have been found to underlie the effects of exercise on neurological diseases and brain function. The results were arranged into logical themes.

## Results

### Effects of exercise on brain structure

It has been discovered that exercise has beneficial impacts on the structure of the brain, including modifications to neuronal connections, gray matter density, and brain volume [18]. The hippocampus, a major brain area involved in memory and learning, has been demonstrated to increase in volume with



**Figure 1. PRISMA 2020 flow diagram for updated systematic reviews, which included searches of databases, registers, and other sources.**

exercise [19, 20]. A study by Erickson et al. (2011) found that older persons who engaged in a year-long program of moderate-intensity aerobic exercise had higher hippocampus volumes than the control group [21]. Similar results from animal studies have been observed that Exercise has been shown to improve the production of new neurons in the hippocampus [22].

Exercise may also have an impact on other brain regions, such as the basal ganglia, which control movement, and the prefrontal cortex, which is related to executive function. Prefrontal brain volume was higher in older persons who completed a six-month aerobic exercise program than in the control group, according to a study by Colcombe et al. (2006) [23]. Additionally, it has been discovered that exercise increases the density of gray matter in specific brain regions, including the anterior cingulate cortex and the prefrontal cortex [24, 25]. This rise in gray matter density could be a reflection of enhanced information processing and brain connections in these areas [26, 27].

Exercise has been shown to improve brain function and cognition in addition to structural alterations. For instance, a single session of moderate-intensity aerobic exercise enhanced preadolescent children's cognitive control and information processing, according to a study by Hillman et al. (2008) [28]. Adult working memory, executive function, and attention in both children and adults have all been demonstrated to be enhanced by exercise.

Exercise appears to have a variety of beneficial impacts on brain structure and function overall, including increases in brain capacity, gray matter density, and neural connections. Exercise's positive benefits on cognition and its ability to prevent age-related cognitive decline and neurological illnesses may be explained by these changes.

#### *Effects of exercise on brain function*

Studies have indicated that physical activity has a variety of advantageous impacts on mental and emotional functions, in addition to physiological alterations in the brain [29].

It has been demonstrated that exercise elevates the synthesis of neurotransmitters like dopamine and serotonin, which play a role in mood, motivation, and emotional stability [30, 31]. It is well known and has been thoroughly researched how dopamine receptors affect the excitability of membrane potentials in striatal neurons [32, 33]. Through a complex process, D1 and D2 receptors modulate motor activities by influencing the excitatory transmission between post-synaptic striatal GABAergic neurons and presynaptic cortical glutamatergic neurons [33]. This complex interaction is essential in determining motor function and coordination. Extensive research on rodents has yielded important insights into the brain's response to sustained exercise. Numerous levels of modifications, including neuroanatomical, neurochemical, and cellular/molecular ones, were identified by these studies [34, 35]. Animal studies investigating the impact of exercise on the brain have shown structural modifications at the molecular (changes in neurotransmission, elevated neurotrophic factors) and cellular (neurogenesis, gliogenesis, synaptogenesis, angiogenesis) levels [36]. Behavioral tasks, particularly spatial tasks, have been used to assess functional activity and aid the study of spatial cognitive skills [32]. These studies offer helpful information about the positive effects of exercise on cognition.

Another study discovered that daily exercise could enhance serotonin availability by increasing the density of serotonin transporters in the brain [37]. The ability to decrease adenylyl cyclase activity is the primary characteristic shared by all six subtypes of the 5-HT1 receptor family (5-HT1A–F), which are members of the Gi-coupled receptor class. The 5-HT1A receptors are highly expressed in limbic areas, with the hippocampus being one of the most prominent postsynaptic receptor locations. They are also expressed as autoreceptors in the somatodendritic regions

**Table 1. Molecular mechanisms of exercise on brain function.**

Items	Mechanism	Principal contributors and outcomes
Molecular mechanisms of exercise on brain function	Neurotrophins and growth factors	Synaptic plasticity and neuronal development are enhanced by BDNF release.
	Mitochondrial biogenesis and oxidative stress	Preserves neurodegenerative damage and enhances cognitive function. Promotes mitochondrial biogenesis, which increases the production of energy. Lowers oxidative stress by elevating antioxidant enzyme levels.
	Synaptic plasticity and neurogenesis	Exercise promotes neurogenesis and synaptic plasticity. Essential for memory, learning, and preventing neurodegeneration.

of the raphe nuclei [38]. These unique distribution patterns show their importance in a variety of cognitive and affective functions by underscoring their critical role in regulating serotonin signaling and neurotransmission. The principal molecular pathways through which exercise influences brain function, including neurotrophin signaling, mitochondrial biogenesis, synaptic plasticity, and inflammatory modulation, are summarized in **Table 1**.

