Molecular Advances in Aging and Neurodegenerative Diseases by Emerging Mechanism, Biomarker and Therapeutic Purpose: A Review

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ABSTRACT

Aging is a major hazard for many neurodegenerative diseases that decline our body movements, and it is included with Alzheimer's disease, Parkinson's disease all these were affected in human health. In aging due to the global population increases rapidly in number of individuals. It is a major complex risk factor and biological process for diseases. In humans Alzheimer's disease causes dementia in adults. All these diseases are caused by genetic mutation from the production of abnormal proteins which deposit in our brain cell that leads to memory loss and cognitive decline. The blood brain barrier is a semi permeable membrane which is obtained from sensitive monitoring diseases which are efficient in drug delivery. In India over 138 million in individuals aged 60 or above constitute from the disorders about 10% of population are expected that in future it rises 20%. It produces a disease in the brain cells by oxidative stress due to cytotoxic consequences and produces the changes in phosphodiesterase-fatty acid. A biomarker like homocysteine and apolipoprotein (ApoE4) in treatment of vascular risk factors in disease development, and synaptic marker measure the blood or brain tissue to assess the synaptic damage. The benefit is that it leads to a better understanding and treatment of the (CNS) and develops a remarkable adaptability. The aim is to study the area of improving the public health issues from the increasing aging population by identifying the degeneration in advancing field as the biomarkers emerges for better clinical research and examining the therapeutic strategies for the prevention of the diseases.

Keywords: Aging, Alzheimer, Parkinson's, biomarkers, neurodegenerative, glycerophospholipid, homocysteine, ApoE4

INTRODUCTION

Aging is a natural process, a progressive and universal change in living organism. It is a complex factor for the loss of neurons particularly for the vulnerable areas in CNS. The neurodegenerative disease including Alzheimer's, Parkinson's, Huntington disease. The effect of aging is on the brain, which is the major risk factor for the development of disorders [Lopez et al,2013]. These diseases are characterized by the gradual loss in nervous system structure and function and the symptoms which lead to a cognitive decline and memory loss in individuals age as biological process are oxidative stress, mitochondrial dysfunction and DNA damage which can contribute to the changes created in environment for the development of neurodegenerative diseases. There is a decline of antioxidants defense in the oxidative damage which leads to neurodegenerative disorder and there is interaction in oxidative stress. The biomarker for the accumulation of amyloid-beta plaques in Alzheimer's or alpha-synuclein in Parkinson disease linked on aging process to a change in metabolism. It is a time dependent progressive functional capacity. The cause of aging is genetic mutation and a gradual deterioration in molecular components which has a loss of gene expression. The factors that affect the vascular changes lead to a reduce on blood flow by increasing the risk factor of dementia, it reduces the cell ability to damage the protein and there is a loss of synaptic dysfunction due to cognitive decline and there is a exposure of pollutants or pesticides which contribute in a disruption of neuronal functioning in diseases causing. Around 60-70% of neurodegenerative disease are age related. The future aspects is the genetic testing to assess the individual susceptibility and improve the accuracy and speed of detection and techniques on diagnosing. As like CRISPR-Cas9 which target a specific genetic mutation. The development of monoclonal antibodies to clear the protein like plaques and develop the age- related hormone in degeneration and there is a therapy to improve the reduce of reactive oxidative species and cellular energy. The challenge in India is that there is a less awareness of this disease and there is a reduction in bio availability because of the pH condition and exposure of the blood brain barrier. Neurodegenerative

disorder is a neurological disease in the CNS and PNS and this process is called neuroinflammation.[Masrori et al,2020]. Aging is a composite process in nervous system, it affects cellular, structural or molecular changes. There is a bidirectional form between the CNS and gut micro-biome which is referred to as a microbiota gut brain which generates a glial function on developing neuron damage. Due to the cause of dementia, in 2019, 50 million people are affected and in 2050 it is expected that this increases to 139 million people. According to WHO neurological diseases are hazardous and become more serious. This disorder is caused by genetic or environmental changes, which is a metabolic debility. In this the genes are transferred from parents to children from that the infectious disease is spreading. Aging is associated by the expanding of reactive ROS level which leads to oxidative stress. The antioxidant uses in OS as coenzyme which help in treatment. When the production of ATP level decreases the ROS increases which reduces the efficiency of mitochondrial dysfunction which also damages the aging [Albert et al,1998]. Neuroinflammation increases the chronic level in older people. The disorders include Alzheimer's disease, Parkinson disease, Huntington disease and amyotrophic lateral sclerosis (ALS). The imaging techniques PET and MRI used for the visualization of the diseases, the protein misfolding this was also used for large scale screening studies. The clinical and experimental methods occurred by providing the neuropathological evidence to demonstrate the loss and rigidity in diseases.

