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The Impact of Vitamin D Deficiency on the Development and Progression of Alzheimer's and Parkinson's Diseases: A Narrative Review

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Aleksandra Katarzyna Klosowicz [1], Aleksandra Olga Pakulska [1], Marcin Marek Dziubiela [1], Aleksandra Maria Bloch [1], Natalia Rzadzinska [1], Sara Paulina Szczepaniak [2]

1. Medicine, Jan Biziel University Hospital No. 2, Bydgoszcz, POL 2. Medicine, Ludwik Rydygier Collegium Medicum, Bydgoszcz, POL

Corresponding author: Natalia Rzadzinska, natalia.rzadzinska@gmail.com

Abstract

In the face of global population aging, neurodegenerative diseases, particularly Alzheimer's disease (AD) and Parkinson's disease (PD), represent a challenge for modern medicine. These progressive and currently incurable conditions are characterized by the irreversible damage of neurons and myelin sheaths, ultimately resulting in profound impairment of motor and cognitive functions. Due to their long asymptomatic period, diagnosis is frequently made at a stage when substantial neuronal degeneration has already occurred. The pathogenesis of these disorders is multifactorial, with emerging evidence suggesting that vitamin D may contribute to their development and progression. Vitamin D plays a key role in the development and functioning of the central nervous system. It possesses neuroprotective properties and supports signaling and repair processes in neurons. Some observational studies report an association between vitamin D deficiency and an increased risk or greater severity of AD and PD, potentially through mechanisms involving impaired neuronal signaling, reduced synaptic plasticity, oxidative stress, and chronic neuroinflammation. However, these associations do not establish causality, and randomized clinical trials have not consistently demonstrated that vitamin D supplementation improves cognitive or motor outcomes, prevents disease development, or slows disease progression. These observations underscore the importance of further evaluating the potential role of vitamin D in neurodegenerative disorders and its implications for clinical management. The aim of this review was to evaluate the available evidence regarding the association between vitamin D deficiency and the development, progression, and severity of symptoms in AD and PD.

Categories: Neurology, Geriatrics, Public Health
Keywords: alzheimer’s disease, cognitive function, neurodegenerative diseases, neuroprotection, parkinson’s disease, vitamin d, vitamin d deficiency

Introduction And Background

Neurodegenerative diseases (NDs), including Alzheimer's disease (AD) and Parkinson's disease (PD), comprise a heterogeneous group of nervous system disorders characterized by progressive and irreversible neuronal loss, leading to the gradual impairment of neurological functions. They represent a major and growing public health concern, with prevalence increasing substantially among individuals aged 65 years and older [1,2].

NDs typically develop gradually and may remain clinically silent for prolonged periods. Early clinical manifestations are typically nonspecific and may not emerge until significant neurodegenerative changes have occurred [3]. Initial manifestations may include impaired fine motor control, memory difficulties, and reduced concentration. As the disease progresses, patients may develop severe physical disability, communication impairment, disorientation, profound memory loss, and behavioral disturbances. Most NDs follow a progressive course without remission, with current therapeutic approaches focusing primarily on symptom management, pain relief, and the preservation of motor and cognitive function [4].

Consequently, NDs are associated with a marked decline in quality of life and may substantially limit patients' ability to obtain or maintain employment [5]. They are also a major cause of disability and contribute considerably to global mortality [6-8]. Although the mechanisms underlying neurodegeneration remain incompletely understood, current evidence suggests that disease development results from complex interactions among aging, genetic susceptibility, and environmental factors. Among the potentially modifiable factors, altered vitamin D status has received increasing attention.