Additionally, it has been discovered that exercise increases cerebral blood flow [39]. Sustaining normal brain function and vital metabolic processes depends on a constant and regular blood supply to the brain [40]. By improving the delivery of nutrients and oxygen to the brain cells, this enhanced blood flow may improve brain function. Furthermore, exercise can promote the development of new capillaries and blood vessels in the brain, which enhances the transport of nutrients and blood flow [41-43]. Previous research suggests that short-term exercise appears to have no appreciable effect on cerebral blood flow (CBF) or the blood vessels' capacity to adapt to variations in blood flow inside and outside of the brain [44]. Young people exhibited this finding, indicating that CBF is rapidly and reliably modulated following acute exercise sessions. Studies on animals have demonstrated that in rats with bilateral common carotid artery embolism, exercise increases the number of neurons in the hippocampus. Furthermore, it was shown that exercise slowed down the deterioration of cognitive function by promoting neurogenesis, the creation of new neurons, and increasing the expression of BDNF, a protein critical to the health and functionality of brain cells [44].

Exercise also influences the amounts of brain-derived neurotrophic factor (BDNF), a protein that supports the development and survival of neurons, which is another way that exercise can enhance brain function [45]. An increase in brain BDNF levels promotes synaptic plasticity, protects against neurodegenerative diseases, and improves learning and memory. [46, 47]. Strong evidence from recent studies suggests that regular, prolonged bouts of aerobic exercise can cause temporal increases in BDNF levels that were initially induced by acute exercise to proceed even further. This shows that aerobic exercise and the upregulation of BDNF are positively correlated, and this could have important effects on cognitive and brain health [48]. The primary player in the body's stress response is cortisol, a hormone released in reaction to a variety of stimuli, including psychological stress, worry, and terror. Stress also affects brain-derived neurotrophic factor (BDNF) concurrently. Increased stress has been associated with changes in BDNF mRNA, which in turn causes a decrease in BDNF expression. The complex relationship

between BDNF and cortisol offers important insights into the neurobiological processes that underlie the impacts of stress on the brain and its possible impacts on brain health and cognitive function [49]. Zheng and colleagues observed a significant inverse relationship between cortisol and brain-derived neurotrophic factor (BDNF) [50]. Working memory can be understood as the cognitive domain that calls for conscious attention and mental effort, as proposed by Baddeley. Temporary information is actively stored, altered, and processed in this functional space, and it is essential to a variety of cognitive tasks and problem-solving activities [51]. According to Gathercole and Alloway, a person's capacity for working memory and their learning capacity are significantly and intricately related [52].