DESCRIPTIONS OF DISEASES

2.1Alzheimer's diseases

It is a batten disease which has a complex form that causes dementia in older adults. The major risk factor occurred in age related disorders which usually effect on the memory loss and thinking of knowledge. The classification of the cause stated from the amyloid-beta plaques its a spherical microscope feature which is surrounded by axonal and neurofibrillary tangles. The structure formed in inner neuron which is composed of tau protein and also has extracellular as hyper phosphorylation in tau angles [Miguel et al,2015]. The relationship between the tau and beta-amyloid is a trigger and also called stagging system which is classified by the protein that initiates the process of the disease and neurofibrillary dysfunction as bullet in neurodegeneration. In adults the disease caused by the obesity or diabetes. After the age of 65 this disease is twice every 5 years. The Apolipoprotein is characterized by the metabolism which regulates this amyloid protein. The treatment of this disorder has occurred by two drugs cholinesterase enzyme inhibitor and methyl aspartate. Uses the antioxidants to increase the diet like fiber and omega3 polyunsaturated fatty acids for protective analyzing. Vitamin E is antioxidants in lipoprotein which is the oxidative pathway and is effective against in vivo oxidation [Svetlana et al,2004].

2.2Parkinson diseases

Parkinson's disease is characterized by the loss of dopaminergic neurons in the substantia nigra, leading to reduced dopamine levels which disrupt motor control, causing symptoms such as stiffness, bradykinesia, tremors, and poor balance [Michel et al, 2019]. The disorder can spread through misfolding of alpha-synuclein proteins, which propagate neuronal dysfunction and are detectable by a toxic marker in diagnostic tests [M.et al, 2015]. The dysfunction and rise of reactive oxidative stress further contribute to neuronal damage, while microbial activation and neuroinflammation release cytokines and are influenced by genetic mutation. PET scans help assess dopamine system dysfunction, and cerebrospinal fluid (CSF) testing can detect alphasynuclein presence; monoclonal antibodies are being explored for targeted therapy [Philip et al., 2021]. Treatment primarily involves levodopa, often combined with carbidopa to prevent premature dopamine breakdown outside of the brain, reducing side effects like nausea. Although there is no cure, these treatments help manage symptoms and improve quality of life. Parkinson's disease has seen a significant rise, affecting approximately 8.5 million people globally by 2019, highlighting the urgent need for continued research and therapeutic development.

2.3Amyotrophic Lateral Sclerosis (ALS)