Vitamin D comprises a group of fat-soluble secosteroids, of which vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol) are the most biologically relevant forms [9,10]. In this review, the term "vitamin D" is used as a general term when referring to the vitamin D system or when the specific compound is not distinguished in the cited literature. Cholecalciferol (vitamin D3) is the parent compound commonly used in supplementation, whereas 25-hydroxyvitamin D (25(OH)D, calcidiol) is the principal circulating metabolite

used to assess vitamin D status. In contrast, 1,25-dihydroxyvitamin D ($1,25(OH)_2D$, calcitriol) is the biologically active hormonal metabolite that binds to the vitamin D receptor (VDR). These compounds differ in their physiological roles and clinical use and are therefore distinguished throughout the review where relevant.

Ergocalciferol is primarily derived from fungi and yeasts, whereas cholecalciferol is present in animal-derived foods, particularly fatty fish. Vitamin D status depends on multiple factors, with sunlight exposure being one of the most important determinants [11]. It is mainly synthesized in the skin in response to ultraviolet B (UVB) radiation, whereas only a limited amount is obtained from dietary sources [12]. However, endogenous production may be insufficient to maintain adequate vitamin D levels, particularly during periods of limited sunlight exposure [13]. Factors associated with reduced vitamin D status include older age, certain chronic diseases, darker skin pigmentation, limited sunlight exposure, skin disorders, and inadequate dietary intake [13,14]. Notably, studies conducted in Spain have demonstrated that vitamin D deficiency can occur even in populations with relatively high year-round sunlight exposure [15].

Vitamin D deficiency is assessed based on serum 25-hydroxyvitamin D (25(OH)D) concentrations, although the diagnostic thresholds vary among organizations and across studies. A serum 25(OH)D concentration below 50 nmol/L is commonly used as a threshold for vitamin D deficiency and has been estimated to affect up to one billion people worldwide [16]. The widespread occurrence of vitamin D deficiency is particularly important in view of the diverse physiological functions of this vitamin. Vitamin D is essential for maintaining calcium and phosphate balance and is therefore closely involved in bone growth and mineralization. Beyond its skeletal effects, it contributes to immune regulation, proper muscle function, and the control of cell proliferation and differentiation [17]. Recent studies have also highlighted its potential involvement in nervous system processes, including neuroinflammation, neurogenesis, and overall brain function [18-20].

In AD, pathophysiology extends beyond amyloid-β and tau to include chronic neuroinflammation, oxidative stress, mitochondrial dysfunction, disrupted calcium homeostasis, and insulin resistance, and vitamin D has been proposed to modulate several of these pathways, including amyloid metabolism, microglial activation, and synaptic integrity [21,22]. In PD, which is characterized by loss of dopaminergic neurons in the substantia nigra and α-synuclein aggregation in Lewy bodies, the VDR is highly expressed in the substantia nigra, and vitamin D may influence dopaminergic signaling, oxidative stress, and neuroinflammation [23]. Importantly, these mechanistic and epidemiological observations do not establish causality or clinical efficacy [22,23].

Review

Methodology

A literature search was conducted to identify relevant articles investigating the association between vitamin D status and neurodegenerative disorders, as well as the potential effects of vitamin D supplementation, with particular emphasis on AD and PD. The PubMed/MEDLINE database was searched for relevant publications in English published between 2010 and 2026. The search strategy included combinations of the following terms: "vitamin D deficiency", "vitamin D supplementation", "vitamin D status", "neurodegenerative diseases", "Alzheimer's disease", "Parkinson's disease", "cognitive function", and "neuroprotection".

Given the heterogeneous nature of the available evidence, broad inclusion criteria were applied. Eligible sources included original research articles, clinical studies, observational studies, and review articles addressing the relationship between vitamin D status or supplementation and AD or PD. Exclusion criteria were conference abstracts without full text available, duplicate publications, and non-English language publications. Due to the narrative nature of the review and the heterogeneity of the available evidence, findings were synthesized narratively, and a formal risk-of-bias assessment was not performed. Following the screening and selection process, 60 studies were included in the present narrative review.

