The importance of lipids in neurodegenerative diseases

Neurodegenerative diseases and lipids

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Abstract

Lipids are vital for membrane structure, energy storage, and cell signaling. Balanced lipid intake is essential for brain health and function. PUFAs like DHA and AA make the brain prone to oxidative stress and inflammation. Lipid peroxidation contributes to neuronal damage and neurodegenerative diseases. Disrupted lipid metabolism is linked to Alzheimer's, Parkinson's, and schizophrenia. Studying brain lipid changes may uncover disease mechanisms and guide new therapies.

Introduction

Lipids are essential for brain structure and function. They maintain membrane fluidity, support signaling, and enable synaptic plasticity. Although the brain is only 2% of body weight, it contains over 20% of the body's lipids. Polyunsaturated fatty acids (PUFAs), especially DHA and AA, are abundant in the brain and prone to oxidation. Disturbed lipid metabolism is linked to Alzheimer's, Parkinson's, and other brain disorders. Lipid peroxidation, inflammation, and membrane defects contribute to neuronal damage. Studying lipid changes may reveal disease mechanisms and new therapeutic targets. This paper examines the role of lipids in neurodegeneration and their clinical relevance.

Lipids

Lipids are a heterogeneous group of water-insoluble organic molecules. They are insoluble in aqueous solutions. Lipids found in the body are usually either present as membrane lipids and triacylglycerol droplets in adipocytes or transported in plasma with proteins as lipoproteins. Being used as the main energy source for the body, lipids also have a hydrophobic barrier function in the cell.[1] Lipids are grouped as simple lipids, complex lipids, lipid precursors, and derivatives.[2] Simple lipids: fats, waxes; complex lipids: phospholipids, glycolipids, other complex lipids (lipoproteins, aminolipids); lipid precursors and derivatives: fatty acids, glycerol, steroids, ketone bodies, fat-soluble vitamins, hormones.

An adult person takes about 60-150 g of fat per day. More than 90% of this amount is triacylglycerol. The remaining amount consists of cholesterol esters, phospholipids, and free fatty acids.[1] The lipid classes called neutral lipid and polar lipid have different functions in the organism. Neutral lipids have a storage function in the process of obtaining energy. Polar lipids act as precursors in eicosanoid production and are structural components of biological membranes.[3,4]

Lipids in neurodegenerative diseases are critical to brain health and function. Sphingolipids and phospholipids have vital functions in the structure and communication of nerve cells. While one-carbon fatty acids are effective in energy metabolism and cellular signaling, a deficiency of essential fatty acids can accelerate neurodegeneration processes by increasing inflammation. Excess of these fatty acids can also cause an imbalance and cause cellular deterioration. As a result, maintaining lipid balance stands out as a key element in the prevention and treatment of neurological diseases. Lipids such as phosphatidylinositol act as signal molecules and are involved in many processes, such as inflammation. In the brain, most of the lipids are formed by oligodendrocytes and are located in myelin. All membranes contain glycosphingolipid, cholesterol, and phospholipid.[5] PUFA; it contributes to brain functions such as membrane fluidity, function of ion channels, production and activity of neurotransmitters, signal production, and activity of neuronal growth factors.[6] The essential fatty acid content of foods directly affects neurotransmitter systems. (ω-3) fatty acid deficiency may cause decreased binding of dopamine receptors, an increase in serotonin receptor density, and changes in dopamine metabolism. The brain needs lipids and cholesterol to maintain its normal functions in the organism. Hypercholesterolemia can cause oxidative stress and neuropathological changes in the brain. There are antioxidant defense enzymes that can detoxify toxic free radicals formed as a result of cellular metabolism in the brain. Glutathione level decreases in hypercholesterolemia and affects oxidative stress. This situation causes the endoplasmic reticulum stress response, which supports neurotoxicity.[7]

Lipid Metabolism and the Brain

Lipids are one of the essential components that maintain the structural integrity of the brain and form the membranes of nerve cells. The brain's lipid composition consists of cholesterol (30%), glycerophospholipids (55%), including phosphatidylcholine (33%), phosphatidylethanolamine (16%), and phosphatidylserine (6%), sphingolipids (6%), and other lipid types (9%).[8] Synaptic plasticity plays a critical role in strengthening the connections between neurons with each other. It is thought that synaptic plasticity is impaired in schizophrenia. The myelin layer surrounding nerve fibers ensures the rapid transmission of electrical signals. Defects in myelination may be effective in the development of schizophrenia symptoms.

