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The Role of Omega-3 Fatty Acids in Neuroprotection: Molecular Mechanisms and Clinical Implications in Neurodegenerative Diseases. Focus on Alzheimer's Disease, Multiple Sclerosis and Parkinson's Disease

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Abstract

Among omega-3 fats, DHA and EPA stand out for their role in keeping the brain and nervous system healthy. Because the body cannot make sufficient amounts by itself, dietary intake is essential. These nutrients help nerve cells remain flexible and support smooth communication in the nervous system. While DHA is especially valuable for memory and mental performance, EPA, on the other hand, is mostly associated with managing brain inflammation.

Omega-3s protect nerve cells by easing inflammation and promoting cell survival. They also help damaged nerve tissue heal and encourage the growth of new brain cells, which supports clear thinking and learning. Certain substances derived from DHA and EPA help protect the brain from stress and cell loss.

Researchers have found that omega-3s may be useful for people dealing with Alzheimer's, Parkinson's and multiple sclerosis. In Alzheimer's disease, these fats might preserve connections between brain cells. In Parkinson's disease, they may assist with movement and nerve function. For people with MS, omega-3s could help by lowering inflammation and

promoting the repair of nerve fibers. While omega-3s aren't a cure, including them in the diet might help protect brain health and slow down the progression of the diseases.

Keywords: omega-3 fatty acids; neurodegeneration; Alzheimer's disease; Parkinson's disease; multiple sclerosis;

Introduction

Omega-3 fatty acids are a group of essential polyunsaturated fatty acids that play a crucial part in the proper functioning of the nervous system. They are critical components of neuronal cell membranes that contribute to membrane fluidity, synaptic transmission and nerve regeneration. Since the human body is unable to synthesize omega-3 fatty acids *de novo*, they must be obtained from dietary intake. The three main types include alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) with DHA and EPA being most biologically active in the central nervous system.[\[1\]](#)

The neuroprotective properties of DHA and EPA stem from their anti-inflammatory, antioxidant and membrane-stabilizing actions. DHA is particularly concentrated in the cerebral cortex and it is vital for neurodevelopment and cognitive function. On the other hand, EPA modulates inflammatory processes and oxidative stress, which are central to the pathogenesis of many neurodegenerative disorders. Numerous studies have demonstrated the potential of omega-3 fatty acids to support brain health and mitigate the progression of diseases such as Alzheimer's disease, Parkinson's disease and multiple sclerosis.[\[2\]](#)

This paper reviews how omega-3 fatty acids function in the nervous system and summarizes current clinical findings about their possible benefits in different neurodegenerative diseases.

Materials and Methods

This review aims to evaluate the role of omega-3 fatty acids in the functioning of the nervous system and their potential therapeutic applications in neurodegenerative diseases. A comprehensive search of literature was performed using the PubMed database using the following search terms: ("Omega-3 fatty acids" OR DHA OR EPA OR ALA) AND ("Nervous

system” OR “Neurodegeneration” OR “Cognitive function”). Studies investigating mechanisms of action (including membrane fluidity, synaptic transmission, inflammation and oxidative stress), as well as clinical outcomes in disorders such as Alzheimer’s disease, Parkinson’s disease, multiple sclerosis, were included. Both human and relevant animal studies were considered. Titles and abstracts were manually screened for relevance and alignment with the objectives of this review. The selected articles were thoroughly analyzed and synthesized to provide an overview of current evidence. As this review was not intended as a meta-analysis, no statistical pooling of data was conducted.

1. Mechanism of Action of Omega-3 Fatty Acids in the Nervous System

Omega-3 polyunsaturated fatty acids (PUFAs), especially DHA and EPA, play a key role in maintaining nerve cells healthy. Because mammals cannot produce these fatty acids, they need to get them through dietary intake or supplementation. DHA is highly concentrated in nerve cell membranes, where it helps stabilize synapses, support cell signalling and protect nerve cells.