Effects of vitamin D on the nervous system

Vitamin D exerts pleiotropic effects on the nervous system and is involved in processes essential for normal brain function. Calcitriol, the biologically active form of vitamin D, binds to the VDR, a ligand-activated transcription factor that regulates the expression of genes involved in neuronal development, survival, and plasticity [24]. Among the proposed neuroprotective mechanisms of vitamin D are the regulation of calcium homeostasis and protection against oxidative stress [24]. By modulating intracellular Ca^{2+} homeostasis, vitamin D may protect neurons against calcium overload and associated cellular damage [24]. Vitamin D also modulates antioxidant pathways and may reduce the accumulation of reactive oxygen species (ROS), thereby limiting oxidative stress and oxidative damage [24]. In animal models, higher vitamin D status or vitamin D supplementation has been associated with improved synaptic function and cognitive performance [25,26]. However, these mechanistic and preclinical findings should not be interpreted as evidence of clinical efficacy or a causal protective effect in humans.

Vitamin D has also been linked to the regulation of neurotrophic factors, including brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) [24]. BDNF plays an important role in neuronal survival, synaptic function, and neuroplasticity and is particularly relevant to learning and memory processes [27]. In addition, vitamin D modulates key neurotransmitter pathways. It regulates the synthesis, release, and expression of dopamine receptors, potentially affecting neural pathways involved in motivation and motor function. Its deficiency promotes dysfunction of dopaminergic pathways observed, among others, in PD [28-30]. In the serotonergic system, acting through the VDR, vitamin D inhibits serotonin reuptake and catabolism, increasing its synaptic availability, which promotes mood regulation as well as learning and memory processes [31]. Lower serum vitamin D levels may also contribute to AD-related neurodegeneration by exacerbating Aβ-associated neurodegeneration in nondemented older adults [32].

Thus, vitamin D deficiency impairs neurotransmitter pathways, increases oxidative stress and inflammation in the brain, and reduces synaptic plasticity and neuroprotection. These mechanisms may accelerate the development of neurodegenerative diseases such as AD and PD, whose association with vitamin D, together with evidence from clinical studies, is discussed below.

Vitamin D and Alzheimer's disease

AD is the most common form of dementia in the older population. It is characterized by deterioration of cognitive function and loss of memory, which may ultimately lead to a loss of functional independence [33]. It is caused by the extracellular accumulation of amyloid plaques composed of β-amyloid protein. In addition, the development of AD is associated with the formation of intracellular neurofibrillary tangles composed of tau protein. This process leads to neuronal degeneration and is accompanied by structural changes in the brain, such as widening of the cerebral sulci and enlargement of the ventricles [34].

A study examining the relationship between serum vitamin D, β-amyloid deposition, and neurodegeneration found no independent association between vitamin D status and either Aβ deposition or hippocampal volume. However, lower serum vitamin D levels were associated with a stronger relationship between Aβ deposition and hippocampal volume loss, suggesting that vitamin D may modulate Aβ-associated neurodegeneration rather than directly influence β-amyloid deposition [32].

In an animal study, vitamin D deficiency was associated with accelerated cognitive decline. It was also associated with increased expression of amyloid precursor protein (APP), greater production and deposition of Aβ, enhanced tau protein phosphorylation, synaptic dystrophy, and neuronal loss [35]. These findings provide a possible biological basis for a role of vitamin D in AD-related neurodegenerative processes; however, findings from animal models cannot be directly extrapolated to clinical outcomes in humans.

A prospective cohort study published in 2024 demonstrated that supplementation with vitamin D was associated with a lower risk of developing AD [36]. However, given the observational nature of the study, these findings should be interpreted with caution when considering the potential preventive effects of vitamin D supplementation. A similar result was obtained in another large prospective study. Vitamin D deficiency was associated with an increased risk of dementia, with the strongest associations observed in individuals with 25(OH)D concentrations <25 nmol/L compared with concentrations of 50-75.9 nmol/L. The results also suggest that increasing 25(OH)D concentrations to 50 nmol/L could prevent 17% of dementia cases [37]. However, this population-attributable estimate reflects the potential population-level contribution of vitamin D status to dementia risk and should not be directly equated with the effects of vitamin D supplementation. Another article reached nearly identical conclusions, reporting that insufficient vitamin D concentrations increased the risk of developing AD [38].