Lipid molecules located in the cell membrane regulate intercellular signaling. Disruption of this signaling can cause disruptions in neuronal functions. Although the brain accounts for only 2% of body weight, it uses approximately 20% of total energy consumption. Lipids are critical for the structural integrity and functionality of the brain. The most common lipids in brain tissue include phospholipids, cholesterol, and sphingolipids. These molecules are major components of cell membranes and play a role in regulating synaptic functions. In addition, they hold an important place in the structure of the myelin sheath and ensure rapid conduction of the action potential.[9,10]

Essential fatty acids are involved in many cellular functions of the brain. Brain free PUFA levels increase due to conditions such as oxidative stress and inflammation. At the same time, oxidative stress causes peroxidation of fatty acids such as (DHA) and (AA), which are at high levels in the brain. This causes neurodegeneration in the dopaminergic system. It has been experimentally stated by many studies that the loss of dopaminergic neurons in the substantia nigra is prevented by DHA. Hippocampal cognitive functions are associated with increased cell plasticity. Arachidonic acid acts as a second messenger molecule in the regulation of enzyme signals in neuronal cell membranes.[6]

DHA [22:6n-3] is a ω-3 fatty acid essential for vision, learning, and neural development. Changes in DHA levels are important for neurodegenerative diseases.[11] PUFAs contribute to brain functions such as membrane fluidity, function of ion channels, production and activity of neurotransmitters, signal production, and activity of neuronal growth factors. Mechanisms for neuroprotection of long-chain ω-3 fatty acids; It is associated with neuronal plasticity, signal transmission, neurotransmission, and regulation of neuronal membranes. The amount of PUFA in the brain changes with age. The amount of LC-PUFA (long chain polyunsaturated fatty acids) decreases with aging. PUFA; With a decrease in the expression of proinflammatory factors such as TNF-α and IL-6, inflammation improves.[6] Deficiency of α-linolenic acid in the diet causes a decrease in DHA level

and high w-6 levels in all brain regions. ω-3 PUFA deficiency is important for the pituitary gland and frontal cortex. Essential fatty acids play a role in numerous cellular functions that affect membrane fluidity, membrane enzyme activities, and eicosanoid synthesis.[12]

Prostaglandins are arachidonic acid derivative molecules. Each type of prostaglandin molecule has its own specific functional pathway and physiological properties. Clinically, it has a positive or harmful effect on the organism depending on the tissue and substrates.[13] Arachidonic acid is formed by the breakdown of phospholipids in the organism. Arachidonic acid forms eicosanoids metabolically in the organism by the cyclooxygenase pathway and lipoxygenase pathway: Via cyclooxygenase, prostanoids are formed. Prostaglandins with prostaglandin synthetase; Prostacyclins with prostacyclin synthetase; Thromboxanes are formed by thromboxane synthetase. Via lipoxygenase; leukotrienes occur.[14] Oxylipins are compounds derived from PUFAs and play a role in inflammation. Oxylipins are derived from ω-3 fatty acids and show anti-inflammatory activity. For example, prostaglandin [PGE2], it is an oxylipin derived from arachidonic acid. Imbalance in ω-3 and ω-6 levels causes inflammation.[6]