One of the main benefits of omega-3 PUFAs is that they help reduce oxidative stress and neuroinflammation, which are linked to diseases like Alzheimer’s, Parkinson’s and multiple sclerosis. EPA and DHA change the structure of nerve cell membranes, affecting certain cell functions and reducing inflammation. For example, they reduce NF- κ B and increase PPAR- γ , which has anti-inflammatory and protective effects. These changes make glial cells less reactive, decrease the release of harmful cytokines and help prevent further nerve cell damage.[\[3\]](#)

EPA and DHA affect inflammatory signals and help make compounds like resolvins and protectins, which reduce and resolve neuroinflammation. Neuroprotectin D1 (NPD1), made from DHA and found in the brain, helps prevent cell death, protects neurons during oxidative stress and shields them from amyloid- β damage. Reducing inflammation quickly is crucial in chronic neurodegenerative diseases because ongoing glial activation and poor waste removal cause continued nerve cell loss.[\[4\]](#)

In addition to their anti-inflammatory properties, omega-3 fatty acids also strongly affect how nerve cells communicate. DHA makes cell membranes more flexible, stabilizes receptors and supports proteins needed for cell signaling. This impacts systems like the dopamine and serotonin pathways, which are important for thinking, mood and behavior. EPA and DHA also affect the enzymes that synthesize and degrade neurotransmitters, which helps maintain balanced nerve signalling in areas at risk for degeneration.[\[5\]](#)

Omega-3s support brain plasticity and help new nerve cells grow in the hippocampus. Supplementation of omega-3s increases the expression of genes linked to nerve growth, synaptic connectivity and memory enhancement. DHA in particular increases BDNF levels, which support synaptic plasticity, dendritic spine growth and neuronal survival. These changes help preserve learning, memory and mental resilience, which often decline early in neurodegenerative diseases.[\[6\]](#)

Moreover, Omega-3s help prevent cell death by stabilizing mitochondrial membranes. They improve how cells produce energy and lower harmful reactive oxygen species. When omega-3s are part of nerve cell membranes, they make the cells more resilient against damage by lipid peroxidation. This helps keep them healthy under stress, which is especially important in diseases where mitochondria do not function well and cells are subject to oxidative damage.[\[7\]](#)

Overall, DHA and EPA work together in many ways. They reduce neuroinflammation, stabilize nerve cell membranes, regulate neurotransmitters, boost brain plasticity and protect against

oxidative stress and cell death. These combined effects help nerve cells survive. For this reason, omega-3 fatty acids are promising as a supplementary treatment to slow the progression of neurodegenerative diseases and strengthen the brain's resilience.

2. Omega-3 Fatty Acids in Alzheimer's Disease

Alzheimer's disease is characterized by progressive cognitive decline, memory loss and neurodegeneration. Key features of AD are the buildup of beta-amyloid (A β) plaques outside cells and neurofibrillary tangles made of hyperphosphorylated tau protein. Chronic inflammation and oxidative stress further contribute to neuronal loss.[\[8\]](#)

Omega-3 polyunsaturated fatty acids, especially DHA, are being studied for their potential to counteract harmful processes in Alzheimer's disease (AD). Their anti-inflammatory and antioxidant effects are well known. In AD, these effects are even more important because they directly affect disease pathways such as microglial activation, amyloid- β buildup and synaptic weakness. Ongoing neuroinflammation caused by high levels of IL-1 β , TNF- α and reactive microglia accelerates amyloid buildup and leads to synaptic loss.[\[9\]](#) In this setting, DHA not only lowers inflammatory mediators but also helps shift microglia from a pro-inflammatory to a pro-resolving state. This change makes it easier for neurons to survive and for amyloid to be cleared.

Evidence suggests that DHA affects amyloid precursor protein (APP) processing, reducing the production of amyloid- β peptide. This shift to non-amyloidogenic pathways is important in the early stages of AD, where limiting A β buildup may slow the shift from mild cognitive impairment (MCI) to full Alzheimer's disease. DHA-derived mediators, like neuroprotectin D1, also help counteract stress caused by A β .[\[9\]](#) This helps keep cell membranes intact and lowers later neurotoxicity. While these effects do not fully stop plaque formation, they may reduce the impact on nearby neural circuits. In this context, the support provided by omega-3 fatty acids becomes clinically meaningful.