Despite evidence from several studies suggesting that vitamin D deficiency may be associated with an increased risk of AD, findings from a 2022 study did not support this hypothesis. In the animal model, transgenic APP/PS1 mice, used to model AD pathology, were fed a vitamin D-rich diet. Notably, the diet did not increase serum vitamin D concentrations and was instead associated with greater β-amyloid deposition in the brain and a worsening of disease progression [39]. The study also examined the effects of vitamin D supplementation in humans. Among individuals without dementia, regular vitamin D supplementation for at least 146 days per year was associated with a 1.8-fold higher risk of developing dementia. In participants with an existing dementia diagnosis, vitamin D supplementation was related to a 2.17-fold higher risk of mortality [39]. These findings contrast with the proposed neuroprotective effects of vitamin D and highlight the complexity of its potential role in the development and progression of neurodegenerative diseases.

However, the findings of this study should be interpreted with caution because of several methodological and terminological concerns. Two letters published in the same journal, Aging Cell, raised concerns regarding the interpretation of the results. One of the authors, Vieth, highlighted several important limitations. First, the animal study used concentrations of vitamin D, calcidiol, and calcitriol that were several times higher than physiological levels, limiting the relevance of these findings. Vieth also questioned the analysis involving human participants, noting that it examined calcitriol ($1,25(OH)_2D$) rather than the commonly used vitamin D3 supplementation. Calcitriol is an active hormonal metabolite primarily used in the treatment of disorders of calcium-phosphate metabolism, including those associated with chronic kidney disease and parathyroid dysfunction. Consequently, Vieth argued that referring to calcitriol simply as

"vitamin D" in the title, abstract, and conclusions of the study represented a significant terminological inaccuracy that could potentially mislead readers [40].

Gombart et al. raised similar limitations. They emphasized that calcitriol, calcidiol, and cholecalciferol differ substantially in their affinity for the VDR and in their physiological significance. Therefore, referring to these compounds collectively as "vitamin D" may affect the interpretation of the study findings. They pointed out that the transgenic APP/presenilin 1 (PS1) mouse model used in the study represents only a specific form of AD pathology and does not reflect the typical course of the disease in humans. In addition, they questioned the reliability of the retrospective analysis based on the Taiwanese National Health Insurance Research Database (NHIRD), noting that it included individuals treated with calcitriol as a prescription medication rather than individuals taking vitamin D supplements. The study population consisted of patients with renal or parathyroid dysfunction who were frequently burdened with numerous comorbidities, such as osteoporosis, thyroid disease, diabetes, dyslipidemia, hypertension, and chronic kidney disease. These conditions may themselves influence the risk of dementia and therefore represent potential confounding factors [41].

Importantly, evidence from randomized interventional studies does not demonstrate a clear preventive or cognitive benefit of cholecalciferol supplementation. In the VITAL study, which included more than 3,400 participants aged ⩾60 years, supplementation with vitamin D3 at a dose of 2,000 IU/day over a mean follow-up period of 2.8 years did not demonstrate a significant effect on cognitive decline compared with placebo [42]. Consistent with these findings, the 24-month, double-blind, randomized VitaMIND trial evaluated 620 individuals over 50 years of age with mild-to-moderate vitamin D deficiency and early cognitive impairment; vitamin D supplementation did not lead to a statistically significant improvement in cognitive function [43]. The absence of a beneficial effect of vitamin D3 supplementation on cognitive function was also confirmed in a 2025 study, in which five years of supplementation with moderate or high doses of vitamin D3 did not reduce the incidence of dementia in healthy older adults with normal baseline vitamin D concentrations [44].