Phosphoglycerides are a class of polar lipids characterized by the backbone of phosphatidic acid. Phosphatidic acid is formed as a result of the esterification of phosphoglyceride with substances such as inositol, serine, ethanolamine, and choline.[15] Glycerophospholipids play a role in DHA transport in the brain.[11] Sphingolipids are a group of polar lipids and contain the sphingosine backbone, which is a long-chain aminoalcohol.[15] Sphingolipids are molecules consisting of one or two hydrophobic acyl chains and a hydrophilic head. The hydrophilic part consists of organophosphate groups or monosaccharides and disaccharides; the hydrophobic part consists of the ceramide molecule.[16] Ceramide, sphingosine, and sphingomyelin, which are digestive products formed as a result of their digestion in the small intestine, have very high biological activity.[17] Processes such as glucocerebroside enzyme deficiency, over-synthesis of glycosphingolipids, and aggregation of α-synuclein; It is associated with risk factors related to motor effects, memory, and neurodegeneration in Parkinson's disease.[18] The conversion of propionyl-CoA to succinyl-CoA is an important source of energy for the brain. This metabolic pathway is involved in the breakdown of fatty acids and some amino acids and contributes to ATP production by integrating into the Krebs cycle. It plays a critical role in maintaining energy balance in the brain. Succinyl-CoA is effective in the synthesis of neurotransmitters and lipid metabolism, supporting neurological health. Deficiency states can trigger the development of neurodegenerative diseases.

ω-3 fatty acids play an important role in processes such as the nervous system, cognitive development, memory-learning relationship, neuroplasticity of nerve membranes, synaptogenesis, and synaptic transport. PUFA, DHA, and AA are important components of neural membranes.[19] The brain consists of three main cell types, namely neurons and glial cells, astrocytes and oligodendrocytes, and neurons make up approximately 1/4 of the brain. Fatty acids are the main components in the brain structure, and they participate in the functioning of the cerebral cell membrane, as they are in the basic cell structure. After adipose tissue, nervous tissue has the highest lipid concentration in the body. While approximately 50% of the neuronal membrane consists of fatty acids, this ratio is 70% in the myelin sheath.[20] Neurotransmitter systems are affected due to the peroxidation of PUFA and cholesterol, which are found at high rates in the brain. Insufficient α-linolenic acid consumption affects brain fatty acid composition. The anti-inflammatory effect of DHA fatty acid is important to slow

Table1. Lipid types and their relationship with neurodegenerative diseases

Literature	Lipid Type	Conclusion
Chen et al., 2022	SCFA	Plasma SCFA levels increase in PD
Meguid et al., 2008	DHA	The risk of AD decreases with increasing DHA intake
Makrides et al., 2009	PUFA	Increased PUFA intake reduces the risk of PD
Kamel et al., 2014	PUFA	Levels are reduced in PD
Nitch et al., 1992	PC and PE (Phosphatidylcholine, Phosphatidylethanolamine)	Levels decrease in AD
Barbash et al., 2017	Seramide	Ceramide level decreases in AD
Mielke et al., 2013	Ceramide	Its level decreases with cognitive loss in PD
Prasad et al., 1998	A.A. (Arachidonic acid), L.A. (Linoleic acid)	levels decrease in AD
Snowden et al., 2017	LA, AA, ALA, EPA, OA	levels decrease in AD
Gonzales et al., 2022	PGE2	PGE2 level also decreases in AD
Irigoyen et al., 2021	TAG (Triacylglycerol), PC	TAG, PC levels decrease in PD
Ahmed et al., 2024	Lipoprotein, Cholesterol	LDL and cholesterol levels can be increased in AD
Chu et al., 2022	EPA, DHA	EPA, DHA levels decrease in AD
Calandria et al., 2023	NPD1 (Neuroprotectin D1, DHA derivative)	Enhances synaptic plasticity, has neuroprotective effects in AD
Taguchi et al., 2022	Gangliosides (glycosphingolipids)	Deficiency associated with dopaminergic neuron loss in PD
Bazinet & Layé, 2023	DHA, ALA, EPA	Omega-3 deficiency increases tau phosphorylation and amyloid-β in AD
Kingwell, 2024	Lipid rafts (cholesterol-rich microdomains)	Lipid raft disruption promotes tau aggregation in AD