Moreover, DHA helps maintain synaptic proteins, spine density and dendritic architecture. These features are most affected in the hippocampus, a region central to memory and one of the earliest sites of AD degeneration. Even modest preservation of synaptic function may translate into measurable cognitive benefits, particularly in individuals with MCI. In these cases, synaptic plasticity remains at least partially intact.[\[10\]](#)

Clinical data on omega-3 supplements in Alzheimer Disease and Mild Cognitive Impairment are complex. Observational studies, including those from the Alzheimer's Disease Neuroimaging Initiative (ADNI), show a clear link between regular omega-3 intake and a lower risk of Alzheimer's. Meta-analyses with many participants also support a dose-dependent link between DHA/EPA intake and reduced cognitive decline, suggesting possible protective effects for the population. However, randomized controlled trials show that the benefits are clearest in the early stages. For people with MCI, supplements have been linked to enhanced memory and overall function. Some studies suggest they help preserve hippocampal volume. These benefits are weaker or missing in moderate-to-severe AD, likely because too many neurons are lost by the time treatment starts.[\[11\]](#)

Genetic factors can affect how people respond to omega-3 supplements. Some studies show that people with the APOE- ϵ 4 gene have a weaker or more varied response. Because of this, omega-3 treatments may work best when used in early stages, before much damage has

occurred. Even though results vary, omega-3 fatty acids are still considered safe, well-tolerated and a reasonable addition to early intervention strategies.[12]

Overall, omega-3 fatty acids are important in Alzheimer's disease because they target crucial mechanisms of the disease, such as altering microglial behavior, affecting APP processing, supporting weak synapses and possibly slowing cognitive decline in early stages of the disease. Current evidence shows these benefits mostly in preclinical and mild cognitive impairment. Once there is major neuron loss and synapse breakdown, as in moderate to advanced Alzheimer's, omega-3 supplements do not provide much clinical benefit. This stage-dependence shows that omega-3s are best used as a preventive or early-intervention strategy for those at risk or in early decline.[13] These results support more research on omega-3s for personalized prevention and early treatment in people likely to develop AD.

3. Omega-3 Fatty Acids in Parkinson's Disease

Parkinson's disease gradually affects the nervous system, leading to difficulties with movement. The disorder begins with the degeneration of the cells that produce dopamine in the substantia nigra, leading to reduced dopamine levels and affecting how the brain controls muscles.[14] As a result, symptoms like tremor, muscle stiffness and slowed movements appear. Over time, the condition gets worse due to several factors, such as the buildup of α -synuclein proteins (forming Lewy bodies), problems with mitochondria, issues clearing out damaged proteins and ongoing inflammation driven by brain support cells and inflammatory signals.[15] Together, these changes cause a range of movement and non-movement problems.

Animal studies have found that omega-3 fatty acids, especially DHA and EPA, can help protect nerve cells that make dopamine and support movement in models of Parkinson's disease. Ongoing brain inflammation and harmful molecules, especially the buildup of α -synuclein protein, disrupt how cells function. Omega-3s help by calming immune cells and lowering levels of inflammatory substances such as TNF- α and IL-1 β .[16] This may slow the loss of nerve cells seen in Parkinson's disease.

DHA-based molecules like neuroprotectin D1 do more than just lower inflammation - they also protect nerve cells directly. They help maintain cell energy systems, reduce harmful substances, block signals that can cause nerve cell death and control calcium levels inside cells. These actions are important for nerve cells under stress in Parkinson's disease.[17] In animal studies, these effects are linked to healthier nerve connections and increased dopamine production, which support movement and reduce problems caused by nerve-damaging chemicals.[18]

Omega-3s can also help brain circuits adapt by becoming part of nerve cell membranes and influencing how cells send signals to each other. They stabilize receptors and enhance the transmission of signals (including dopamine) between nerve cells, which is crucial for movement. [19] Omega-3 supplements may also increase growth factors like BDNF, which help nerve branches grow and strengthen connections.[20] This may help prevent early nerve loss in Parkinson's disease and support better movement and function.