Recent evidence indicates that insufficient vitamin D concentrations may be associated with an increased risk of developing AD. However, the available evidence suggests that cholecalciferol supplementation in older adults does not consistently result in improvements in cognitive function or prevent cognitive decline [42-44]. The heterogeneity of findings across studies underscores the need for further research and the development of standardized guidelines regarding vitamin D supplementation and its potential role in AD. The potential mechanisms linking vitamin D deficiency to AD pathophysiology and the proposed neuroprotective effects of vitamin D are illustrated in Table *1* and Figure *1*.

Pathophysiological mechanism	Potential role of vitamin D	Relevant references
Amyloid-β (Aβ) metabolism	Vitamin D signaling may influence Aβ clearance and microglial activity. However, evidence that vitamin D directly reduces Aβ deposition in humans remains inconclusive.	[32,34,35]
Tau pathology	Experimental evidence suggests that vitamin D deficiency may be associated with increased tau phosphorylation and neuronal injury.	[34,35]
Neuroinflammation	Vitamin D receptor (VDR) signaling may modulate microglial activation and inflammatory pathways, potentially limiting inflammation-associated neuronal damage.	[18-20,24]
Oxidative stress	Vitamin D may support antioxidant defenses and reduce reactive oxygen species (ROS), which contribute to neuronal dysfunction and degeneration.	[24,35]
Calcium homeostasis and neuronal survival	Regulation of intracellular calcium signaling may help maintain neuronal function and reduce calcium-associated excitotoxic injury.	[18,24]
Synaptic plasticity and neurotrophic signaling	Vitamin D may influence neurotrophic pathways and synaptic function involved in learning, memory, and neuronal maintenance.	[24-27]
Hippocampal neurodegeneration	Lower serum 25(OH)D levels were associated with a stronger relationship between Aβ deposition and hippocampal volume loss, although no independent associations were observed between serum 25(OH)D levels and Aβ deposition or hippocampal volume	[32]

TABLE 1: Potential mechanisms of vitamin D action in Alzheimer's disease

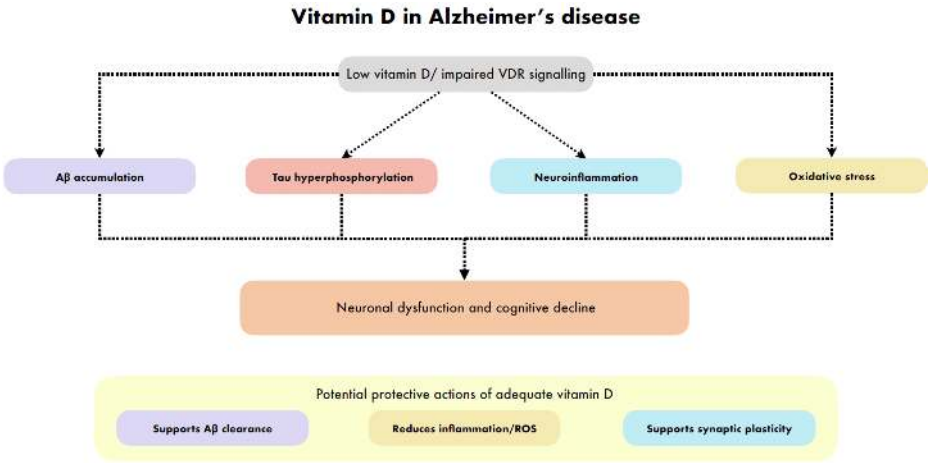


FIGURE 1: Potential role of vitamin D in the pathophysiology of Alzheimer's disease

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Vitamin D and Parkinson's disease

PD is the second most common neurodegenerative disorder after AD, affecting approximately 1-2% of individuals aged 65 years and older [45]. The increasing incidence of PD has been attributed primarily to population aging, the rising prevalence of chronic diseases, and exposure to potentially harmful industrial pollutants [46]. The typical clinical presentation includes motor symptoms, such as bradykinesia, rigidity, and resting tremor [47]. In addition, patients may experience a wide range of non-motor manifestations, including sensory, neuropsychiatric, autonomic, and sleep disturbances [48].