down the process in this disease.[19] LCPUFA has been observed to be important in neurodegeneration and neural development in some clinical and animal studies. Dietary intake of ω-3 in patients with depression affects the disease positively.[21] In a study conducted, arachidonic acid, which is a ω-3 fatty acid, was found to alleviate depression symptoms at a high rate.[22] According to Wu et al. (2022 study), it has been determined that serum SCFA (short-chain fatty acids) levels change in Parkinson's patients. Decreased serum propionic acid level is closely related to motor symptoms. Propionic acid supplementation can improve motor symptoms in Parkinson's patients.[23] According to Zhang et al. (2022 study), low triglyceride (TG) level in serum is associated with motor symptoms in Parkinson's patients. The TG molecule may be a defining biomarker in Parkinson's disease. Palmitic acid is a fatty acid that has physiological functions in brain cells.[24] Lipid metabolism and neurodegenerative diseasesDisturbances in lipid metabolism may contribute to the pathophysiology of many neurodegenerative diseases. Accumulation of lipids can lead to neuronal damage through oxidative stress and inflammation. Below, we will examine how lipid metabolism is affected in neurodegenerative diseases.

Alzheimer's Disease

In Alzheimer's disease (AD), in addition to the accumulation of β-amyloid plaques and tau tangles, disruptions in lipid metabolism are increasingly recognized as critical factors in disease progression. The apolipoprotein E (ApoE) gene, particularly the ApoE4 variant, is the strongest genetic risk factor for late-onset Alzheimer's. ApoE is essential for lipid transport and metabolism in the brain, and individuals carrying the ApoE4 variant have impaired lipid transport, leading to the accumulation of cholesterol and phospholipids in the brain.[25] The disruption of lipid homeostasis in the brain, especially in the context of synaptic membranes, has been shown to impair neuronal function. Cholesterol and phospholipids are crucial for maintaining synaptic integrity, and their imbalances can lead to impaired synaptic signaling, plasticity, and ultimately, neurodegeneration.[26] Furthermore, the altered lipid environment caused by the ApoE4 variant can exacerbate amyloid-beta deposition and tau pathology, creating a harmful feedback loop that accelerates disease progression. This points to lipid metabolism as a promising target for therapeutic interventions in AD.[27] The link between lipid metabolism and Alzheimer's disease is gaining more attention, with research exploring the roles of specific lipids, such as ceramides, sphingolipids, and gangliosides, in AD pathogenesis. Understanding these mechanisms could open new avenues for targeted therapies aimed at modulating lipid metabolism to slow or prevent neurodegeneration.[28,29]

Parkinson's Disease

In Parkinson's disease (PD), loss of dopaminergic neurons and accumulation of Lewy bodies are observed. Disorders in lipid metabolism also play a role in this process. In particular, the alpha-synuclein protein interacts with lipids and contributes to the formation of Lewy bodies. Additionally, disruption of mitochondrial lipid metabolism can lead to decreased cell energy and neuronal damage.[30,31] Several academic studies discuss the role of lipid metabolism in PD, in relation to the accumulation of alpha-synuclein and Lewy bodies. One key factor is the interaction between alpha-synuclein and lipids, which contributes to the formation of Lewy bodies, the hallmark of PD. Research shows that an imbalance in lipid metabolism, particularly phospholipids, promotes the aggregation of alpha-synuclein into its pathological form, which is central to neurodegeneration in PD. This process disrupts synaptic vesicle membranes, leading to neuronal damage.[32] Moreover, mitochondrial dysfunction in lipid metabolism has been linked to reduced cellular energy production and oxidative stress, which exacerbates neuronal damage in PD. Mitochondria rely on proper lipid metabolism to function, and when this is disrupted, it accelerates alpha-synuclein aggregation, creating a cycle that further harms neurons.[33] These interactions between lipids, alpha-synuclein, and mitochondria offer potential targets for therapeutic strategies aimed at modulating lipid metabolism to mitigate neurodegeneration in PD.[34]