Although clinical evidence is limited, it supports these findings. Small studies show that omega-3 supplements, especially when combined with antioxidants such as vitamin E, may lead to improvements in patients' motor and non-motor symptoms, as reflected in better scores on the UPDRS (Unified Parkinson's disease rating scale).[21] The benefits are less clear in people with more advanced disease, where nerve loss and protein buildup are harder to treat. These results

highlight the value of early treatment and suggest that omega-3s may work best as a preventive or add-on therapy, not as a main treatment for Parkinson's disease.

Overall, omega-3 fatty acids are important in Parkinson's disease because they can affect several disease processes. They help reduce overactive microglia, lower oxidative stress, stabilize vulnerable dopamine-producing neurons, preserve important nerve connections and support the brain's ability to adapt. These combined effects support more research into using omega-3s as part of early, personalized treatments for people at risk of Parkinson's disease. However, their benefits in moderate to advanced disease are limited and they should not be seen as a cure.

4. Omega-3 Fatty Acids in Multiple Sclerosis

Multiple sclerosis (MS) is a long-term autoimmune disease that damages the central nervous system. It causes specific areas of damage to myelin and nerve fibers, making it harder for nerves to send signals. This leads to symptoms such as muscle weakness, loss of sensation, vision problems and trouble thinking. MS often comes and goes in episodes, however some people develop a form that gets worse over time.

The disease process in MS involves immune cells called T cells and B cells that enter the central nervous system.[\[22\]](#) They release inflammatory substances, produce autoantibodies and special immune proteins. All of that contributes to the death of oligodendrocytes that produce myelin in the central nervous system. Other cells, such as microglia and macrophages, contribute to the damage by making harmful molecules and causing more inflammation. Infection with the Epstein-Barr virus and problems with certain T cells can keep the immune system active.

MS mainly affects the white matter near the brain's ventricles, the optic nerves, nerve pathways, the lower part of the brain and the spinal cord. Ongoing issues, such as problems with cell energy, buildup of harmful molecules and scar tissue, cause additional nerve loss and make symptoms worse. These combined problems explain why MS symptoms return and persist.[\[23\]](#)

Omega-3 polyunsaturated fatty acids (PUFAs), particularly EPA and DHA, might help slow down harmful changes in MS. In this disease, chronic inflammation and toxic molecules primarily damage the myelin that protects nerves. Omega-3 PUFAs can help by reducing the activity of certain support cells and lowering inflammation, which may limit further harm.[\[24\]](#) Compounds based on DHA also support the cells that build myelin, helping to maintain the protective layer around nerves and possibly aiding in the repair of injured areas in the brain or spinal cord.[\[25\]](#)

Clinical trials indicate that omega-3 supplementation may ease fatigue, boost physical functioning and improve quality of life for people with MS. Some research has found improvements in walking ability and endurance as well as reductions in inflammation markers, sometimes with different effects in men compared to women. [\[26,27\]](#) A higher intake of omega-3s, especially from fish, is also linked to fewer MS relapses, a slower increase in disability and better long-term results.

Omega-3s cannot stop MS on their own, but because they reduce inflammation, protect nerve cells and support repair, they can be a useful part of MS treatment. By limiting these harmful processes, omega-3s may help keep nerves healthy, support daily activities and improve well-being, especially when combined with regular medical care and healthy habits.

5. Conclusion

Considering the facts presented in this review article, omega-3 fatty acids, particularly EPA and DHA, represent a promising adjunct in the treatment of neurodegenerative diseases. Their ability to modulate inflammation, counteract oxidative stress and support neurodegeneration makes them attractive therapeutic agents when fighting conditions such as Alzheimer's disease, Parkinson's disease and multiple sclerosis. While many clinical trials show encouraging results, further research is necessary to determine optimal dosing strategies, treatment windows and patient subgroups that may benefit most. As understanding deepens, omega-3s may become progressively more important in the prevention and management of neurodegenerative disorders.

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