The development of PD is associated with the progressive loss of dopaminergic neurons in the substantia nigra of the midbrain, as well as with the formation of protein aggregates composed predominantly of α-synuclein, which accumulate in neurons in the form of Lewy bodies [49]. The pathological process also extends beyond the central nervous system and may involve peripheral autonomic nerves, visceral nerves, salivary glands, and the skin [50]. Consequently, PD is associated not only with alterations in dopaminergic neurotransmission but also with disturbances in adrenergic, cholinergic, serotonergic, glutamatergic, and GABAergic signaling [51]. Several molecular and immunological mechanisms are currently considered to play a role in the pathogenesis of PD [52]. Vitamin D may be involved in the modulation of several of these pathways, particularly those related to immune regulation and mitochondrial function.

Mechanistic and preclinical evidence suggests that vitamin D may influence pathways relevant to PD, particularly those related to immune regulation, oxidative stress, and mitochondrial function. Studies investigating immune alterations in PD have suggested that Th17 cells may contribute to neuroinflammatory processes, whereas regulatory T cells (Tregs) may exert protective effects on dopaminergic neurons [45]. Vitamin D may influence the balance between Th17 and Treg responses [45], supporting a potential immunomodulatory role in PD.

Vitamin D has also been proposed to influence mitochondrial function and oxidative stress. Mitochondrial dysfunction is considered an important component of PD pathogenesis [52]. Available mechanistic evidence suggests a potential relationship between vitamin D signaling, mitochondrial homeostasis, and the regulation of ROS [53,54]. Together, these findings provide a biological rationale for investigating the potential role of vitamin D in PD-related neurodegenerative processes.

Clinical studies evaluating vitamin D supplementation have reported heterogeneous but potentially relevant findings. Li et al. investigated patients with PD and vitamin D deficiency who received vitamin D3 supplementation for three months [45]. Supplementation was associated with changes in Th17 and Treg cell populations and with improvement in motor function. These findings suggest that vitamin D supplementation may influence both immune-related biomarkers and clinical outcomes in selected patients with vitamin D deficiency.

Similarly, Bytowska et al. evaluated BMI-adjusted vitamin D3 supplementation over 12 weeks and reported improvements in selected measures of physical performance [55]. A trend toward a decrease in inflammatory status was also observed, suggesting a possible relationship between vitamin D supplementation, physical function, and inflammatory activity. Barichella et al. reported favorable functional outcomes in patients receiving a nutritional intervention containing vitamin D together with

protein, leucine, and rehabilitation [56].

Other studies have reported less pronounced effects. Hiller et al. did not find a significant overall improvement in balance following vitamin D supplementation, although exploratory subgroup analyses suggested a possible age-dependent effect [57]. Luthra et al., in a longitudinal observational cohort of patients with early PD, found no significant difference in disease progression according to reported vitamin D supplement use [58].

Observational studies have also frequently reported lower circulating vitamin D concentrations in patients with PD compared with individuals without PD [30,59]. A recent systematic review and meta-analysis including 63 studies and approximately 10,700 participants confirmed that patients with PD had significantly lower vitamin D concentrations and were more likely to meet criteria for vitamin D deficiency or insufficiency than healthy controls [59]. Vitamin D supplementation was associated with only a small and statistically non-significant improvement in motor symptoms in the pooled analysis [59].

Evidence from Mendelian randomization provides an additional perspective on the relationship between vitamin D status and PD risk. Larsson et al. found no significant association between genetically predicted lower 25-hydroxyvitamin D concentrations and PD risk [60], suggesting that the causal nature of this relationship remains uncertain.