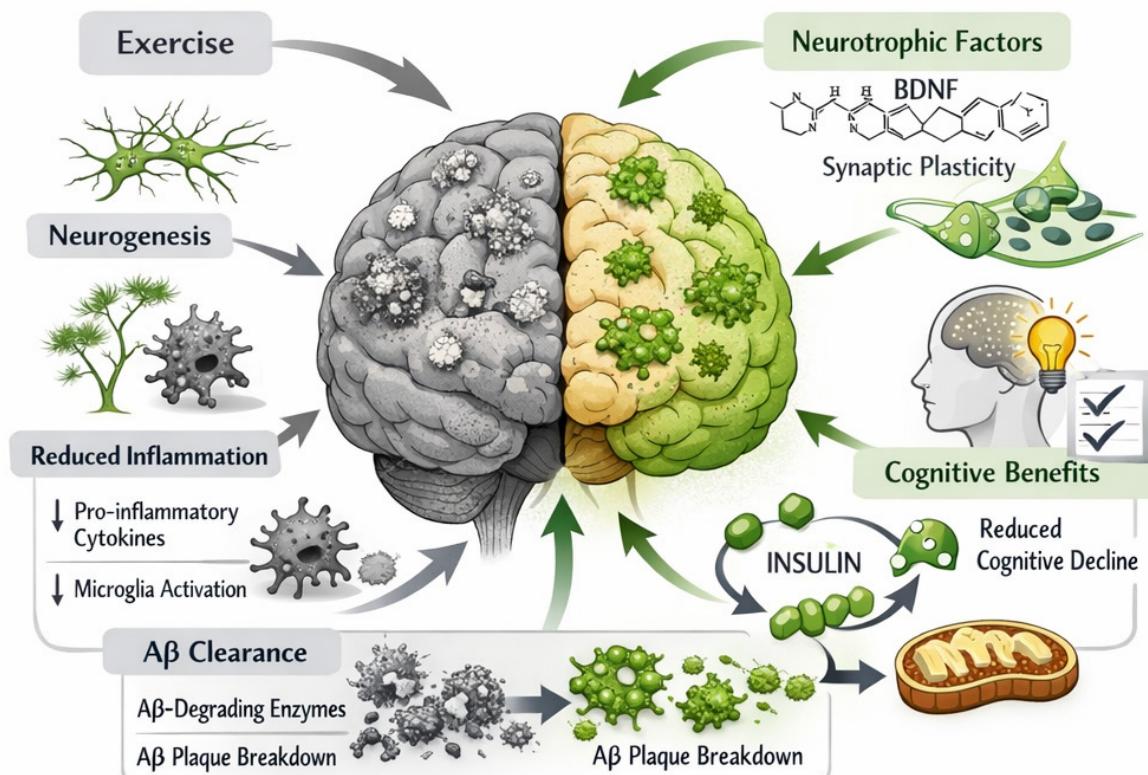
#### *Cognitive benefits of exercise*

Studies indicate that the effects of exercise on cognition may be due to modifications in brain structure and function caused by exercise [53]. The nervous system's ability to adapt and alter in response to events and learning is known as neuroplasticity. This amazing property allows the brain to rewire itself and create new connections, which affects how the brain functions and behaves [54]. Because of this, physical activity is shown to be a very beneficial environmental component that enhances and supports neuroplasticity, which in turn favorably affects the brain's ability to alter and restructure itself in response to experiences and learning. Exercise has been proven in numerous studies to increase the volume of the hippocampus, a part of the brain essential for learning and memory, which may help to explain why exercise can enhance memory function [23, 55]. Exercise has been shown to have positive effects on cognitive performance at every stage of life, from early childhood to old age. Numerous studies have repeatedly demonstrated how exercise improves a range of cognitive functions, promoting brain health and cognitive capacities across the lifetime [56]. The variation noted amongst studies can potentially be linked to distinct factors that attenuate the effects of exercise on cognition. Genetic variations, such as the apolipoprotein E (APOE) ε4 allele and the brain-derived neurotrophic factor (BDNF) Val66Met single-nucleotide polymorphism, can modulate the relationship between exercise and brain health. Genetic influences are among the factors that significantly influence this relationship. Exercise response and its effects on brain function and cognitive ability can be influenced by these hereditary factors [57, 58]. Strong evidence that increased physical activity is substantially associated with a lower incidence

of cognitive decline and dementia was found through a meta-analytic assessment of 21 longitudinal studies including 89,205 persons 40 years of age and older [59]. An additional important meta-analysis including 15 prospective trials, showed that regular physical activity considerably decreased the chance of cognitive decline in participants by 38% [60]. Furthermore, there is strong evidence to support the idea that mind-body workouts can improve older persons' cognitive function. In an extensive meta-analysis carried out by Wu et al. [61], after taking part in 32 randomized controlled trials, older persons with and without cognitive impairment showed exceptional improvements in their learning, verbal fluency, working memory, cognitive flexibility, and global cognition. Zhang et al. conducted an extensive meta-analysis that included 11 randomized controlled trials [62], regardless of the presence of cognitive impairment, mind-body exercise has been shown to have substantial benefits on a range of adult cognitive functions. Notably, benefits were seen in language, learning, memory, executive function, and global cognition.