Amyotrophic Lateral Sclerosis (ALS)

Amyotrophic lateral sclerosis (ALS) is a progressive disease characterized by the loss of motor neurons. Abnormalities in lipid metabolism have also been observed in this disease. Various studies show that plasma lipid levels and genes involved in lipid metabolism differ in ALS patients. In particular, lipid peroxidation and lipid accumulation contribute to the induction of oxidative stress. The relationship between ALS and lipid metabolism has been examined in various studies. Abnormalities in lipid metabolism, including alterations in plasma lipid levels, lipid peroxidation, and lipid accumulation, have been observed in ALS patients. These changes contribute to the induction of oxidative stress, a key pathological mechanism in ALS.

Studies show that lipid peroxidation, a process where reactive oxygen species (ROS) damage lipids, plays a significant role in the oxidative stress seen in ALS. This oxidative damage affects cell membranes and proteins, contributing to motor neuron degeneration. Increased lipid peroxidation and accumulation of oxidative damage biomarkers, such as malondialdehyde (MDA), are prominent in ALS patients, particularly in spinal cord tissues.[35] Furthermore, research on lipid rafts (specialized membrane domains rich in lipids) in ALS suggests significant changes in their lipid composition and structure. These changes impact cell signaling and membrane fluidity, further implicating lipid metabolism in the disease's progression.[36] These findings highlight the importance of lipid metabolism and oxidative stress in ALS pathogenesis and suggest potential therapeutic targets to mitigate these processesi.[37]

Schizophrenia

Schizophrenia is a complex disorder affecting brain function. The role of lipid metabolism in its pathophysiology is gaining interest. Lipids support neuronal function and synaptic transmission. Altered lipid metabolism has been observed in schizophrenia patients. Low levels of ω-3 fatty acids and phospholipid abnormalities are common. Disrupted phospholipids may impair membrane structure and neurotransmitter release.[38] ω-3 fatty acid deficiency (DHA and EPA) may contribute to schizophrenia development.[39] These fatty acids reduce inflammation

and support brain cell function. Low ω-3 levels can trigger neuroinflammation and impair synaptic transmission.[39] Brain cholesterol is crucial for membrane structure and synaptic plasticity. Cholesterol metabolism disorders have been found in schizophrenia.[34] Low cholesterol may impair neurotransmission and synaptic function.[34]

Effects of Lipid Abnormalities
Disturbances in lipid metabolism may impact schizophrenia in several ways:

Abnormal lipid metabolism, especially low PUFA levels, can trigger brain inflammation in schizophrenia.[40] Lipid imbalances disrupt neuronal membrane integrity and signaling. Altered membrane lipids are common in schizophrenia.[41,42] Lipids support mitochondrial energy production. Mitochondrial dysfunction linked to lipid peroxidation is seen in schizophrenia and impairs neuronal function.[43]

Molecular Mechanisms
ApoE, especially the ApoE4 variant, impairs brain lipid transport and increases neuronal damage in Alzheimer's disease.[44,45] It also affects microglial lipid metabolism and promotes toxic lipid droplet accumulation.[45] Oxidative stress induces lipid peroxidation, damaging neuronal membranes and contributing to Alzheimer's and Parkinson's disease.[46,47] Disrupted cholesterol homeostasis impairs synaptic function and promotes amyloid plaque formation in Alzheimer's.[48] Large-scale studies show that LDL cholesterol fluctuations can raise dementia risk by up to 60% in the elderly.[49]

Targeting Lipid Metabolism
Understanding the role that lipid metabolism plays in neurodegenerative diseases may allow the development of new treatment strategies targeting these processes.