The current evidence should be interpreted in light of several limitations. Mechanistic and preclinical findings provide biological plausibility but do not directly establish clinical efficacy or causality in humans. Changes in immune or inflammatory biomarkers, including Th17 and Treg responses, should also be distinguished from clinical outcomes such as motor function or disease progression. Clinical supplementation studies are limited by relatively small sample sizes, short follow-up periods, heterogeneous supplementation protocols, and differences in baseline vitamin D status and patient characteristics. In addition, observational associations between low vitamin D concentrations and PD may be influenced by confounding and reverse causation, including reduced mobility, lower physical activity, and limited sunlight exposure after disease onset. Therefore, although available findings support further investigation of vitamin D in PD, current evidence is insufficient to establish vitamin D supplementation as a disease-modifying treatment.

Overall, observational studies frequently report lower vitamin D concentrations in patients with PD, whereas interventional studies have not consistently demonstrated clinically meaningful benefits of supplementation [30,45,55,57-59]. Mendelian randomization data also do not support a clear causal relationship between lower vitamin D status and PD risk [60]. These findings suggest an association between vitamin D status and PD, but the clinical relevance of supplementation remains uncertain. Table *2* and Figure *2* provide a schematic overview of the molecular and cellular pathways through which vitamin D may influence PD pathophysiology, with particular emphasis on dopaminergic neuronal function, neuroinflammation, oxidative stress, and mitochondrial homeostasis.

Pathophysiological mechanism	Potential role of vitamin D	Relevant references
Dopaminergic neuron survival	VDR signaling may contribute to the maintenance of dopaminergic neuronal function and survival, although evidence of direct neuroprotection remains predominantly experimental.	[29,53]
Dopaminergic neurotransmission	Vitamin D may regulate processes involved in dopaminergic neuronal differentiation, dopamine synthesis, and neurotransmitter signaling.	[28,29]
Neuroinflammation	Vitamin D may modulate immune responses, including the balance between pro-inflammatory Th17 cells and regulatory T cells (Tregs), potentially influencing inflammatory injury to dopaminergic neurons.	[45,53]
Oxidative stress	Experimental evidence suggests that VDR-mediated signaling may regulate antioxidant responses and attenuate ROS-associated neuronal damage.	[24,53]
Mitochondrial dysfunction	VDR-related mechanisms may contribute to mitochondrial homeostasis and protection against mitochondrial dysfunction, although their clinical relevance remains uncertain.	[52-54]

TABLE 2: Potential mechanisms of vitamin D action in Parkinson's disease

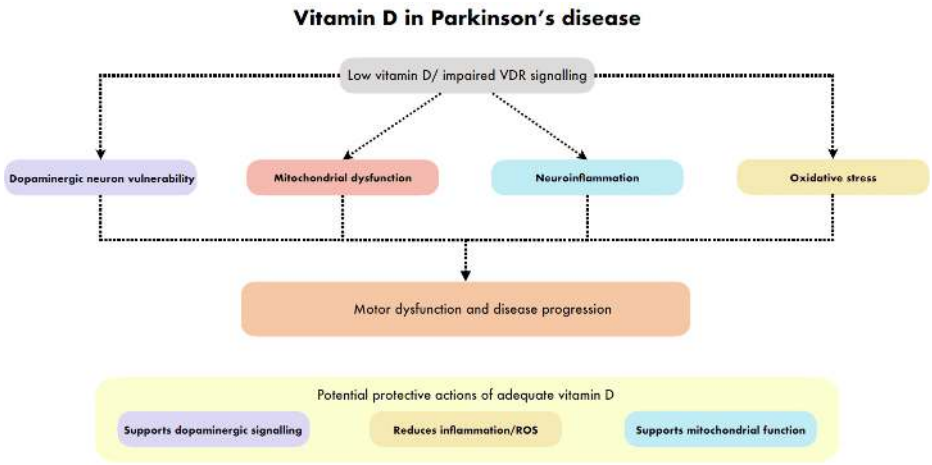


FIGURE 2: Potential role of vitamin D in the pathophysiology of Parkinson's disease

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Discussion

A review of the available literature concerning the relationship between vitamin D deficiency and the development and progression of AD and PD highlights the complexity and multifactorial nature of this issue. A notable discrepancy can be observed between observational and interventional studies. Whereas observational studies frequently report an association between low vitamin D concentrations and an increased risk or greater severity of these disorders, interventional trials have generally failed to demonstrate a clear therapeutic benefit of vitamin D supplementation [16,30,36,38,42-44,55,57,59].