Exercise can also promote cerebral vascular function, which increases blood flow and oxygen supply to the brain, hence promoting neuronal activity and cognitive performance [63]. Exercise also lowers the risk of cardiovascular disease, oxidative stress, and inflammation, all of which have a detrimental effect on brain function [64]. Risk factors for dementia and cognitive impairment include hypertension, dyslipidemia, diabetes, and hyperinsulinemia. These conditions also increase the risk of cerebrovascular disease and cardiovascular disease. These risk factors compound to degrade brain health, highlighting the need to manage and address vascular health to potentially reduce the risk of dementia and cognitive decline [65]. Researchers found that rising blood pressure and higher fasting blood glucose levels were linked to an increased risk of cognitive impairment and dementia in an extended observational trial that lasted 25 years and involved 3,381 participants [66]. Numerous studies have conclusively demonstrated the positive effects of exercise on cardiovascular and cerebrovascular health [67, 68]. A noteworthy correlation was

## Exercise and Alzheimer's Disease



### Benefits of Exercise in Alzheimer's Disease

Neurotrophic Factors	↑ BDNF, ↑ Synaptic Plasticity
Reduced Inflammation	↓ Pro-inflammatory Cytokines, ↓ Microglia Activation
Aβ Clearance	↑ Aβ-Degrading Enzymes, ↓ Aβ Plaques
Improved Insulin Signaling	↑ Glucose Uptake, ↑ Energy Metabolism

**Figure 2.** Exercise modulates neurotrophic signaling, neuroinflammation, amyloid- $\beta$  clearance, and metabolic pathways to reduce cognitive decline in Alzheimer's disease.

found between physical fitness, cerebrovascular regulation, and cognitive performance by Brown et al. in a cross-sectional study involving forty-two healthy older women [68], and by performing a mediational analysis within their randomized controlled trial (RCT) with 57 older persons, Smiley-Oyen and her team provided more data refuting the cardiovascular fitness hypothesis. The findings demonstrated that those who participated in aerobic exercise showed gains in executive function [69].

### **Molecular mechanisms underlying the beneficial effects of exercise on brain function**

#### *Neurotrophins and growth factors*

Increased synthesis and release of neurotrophins and growth factors is one of the primary methods that exercise supports brain function [70]. In the brain, these proteins are essential for the growth, repair, and survival of neurons. Specifically, the beneficial effects of exercise on brain function have been linked to brain-derived neurotrophic factor (BDNF) [71]. BDNF enhances synaptic plasticity and neurogenesis in addition to promoting the growth and survival of neurons [72]. According to multiple studies, Exercise boosts levels of BDNF in the brain, which has been linked to better cognitive performance and defense against neurodegenerative disorders, including Parkinson's and Alzheimer's [73].

#### *Mitochondrial biogenesis and oxidative stress*

The enhancement of mitochondrial biogenesis and the mitigation of oxidative stress are two additional significant ways that exercise improves brain function [74]. The powerhouses of the cell, mitochondria, are essential for the synthesis of energy. They are also crucial for preserving the homeostasis of cells and guarding against oxidative damage [75]. It has been demonstrated that exercise increases mitochondrial biogenesis, which enhances cellular function and increases energy output. Exercise may decrease oxidative stress by lowering the generation of reactive oxygen species (ROS) and raising the production of antioxidant enzymes [76].

#### *Synaptic plasticity and neurogenesis*

Furthermore, research has demonstrated that exercise promotes neurogenesis and synaptic plasticity, two critical processes for brain health [77]. Neurogenesis is the process through which new neurons are formed in the brain, whereas synaptic plasticity is the capacity of neurons to change their connections in response to experience [78]. Both of these processes are vital for memory and learning, and neurological conditions like Parkinson's and Alzheimer's frequently affect them. Exercise has been demonstrated to increase neurogenesis and synaptic plasticity, which improves cognitive function and guards against neurodegenerative disorders [79].

### **Molecular mechanisms underlying the beneficial effects of exercise on neurological disorders**

#### *Alzheimer's disease and dementia*

1. Neurotrophic factors. Frequent physical exercise stimulates the release of neurotrophic factors, specifically brain-derived neurotrophic factor (BDNF) [80]. BDNF promotes neurogenesis, synaptic plasticity, and neuronal survival [81]. It promotes the growth of new synapses, which enhances cognitive function and

could slow down cognitive aging [82].