Statins: These cholesterol-lowering drugs, traditionally used for cardiovascular diseases, are also being investigated for their neuroprotective effects in diseases like Alzheimer's. Research suggests that statins might help reduce amyloid plaque formation and oxidative stress in the brain, though more studies are needed to confirm these effects in neurodegenerative contexts.[50] Antioxidants: Lipid peroxidation, a process where free radicals damage lipids in neuronal membranes, is a major contributor to neurodegeneration. Antioxidant therapies aim to reduce this oxidative stress, potentially preventing further neuronal damage in conditions like Alzheimer's and Parkinson's.[24] Gene Therapy: In particular, approaches targeting the ApoE4 allele, which is linked to impaired lipid metabolism in the brain, are being explored. Gene therapy could help regulate lipid metabolism and reduce the neurotoxic effects seen in neurodegenerative diseases.[51]

Trending Lipid Molecules and their Relationship with Neurodegenerative Diseases
Recent studies have provided a better understanding of the role of lipid metabolism in neurodegenerative diseases. Specifically, molecules phosphatidylserine (PS), sphingomyelin (SM), oxysterols, lipid rafts, and fatty acid derivatives have been shown to play a crucial role in neuronal protection and slowing disease progression.

Phosphatidylserine (PS) and Neuroprotection
Phosphatidylserine is a fundamental phospholipid found in cell membranes and plays a critical role in brain health. Studies have shown that PS supplementation may support cognitive functions in Alzheimer's disease and slow down age-related cognitive decline.[49] Additionally, PS exerts a neuroprotective effect by suppressing neuroinflammation.

Phosphatidylserine has also been investigated for its role in supporting dopamine production in Parkinson's disease, potentially improving motor functions.[52] Experimental studies have demonstrated that PS enhances synaptic plasticity in the hippocampus and prefrontal cortex, improving learning and memory.[53] Furthermore, PS supplementation has been reported to balance cortisol levels, thereby supporting cognitive functions.[54] Additionally, PS is suggested to support mitochondrial function, enhancing energy production, which contributes to neuroprotection.[55] Therefore, PS has emerged as a promising therapeutic target in slowing the progression of neurodegenerative diseases.

Sphingomyelin and Lipid Rafts
Sphingomyelin is a crucial component of cell membranes, contributing to neuronal signaling and maintaining membrane integrity. Studies have found that sphingomyelin levels decrease in Parkinson's disease, correlating with α-synuclein aggregation. Recent research has shown that disruptions in sphingomyelin metabolism are linked to neuroinflammation and oxidative stress mechanisms.[56] A deficiency in gangliosides, a subgroup of glycosphingolipids, has been associated with accelerated dopaminergic neuron degeneration in Parkinson's patients.[57]Lipid rafts are specialized microdomains in cell membranes that function as signaling platforms between neuronal cells. Studies have shown that lipid raft composition is disrupted in Alzheimer's disease, contributing to beta-amyloid plaque formation.[48] Changes in cholesterol and sphingolipid balance disrupt lipid raft structures, promoting tau protein aggregation.[58] Recent research suggests that lipid raft modulation may reduce amyloid beta toxicity, thereby protecting neurons.[59]

Oxysterols and Brain Health
Oxysterols are oxidized derivatives of cholesterol that play a crucial role in brain cholesterol homeostasis. Studies have found increased levels of 24-hydroxycholesterol in Alzheimer's patients, whereas 27-hydroxycholesterol levels are decreased in Parkinson's disease.[45] Oxysterols can contribute to neuroinflammation, exacerbating disease progression.Recent findings indicate that 24-hydroxycholesterol promotes amyloid-beta peptide accumulation, accelerating Alzheimer's disease.[60] Reduced 27-hydroxycholesterol levels have been linked to dopaminergic neuron loss in Parkinson's disease.[61] Oxysterols are thought to influence neurodegeneration through glial cell activation and the release of pro-inflammatory cytokines, enhancing microglia-mediated inflammation.[62] Emerging research suggests that oxysterol modulation may serve as a potential therapeutic target in slowing neurodegenerative diseases.[63]