The findings from observational studies are supported by the proposed neuroprotective effects of vitamin D, including the attenuation of oxidative stress and neuroinflammation and the modulation of neuronal signaling [18-20,24,35]. However, these associations should be interpreted with caution, as they do not necessarily indicate a causal relationship [37]. Several potential confounding factors, including older age, reduced physical activity, limited sunlight exposure, poor nutritional status, and chronic diseases, may be associated with both lower vitamin D concentrations and an increased risk of neurodegeneration [12,13,15]. Moreover, reverse causation cannot be excluded, as neurodegenerative diseases may themselves contribute to reduced physical activity, decreased outdoor exposure, changes in dietary intake, and other factors that may subsequently lead to lower vitamin D concentrations. Thus, the observed association between vitamin D status and neurodegenerative disease may partly reflect shared risk factors or consequences of disease rather than a direct causal effect of vitamin D deficiency.

The results of large randomized interventional studies, including VITAL, VitaMIND, and the Finnish vitamin D supplementation trial, have not conclusively demonstrated that cholecalciferol supplementation in older adults prevents cognitive decline or dementia [42-44]. Evidence concerning PD is similarly limited. In particular, findings from the recent PRISMA-compliant meta-analysis indicate only a small and statistically non-significant improvement in motor symptoms following vitamin D supplementation [59].

The discrepancies between individual studies may partly result from methodological differences, including variations in study populations, baseline vitamin D status, supplementation dose and duration, outcome measures, and thresholds used to define vitamin D deficiency [11,34,37,42-44]. Another important issue is the distinction between cholecalciferol and its active metabolites, as these compounds differ in their biological activity and clinical use [34]. Failure to clearly distinguish between them may lead to misinterpretation of clinical findings [40,41].

Given the chronic course of AD and PD and the lack of curative treatment options, further research into the potential role of vitamin D is warranted. Future randomized clinical trials should focus on individuals with clearly defined vitamin D deficiency, use standardized supplementation protocols, account for baseline vitamin D status, and clearly distinguish between different forms of vitamin D and its metabolites. Such studies may help determine whether vitamin D supplementation provides a clinically meaningful benefit and identify the patient populations most likely to benefit.

Conclusions

Current evidence suggests that vitamin D deficiency may be associated with AD and PD, although a clear

causal relationship has not been established. Although some observational and experimental studies suggest potential neuroprotective effects of vitamin D, current evidence does not establish vitamin D supplementation as an effective preventive or therapeutic intervention for AD or PD. Randomized clinical trials have not consistently demonstrated significant benefits of supplementation for disease prevention and clinical outcomes. Further well-designed studies are needed to determine whether vitamin D supplementation may provide meaningful benefits in specific patient populations, particularly those with confirmed vitamin D deficiency. Future research should also use standardized definitions of vitamin D deficiency and clearly distinguish between the different forms of vitamin D and its metabolites.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Natalia Rzadzinska, Aleksandra Maria Bloch, Sara Paulina Szczepaniak, Aleksandra Katarzyna Klosowicz, Marcin Marek Dziubiela

Critical review of the manuscript for important intellectual content: Natalia Rzadzinska, Aleksandra Maria Bloch, Aleksandra Katarzyna Klosowicz

Supervision: Natalia Rzadzinska, Aleksandra Maria Bloch, Aleksandra Katarzyna Klosowicz

Drafting of the manuscript: Sara Paulina Szczepaniak, Aleksandra Olga Pakulska, Marcin Marek Dziubiela

Acquisition, analysis, or interpretation of data: Aleksandra Olga Pakulska

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