2. Inflammation and oxidative stress. Exercise reduces inflammation by changing cytokine profiles and triggering immune cells, such as microglia [83]. By doing this, neuroinflammation is reduced, which minimizes the pathophysiology of Alzheimer's [84]. Exercise additionally strengthens the body's natural antioxidant defenses, preventing oxidative stress from damaging neurons [85].
3. A $\beta$  Clearance: The hallmark of Alzheimer's disease, amyloid-beta (A $\beta$ ) plaques, is eliminated by exercise [86]. It increases cerebral blood flow and upregulates proteolytic enzymes that break down A $\beta$ , making it easier for the brain to eliminate A $\beta$  [87]. Insulin signalling and glucose metabolism. Exercise improves glucose utilization and insulin sensitivity [88]. Exercise promotes neuronal function and indirectly supports brain energy metabolism by improving peripheral insulin resistance [89]. Further, insulin is also essential for maintaining proteostasis. It influences the excretion of amyloid  $\beta$  peptide and the phosphorylation of tau, two important markers in Alzheimer's disease [90].
4. Synaptic plasticity and neurogenesis. Exercise increases synaptic connections and stimulates hippocampal neurogenesis [91]. Important roles are played by BDNF and other growth factors in the maintenance of cognitive capacities [92]. The importance of adult hippocampal neurogenesis in cognition is being highlighted by an increasing number of studies from research on humans and animals. Additionally, there is a strong correlation between neurodegenerative diseases such as Alzheimer's disease (AD) and age-related cognitive loss [93]. The major molecular pathways through which exercise influences Alzheimer's disease pathology, including neurotrophic signaling, neuroinflammation, amyloid- $\beta$  clearance, and metabolic regulation, are illustrated in **Figure 2**.