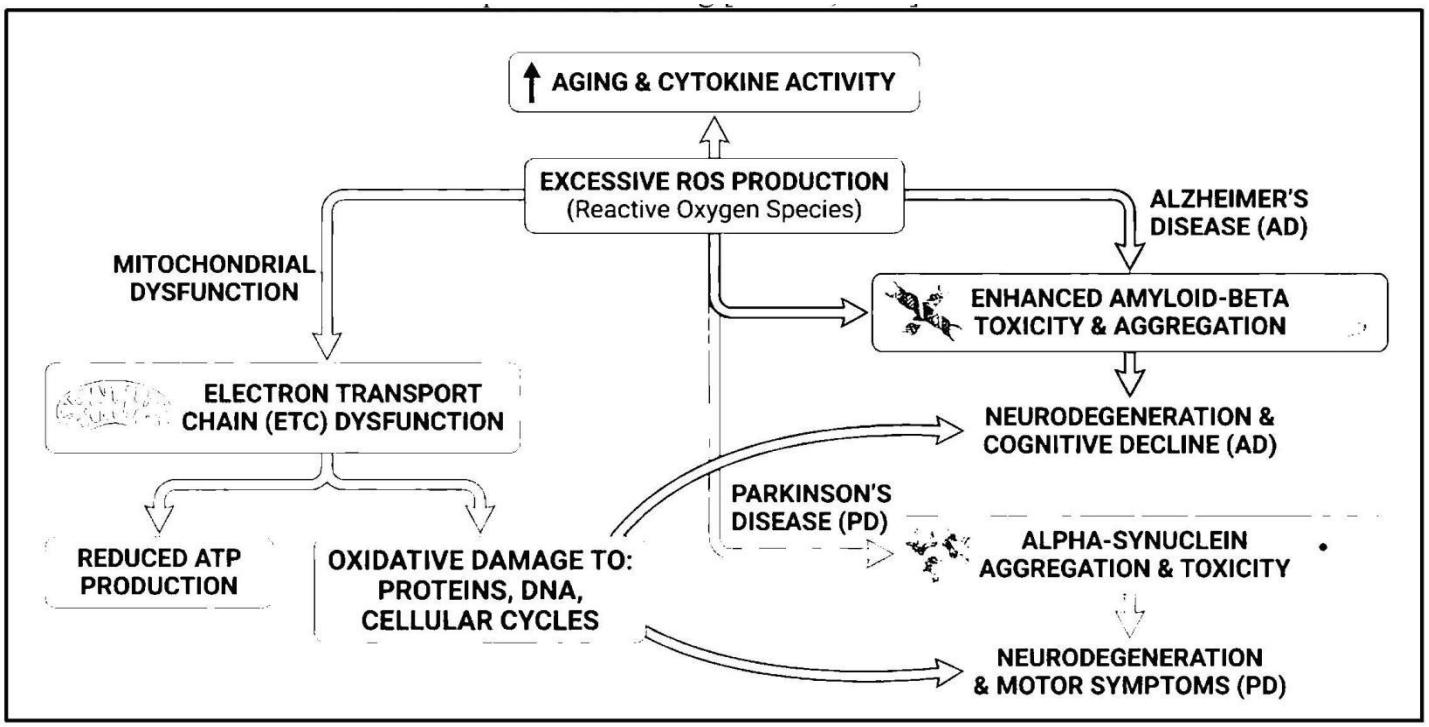
This disorder is a progressive form in our nervous system that affects nerve cells and spinal cord and brain in motor neuron [De Strooper et al,2016]. The symptoms of the diseases are muscle weakness respiration problem and death may cause. These diseases develop in the older age of 55years and generally it affects in men as compared to women. And 75-80% are affected by the disorder. The hallmark of this ALS is selective motor

neuronal dysfunction and genetic mutation like SOD1 for oxidative stress. The key features are dementia, motor neurons and molecular function. The disorders are amyloidosis, TAR DNA-binding protein [Neumann et al,2006]. Still the causes are unknown but there is a development and provides the vulnerable phase. Biomarkers are developed to diagnosis the disease essentially and antioxidants are provided in brain and tissues which analyze the reduction of OS. Proteomics are quantitative analysis of protein in tissue, cells, plasma membrane and CSF that identify biomarkers like ALS and PD develop TDP43 and alpha synuclein. In ALS the TAR DNA misfolded protein fused in liposarcoma for effective treatment in neurodegenerative disorder.

MECHANISM OF AGING AND NEURODEGENERATIVE DISEASES

Excessive production of reactive oxygen species (ROS) impairs the mitochondrial function, often initiated by cytokines activity, leading to reduced ATP production through electron transport chain (ETC) dysfunction and increased the damage to proteins misfold, DNA, and cellular cycles. In fig.1Alzheimer's disease (AD), ROS enhances amyloid-beta toxicity; in Parkinson's disease (PD) the alpha-synuclein aggregation contributes to dopamine neuron loss; and in amyotrophic lateral sclerosis (ALS), mitochondrial dysfunction affects beta-oxidation. This has an interconnection in cellular and molecular mechanism. The protein aggregation, often caused by oxidative phosphorylation imbalances, leads to toxic misfolded on oligomers that disrupt cell functioning. Neuroinflammation, involving microglia and astrocytes, initially offers protection but becomes damaging when chronic, breaking the blood cells [Tahira et al., 2009]. Hayes antioxidants like Coenzyme Q10 and curcumin can reduce oxidative stress, while omega-3 fatty acids mitigate neuroinflammation and promote therapeutic benefits. Mitochondrial DNA mutations impair energy production and expand the ROS levels, with reactive species such as OH and NO further damaging cellular components; antioxidants and telomerase play the protective roles in these pathways and help on mitochondrial DNA mutations impair the further damaging of cellular components; and also the antioxidants and telomerase involves in these pathways [Hasna et al, 2019]. Neuronal cells when exceed it affect and reduces the neurogenesis and SASP also effect on tissue damaging and also the autophagy failure introduced in aggregation of protein accumulation.As mitochondrial dysfunction affects oxidative phosphorylation, ATP synthesis, calcium regulation, and metabolic processes such as fatty acid and amino acid oxidation, it becomes a central issue in neurodegenerative diseases, often driven by mutations in mitochondrial DNA and protein misfolding [M. et al, 1995]