Fatty Acid Derivatives and Neuronal Protection
Unsaturated fatty acids play significant roles in brain function. Recent studies have highlighted the neuroprotective effects

of DHA derivatives (docosahexaenoic acid metabolites), such as NPD1 and resolvins. These molecules exhibit anti-inflammatory properties and may slow the progression of Alzheimer's and Parkinson's diseases.[11] Studies indicate that NPD1 (Neuroprotectin D1) enhances synaptic plasticity, thereby supporting cognitive functions.[64] Additionally, resolvins have been shown to suppress microglial activation, reducing neuroinflammation, a mechanism effective in slowing neurodegeneration in Parkinson's disease.[65] Furthermore, deficiencies in essential fatty acids (EFAs) have been associated with increased tau hyperphosphorylation and amyloid-beta production in Alzheimer's disease.[66] ω-3 fatty acids, such as DHA and EPA, improve neuronal membrane stability and enhance cellular resilience.[67] Recent data suggest that lipid-based drug delivery systems are being developed to enhance the therapeutic potential of omega-3 derivatives.[10]

New therapeutic approaches: lipid modulation for treatment
With the growing understanding of lipid metabolism's role in neurodegenerative diseases, new lipid-based therapeutic approaches are emerging:

• Statins: They have been shown to regulate brain lipid balance and slow Alzheimer's disease progression.[50] Some studies suggest that statins may also alleviate motor symptoms in Parkinson's disease by reducing neuroinflammation.[68]

• ω-3 and DHA Supplements: ω-3 fatty acids, particularly DHA, have been found to support brain function and exhibit anti-inflammatory effects in Alzheimer's and Parkinson's patients.[24] Recent studies suggest that EPA and DHA reduce microglia-mediated inflammation, providing neuroprotection.[69]

• Antioxidant Therapies: Antioxidants vitamin E and coenzyme Q10 are being investigated to prevent lipid peroxidation caused by oxidative stress.[37] Recent research indicates that polyphenols like resveratrol and curcumin may regulate lipid metabolism and slow neurodegenerative disease progression.[70]

• Lipid-Based Drug Delivery Systems: Advanced therapeutic approaches include lipid nanoparticles and lipophilic drug carriers, which facilitate more effective drug delivery by crossing the blood-brain barrier.[10]

Ethics Approval

This narrative review is based solely on previously published studies; therefore, ethics committee approval was not required.

Statistical Analysis

No statistical analysis was performed, as this study is a narrative review of the literature.

Reporting Guidelines

This manuscript was prepared in accordance with general principles for narrative reviews.

Conclusion

Lipid metabolism is essential in the pathogenesis of neurodegenerative diseases. Lipid accumulation, peroxidation, and transport defects contribute to neuronal damage. ω-3 fatty acid deficiency alters dopamine and serotonin signaling. DHA protects dopaminergic neurons in the substantia nigra. Excess cholesterol increases oxidative stress and disease risk.

Dietary fatty acids significantly influence neurodegenerative processes. Measuring cholesterol and essential fatty acids may help reveal disease mechanisms. Neuroprotective lipids include phosphatidylserine, sphingomyelin, lipid rafts, oxysterols, and fatty acid derivatives. Modulating lipid metabolism could slow disease progression.

Targeting lipid pathways offers potential for novel therapies. Future research will clarify the impact of neurodegeneration on lipid homeostasis.

Abbreviations
AD: Alzheimer's disease
PD: Parkinson's disease
ALS: Amyotrophic lateral sclerosis
PUFA: Polyunsaturated fatty acid
DHA: Docosahexaenoic acid
EPA: Eicosapentaenoic acid
AA: Arachidonic acid
ApoE: Apolipoprotein E
SCFA: Short-chain fatty acid
LDL: Low-density lipoprotein

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