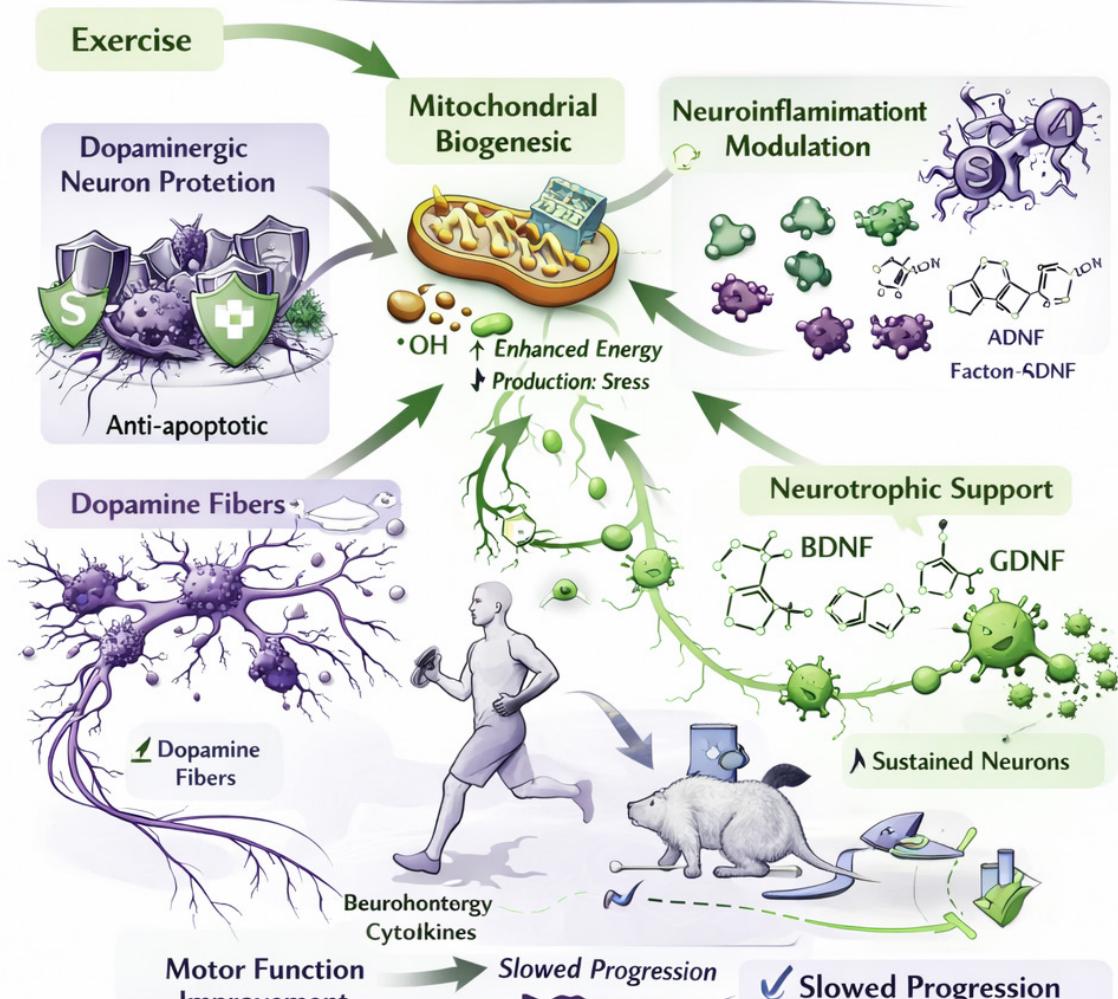
#### *Parkinson's disease*

1. Dopaminergic neurons protection. By strengthening anti-apoptotic pathways, exercise may protect dopaminergic neurons and lessen the neuronal loss associated with Parkinson's disease [94].
2. Mitochondrial biogenesis. Exercise improves mitochondrial biogenesis and function, which is essential for generating energy and reducing oxidative stress, which is a key contributor to the development of Parkinson's disease [95, 96].
3. Neuroinflammation modulation. Frequent exercise influences cytokine profiles and microglial activation, which lowers neuroinflammation and may slow the progression of Parkinson's disease [97, 98].
4. Neurotrophic support. To maintain neuronal survival, function, and plasticity, exercise activates growth factors such as BDNF and glial cell line-derived neurotrophic factor (GDNF) [99]. As Parkinson's disease progresses, there is an increasing amount of evidence that suggests a connection between diminishing BDNF levels and the condition [100]. Exercise-induced neuroprotective mechanisms in Parkinson's disease, including dopaminergic neuron preservation, mitochondrial biogenesis, and neurotrophic support, are summarized in **Figure 3**.

#### *Multiple sclerosis*

1. Immune system regulation. Exercise can potentially reduce the autoimmune attack in multiple sclerosis by moderating the immune response and causing it to shift toward an anti-inflammatory state [101, 102].
2. Neuroprotection. Neuroprotective factors are released in response to exercise, protecting neurons from axonal injury and demyelination [103]. Contradictory results have been obtained from studies on the variations in BDNF levels in people with

## Molecular Mechanisms of Exercise in Parkinson's Disease



**Figure 3.** Exercise promotes dopaminergic neuron survival, mitochondrial function, and neurotrophic support, thereby slowing disease progression and improving motor function in Parkinson's disease.

multiple sclerosis (PwMS). In general, BDNF levels tend to remain normal during times of remission while increasing during relapses [104].

3. Blood-brain barrier integrity. Exercise reduces immune cell infiltration and the possibility of a worsening of multiple sclerosis by maintaining the integrity of the blood-brain barrier [105, 106].

4. Functional compensation. Exercise increases the flexibility of brain networks, allowing the central nervous system to heal damaged areas [107]. In a healthy brain, an increase in neuronal activity can lead to new myelination and subsequent behavioral changes [108]. Using the natural ability of neuronal activity to direct myelination in conjunction with non-invasive techniques that can elicit neuronal activity could be a novel strategy for myelin repair in multiple sclerosis (MS) [109].

### Depression and anxiety

1. Neurotransmitter regulation. Physical exercise affects

neurotransmitter levels, elevating the release of serotonin and dopamine, which help to regulate mood and reduce feelings of anxiety and depression [110, 111].

2. Neuroplasticity and BDNF. Exercise promotes the synthesis of BDNF and neuroplasticity, which allows for neural adaptations to counteract the neuronal atrophy frequently seen in depression and anxiety [112-114].

3. Hypothalamic-Pituitary-Adrenal (HPA) axis modulation. Exercise lowers cortisol levels linked to mood disorders and chronic stress by normalizing the HPA axis [115, 116].