Figure 1. This figure demonstrates the activity of cytokines and aging of molecular pathway in alziemer disease, the ROS production increases that enhances the activity of amyloid beta toxicity and aggregation of protein and Parkinson's the neuroinflammation causes on cellular damaging also on dysfunction disorder and alpha synuclein in Etc that reduced the production of ATP and damage in oxidative phosphorylation affect in cellular cycle.



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MOLECULAR BIOMARKER OF NEURODEGENERATIVE DISEASES

Alterations in biomarkers such as amyloid-beta (Aβ) and tau protein on identification of diseases and neurofibrillary tangles that reduces the Aβ1-42 levels in CSF and serum observed in both early and advanced Alzheimer's disease (AD), alongside decreased APP fragments. In tau protein levels, particularly total tau (t-tau) and phosphorylated tau (p-tau), increase in blood and CSF across several neurodegenerative disorders including Lewy body dementia (LBD), ALS, and prion diseases, correlating with cognitive decline and poor outcomes. Elevated α-synuclein levels in biofluids that are linked with the synaptic loss and neuronal degeneration, especially in PD and LBD. Neurofilament light chain (NF-L), a marker of axonal damage, shows significant increases in blood across multiple neurodegenerative conditions, reflecting structural disconnection. Additionally, while α-synuclein, BACE1, and SNAP-25 are enriched in presynaptic terminals, neurogranin—a postsynaptic protein of glutamatergic neurons—rises in biofluids as an indicator of dendritic spinal loss. These biomarker profiles can be influenced by comorbidity and age-related conditions, including seizure activity, highlighting the complexity of neurodegenerative disease pathology and the need for integrated biomarker research [Ali.N et al,2025].

4.1Amyloid Beta (Aβ)

Amyloid-beta (Aβ) plaque accumulation, a hallmark of Alzheimer's disease (AD), originates from the cleavage of amyloid precursor protein (APP), with Aβ fragments aggregating to disrupt synaptic function and trigger inflammation; detection is possible via fluid-based analysis with magnetic resonance imaging or PET imaging. Similarly, hyper phosphorylated tau forms neurofibrillary tangles in AD and tauopathies, impairing microtubule stability and neuronal transport, with levels of phosphorylated tau (p-tau) and total tau (t-tau) measurable or blood (Table-4). In Parkinson's disease, AD and Lewy body dementia, misfolded α-synuclein aggregates into Lewy bodies, causing mitochondrial dysfunction and neurotoxicity, and is detectable in CSF, blood, or skin biopsies [King E et al,2019]. Neurofilament light chain (NFL), an axonal damage marker, reflects neuronal injury and disease progression across neurodegenerative disorders like ALS, AD and plasma. Emerging biomarkers such as DNA methylation and histone modifications are linked to gene expression alterations in aging and neurodegeneration, while exosomes extracellular vesicles carrying disease-specific proteins like Aβ, tau, and α-synuclein—offer promising potential for early diagnostics and tracking intercellular communication in neurodegenerative diseases.

Table-4 The table shows the diseases, symptoms and prevention of neurodegenerative disorders by elaborating the loss of neuronal dysfunction structure, function and leads to the manifestation and has the disability on ETC and mitochondrial mechanism:

Disease	Symptoms	Prevention
1.Alzheimer Diseases [Swardlow et al,2018]	Memory loss, Confusion	Mental activity, Exercise
2.Amyotrophic Lateral Sclerosis (ALS) [Hardiman O et al,2017]	Muscle Weakness, Paralysis	Riluzole, Respiratory support
3.Frontotemporal Dementia (FTD) [Wang W.et al,2020]	Personality change, loss of empathy	Behaviour therapy, Supportive care
4.Lawy body dementia [Mc Keith.et al,2017]	Hallucinations	Cholinesterase inhibitors, movement therapy
5.prion diseases (CID) [ChenS et al,2016]	Rapid dementia, loss of coordination	No cure supportive care only
6.Multiple Sclerosis [Reich DS et al,2018]	Vision loss, fatigue	Immunotherapy
7.Spincerebellar ataxia [Mento m et al,2012]	Poor condition slurred speech	Physical therapy, genetic testing
8.Vascular dementia [kalaria et al,2016]	Memory loss	Control blood pressure, healthy diet
9.Normal Pressure hydrocephalus (NPH) [Damasceno et al,2015]	Walking difficulty	Surgical shunt placement
10.Cerebellar degeneration [Fatemi et al, 2012]	Slurred speech	Supportive care

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THERAPEUTIC STRATEGIES

Natural therapeutic strategies for neurodegenerative deficiency focuses on significantly the antioxidants due to their ability to counteract the damaging effects of reactive oxygen species , which contribute on neuronal injury, conformationally alter the protein, and mitochondrial dysfunction. Curcumin, a polyphenolic compound from turmeric, exhibits as strong antioxidant, anti-inflammatory, and anti-amyloidogenic properties. Its mechanism includes scavenging ROS, suppressing lipid peroxidation, increasing glutathione levels, and modulating the transcription factors such as NF db. Studies have shown that curcumin reduces amyloid-β plaques, lowers tau hyperphosphorylation, and improves memory in Alzheimer's disease (AD) mouse models (Ahmed et al., 2020). However, its poor bioavailability remains with a limitation, which is being addressed through advanced delivery systems like liposomal and nanoparticle-based formulations. Similarly, resveratrol, a polyphenol found in grapes, berries, and red wine, improves mitochondrial function, promotes autophagy, and activates sirtuin-1 (SIRT1), thereby reducing oxidative stress and inflammation. The natural inflammatory occurred in omega3fatty acid and EGCG green tea extract this uses to reduce the dementia risk by protecting the functioning. A phase II clinical trial demonstrated that resveratrol could stabilize AD-related cerebrospinal fluid (CSF) biomarkers (Turner et al., 2015), though its therapeutic use is limited by low bioavailability and rapid metabolism. Coenzyme Q10 (CoQ10), a lipid-soluble antioxidant crucial for mitochondrial energy production, restores ATP synthesis, reduces lipid peroxidation, and alleviates oxidative mitochondrial damage (Yang et al., 2019). In addition to antioxidants, anti-inflammatory agents derived from natural sources are gaining attention for their neuroprotective effects. Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) from fish oil, enhance the production of anti-inflammatory mediators (resolving and protections) and suppress the release of pro-inflammatory cytokines like TNFα and IL-6. The DHA supplementation in preclinical AD models has shown cognitive improvement and reduced amyloid burden (Dyall, 2015). The compound is epigallocatechin gallate (EGCG), a major catechin in tea extract. EGCG lowers neuroinflammation by inhibiting microglial activation and blocking the NF-κB pathway. It also reduces ROS and amyloid-β aggregation, with studies in AD and Parkinson's disease (PD) models demonstrating its ability to preserve synaptic function and decrease neuroinflammation (Mandel et al., 2018).

DISCUSSION

Neurodegenerative diseases, such as Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), and amyotrophic lateral sclerosis (ALS), are characterized by the progressive loss of neurons in specific regions of the brain or spinal cord. Biomarkers for these diseases play a crucial role in diagnosis, prognosis, and monitoring treatment efficiency. Genetically, variants such as the APOE ε4 allele significantly increase susceptibility to Alzheimer's by promoting amyloid-beta (Aβ) deposition such as cholinesterase. Biomarkers for these diseases play a crucial role in diagnosis, prognosis, and monitoring treatment efficiency. Genetically, variants such as the APOE ε4 allele significantly increases significantly increase susceptibility to Alzheimer's by promoting amyloid-beta (Aβ) deposition and neuroinflammation, while mutations in genes like SNCA (α-synuclein) are associated with Parkinson's disease, linking aging-related mitochondrial dysfunction and protein aggregation. Moreover, epigenetic changes such as DNA methylation and histone modifications, which accumulate with age, regulate the expression of key neurodegenerative genes, further integrating aging into disease pathology. Imaging markers that bridge aging and neurodegeneration by visualizing age-related changes in brain structure and function. Techniques like positron emission tomography (PET) detect Aβ and tau protein deposits in Alzheimer's, while functional MRI (fMRI) reveals connectivity decline in default mode networks commonly seen in aging brains. Structural MRI identifies brain, especially in regions like the hippocampus, which is vulnerable to both aging and neurodegeneration. Importantly, these markers interact; for instance, genetic predispositions (e.g., APOE ε4) amplify age-associated reductions in cerebral glucose metabolism, detectable through FDG-PET imaging. The convergence of genetic and imaging biomarkers which affect aging and neurodegeneration, enabling earlier diagnosis and precise therapeutic targeting, The linking of interconnected diseases in aging-related mitochondrial dysfunction and protein aggregation. Moreover, epigenetic changes such as DNA methylation and histone modifications, which accumulate with age, regulate the expression of key neurodegenerative genes, further integrating aging into disease pathology. Imaging biomarkers also bridge aging and neurodegeneration by visualizing age-related changes in brain structure and function. The deficiency reveals the connectivity decline in default mode networks commonly seen in aging