4. Endorphin release. Endorphins are natural painkillers that naturally occur and cause feelings of well-being and anxiety to decrease as one engages in physical exercise [117-119].

The disease-specific molecular effects of exercise across major neurological disorders are summarized in **Table 2**.

5. Implications for clinical populations. It's vital to take into account exercise's possible advantages for clinical populations given its many beneficial impacts on the brain. For those suffering

**Table 2. Impacts of exercise on neurological disorders.**

Items	Mechanism	Impacts
Impacts of exercise on Alzheimer's disease and dementia	Neurotrophic factors	Release of BDNF promotes synaptic plasticity and reduces cognitive deterioration.
	Inflammation and oxidative stress	Workout strengthens antioxidant defenses and lowers neuroinflammation.
	A $\beta$ clearance	Enhances cerebral blood flow and encourages the removal of A $\beta$ plaques.
	Insulin signalling and glucose metabolism	Promotes insulin sensitivity and energy metabolism in the brain.
Impacts of exercise on Parkinson's disease	Dopaminergic neurons protection	Reducing neuronal loss, exercise may protect dopaminergic neurons.
	Mitochondrial biogenesis	Promotes mitochondrial performance and reduces oxidative stress.
	Neuroinflammation modulation	Minimizes inflammation of the neurons, thus reducing Parkinson's.
	Neurotrophic support	Promotes the growth factors that sustain the life and functionality of neurons.
Impacts of exercise on multiple sclerosis	Immune system regulation	Exercise can potentially reduce the severity of an autoimmune attack by moderating the immunological response.
	Neuroprotection	Activates neuroprotective factors, preventing demyelination of neurons.
	Blood-brain barrier integrity	Reduction of immune cell infiltration and preservation of the integrity of the blood-brain barrier.
	Functional compensation	Boosts the flexibility of brain networks to allow for functional correction.
Impacts of exercise on depression and anxiety	Neurotransmitter regulation	Serotonin and dopamine are influenced by exercise, which helps regulate mood.
	Neuroplasticity and BDNF	Reduces brain atrophy by increasing neuroplasticity and BDNF synthesis.
	HPA axis modulation	Reduces cortisol levels linked to long-term stress by aiding in the HPA axis' normalization.
	Endorphin release	Causes the release of endorphins, which elevate mood and decrease anxiety.

from anxiety or depression as well as cognitive impairment, exercise may be a helpful solution.

6. Future directions. Although progress has been made, much remains unknown about how exercise impacts the brain. Future research should explore its mechanisms, benefits for clinical populations, and the optimal types and intensities for different neurological conditions and demographics, enabling tailored treatments that maximize benefits across all ages and health situations.

## Conclusions

In conclusion, this thorough examination highlights the various advantages of physical activity for neurological conditions and brain health. Exercise can improve mood, cognition, and resistance to neurodegenerative illnesses through molecular mechanisms such as gene expression, neurotransmitter release, and an increase of neurotrophic factors. The methodological rigor of this review, by PRISMA principles, guarantees a thorough evaluation of pertinent papers. As exercise emerges as a therapeutic tool, future research should delve into tailored interventions for neurological conditions.

As we conclude the present study, it is clear that exercise, with

its complex chemical processes, is essential for maintaining brain function and has potential as a comprehensive strategy for treating and preventing neurological conditions. Future studies should focus more on specifically designed exercise programs for diverse neurological disorders to ensure that the benefits are maximized across a range of demographics and health situations. This review adds to the expanding body of research demonstrating that exercise plays a vital role in maintaining brain health and managing neurological disorders.

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## Ethics approval

No applicable.

## Data availability

This narrative review is based on previously published studies and publicly available data. No new datasets were generated or

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## Authors' contribution

Syed Muhammad Essa, Conceptualization, manuscript drafting, and overall supervision; Amanullah Kakar, Data collection and analysis; Noor Ahmed Khosa, Literature review and methodology support; Ismaiel A. Ibrahim, Statistical analysis and interpretation; Milica Jovanovic, Experimental design and validation; Maria Louise McLaughlin, Writing, review, and editing; Muhammad Ibrahim, Data curation and visualization; Karolina Riddle, Project administration and technical support.

## Competing interests

The authors declare no competing interests.

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