brains. Structural MRI identifies brain, especially in regions like the hippocampus, which is vulnerable to both aging and neurodegeneration. Importantly, these markers interact; for instance, genetic predispositions (e.g., APOE ε4) amplify age-associated reductions in cerebral glucose metabolism. The convergence of genetic and imaging biomarkers which affect aging and neurodegeneration, enabling earlier diagnosis and precise therapeutic targeting and neuroinflammation, while mutations in genes like SNCA (α-synuclein) are associated with Parkinson's disease that further integrating in aging into disease pathology. Imaging biomarkers also bridge aging and neurodegeneration by visualizing age-related changes in brain structure and function. Techniques like positron emission tomography (PET) detect Aβ and tau protein deposits in Alzheimer's, while functional MRI (fMRI) reveals connectivity decline in default mode networks commonly seen in aging brains. Importantly, these markers interact; for instance, genetic predispositions (e.g., APOE ε4) amplify age-associated reductions in cerebral glucose metabolism, detectable through FDG-PET imaging. The convergence of genetic biomarkers, while the diseases involves the protein misfolding to form lewy bodies inside the neuron like SNCA (α-synuclein) are associated with Parkinson's disease, linking aging-related mitochondrial dysfunction and protein aggregation. Imaging biomarkers also bridge aging and neurodegeneration by visualizing age-related changes in brain structure and function. Structural MRI identifies brain, especially in regions like the hippocampus, which is vulnerable to both aging and neurodegeneration. Importantly, these markers interact; for instance, genetic predispositions (e.g., APOE ε4) amplify age-associated reductions in cerebral glucose metabolism, detectable through FDG-PET imaging. The convergence of genetic and imaging biomarkers which affect aging and neurodegeneration, enabling earlier diagnosis and precise therapeutic targeting. The comparison that occurred between the biomarkers and therapeutic strategies by classifying that the biomarker has aggregation of protein, neuron loss and evidences provided for visualization and mutant level detection and in therapies by neuroprotection as antioxidants and coenzymeQ10 for stabilization and growth factor.

CONCLUSION

The intersection of aging and neurodegenerative disorders presents a multifaceted challenge that demands continued scientific attention. With the rise in age-related conditions like Alzheimer's, Parkinson's, and ALS, there is an urgent need for more effective diagnostic and therapeutic strategies. Aging significantly contributes to the underlying pathology of these diseases, disrupting vital cellular processes and accelerating neurodegeneration. The treatment provided for the treatment of protein misfolding and Alzheimer diseases occurred in older adults by causing memory loss and that the diagnosis of this not yet established this is challenging. While current treatments offer limited symptomatic relief, emerging research into aging-related mechanisms and advanced technologies such as gene editing and novel biomarkers holds great promise. Ultimately, a deeper understanding of how aging drives neurodegeneration is critical to developing early detection tools and transformative treatments that can improve the hallmark of the patient, vitalize the outcomes and reduce the global healthcare burden. The future research occurred towards on transitional approaches for overcoming the diseases, the consequences that produces by the neuron loss, eliminating the analytical gaps by providing the specificity, sensitivity and reproducibility of the disorders on approval of the biomarker that developed for treatment.

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Conflict of Interest

The author declares that there is no Conflicts of interest.

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