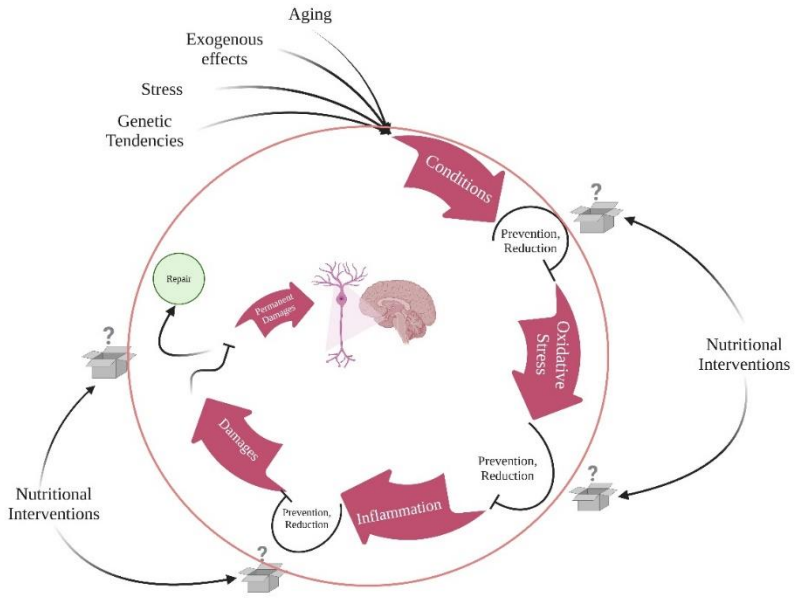
Journal of Vasyl Stefanyk Precarpathian National University. Biology
https://journals.pnu.edu.ua/index.php/jpnubio/
Vol. 11 (2024), P44-P56

UDC 57.022, 57.023
doi: 10.15330/jpnubio.11.44-56

NUTRITIONAL INTERVENTIONS IN NEUROLOGICAL PATHOLOGIES: TARGETING INFLAMMATION AND OXIDATIVE STRESS

ANDRII DIVNYCH, VOLODYMYR LUSHCHAK

Abstract: Neurological pathologies encompass various disorders affecting the central and peripheral nervous systems, arising from structural, biochemical, or electrical abnormalities in the brain, spinal cord, or peripheral nerves. These pathologies manifest through diverse symptoms, including numbness, cognitive impairment, impaired motor coordination, seizures, and altered states of consciousness. According to the World Health Organization, neurological disorders affect individuals across all age groups and geographical regions, with nearly one billion people currently impacted globally. The etiology of neurological pathologies is evidently multifactorial, encompassing genetic mutations, disruptions in cellular systems and pathways that lead to neuronal disturbances, and various environmental factors that may accelerate disease progression.



Graphical overview of the review targets

The illustration shows a cyclic relationship between oxidative stress and inflammation where each amplifies the other, leading to progressive neuronal damage. This cycle, influenced by aging, stress, and genetic predispositions, can result in permanent damage. The review article explores nutritional interventions to disrupt this loop, preventing or reducing oxidative stress and inflammation to promote repair and protect neuronal health. Created in BioRender. Divnych, A. (2025) https://BioRender.com/y65k654

This review focuses on how inflammation and oxidative stress contribute to developing neurological disorders, with an overview of potential nutritional interventions. First, we define and describe the concept of neurological pathology and emphasize the critical role of animal models in advancing research in this field. Subsequently, we discuss oxidative stress and inflammation, their impacts on neuronal cells, and evidence-based nutritional strategies that may mitigate these effects. The primary objective is to underscore the potential of dietary approaches in reducing the risk of neurological disorders by targeting key mechanisms such as oxidative stress and inflammation. We propose that a carefully designed nutritional regimen can enhance the balance between cellular damage and repair, thereby decreasing the likelihood of irreversible neuronal damage, extending lifespan and especially healthspan, and improving the overall quality of life.

Keywords: Neurological Disorders, Antioxidant System, Inflammation, Oxidative Stress.

1. INTRODUCTION

Neurological disorders constitute a diverse group of complex conditions arising from a combination of genetic factors, congenital abnormalities, and environmental or lifestyle influences (Mukherjee et al., 2023). This multifactorial etiology poses significant challenges to understanding, treating, and preventing these disorders comprehensively. Affecting millions of individuals globally, neurological disorders are a leading cause of disability-adjusted life years (DALYs) and represent a substantial global health burden. According to the Global Burden of Disease Study 2021, 37 neurological conditions were identified as the leading contributors to DALYs, collectively accounting for 443 million DALYs worldwide. This extends to an estimated 3.4 billion individuals, or approximately 43% of the global population, reflecting an 18.2% increase in DALY counts since 1990 (Steinmetz et al., 2024). Their effects go beyond the individuals who have them, creating challenges for families, communities, and healthcare systems.

Consequently, neurological disorders have emerged as a major focus of scientific research, driving efforts to develop effective treatment strategies, reducing their societal and economic burden, and enhance preventive measures. Research on neurological disorders can be approached from multiple perspectives, with oxidative stress and inflammation emerging as critical focus areas due to their pivotal roles in disease pathogenesis and therapeutic interventions (Degan et al., 2018; Hassan et al., 2022). The brain's unique metabolic profile, characterized by the activity of excitatory amino acids and neurotransmitters, generates substantial amounts of reactive oxygen species (ROS), rendering it particularly susceptible to oxidative stress for several reasons (Uttara et al., 2009). Harmful effects of ROS on human cells can lead to oxidative damage, and, in severe cases, trigger programmed cell death (apoptosis) (Salganik, 2001). The mitochondrial electron transport chain is recognized as the primary source of ROS, which makes mitochondria the first target for many types of oxidative damage. For example, increased mitochondrial membrane permeability facilitates the release of damage-associated molecular patterns (DAMPs), mitochondrial DNA (mtDNA), cytochrome c, and N-formylated peptides into the cytoplasm, triggering inflammatory pathways. This process, intensified by mitochondrial dysfunction, significantly contributes to neuroinflammation. In response to the accumulation of damaged mitochondria, protective mechanisms such as autophagy and mitophagy are activated to mitigate further damage. However, prolonged oxidative stress can compromise these defenses, reducing mitochondrial biogenesis and increasing neuronal damage (Dmytriv et al., 2023). These processes affect glial cells and post-mitotic neurons which are particularly vulnerable to oxidative damage. The resulting neuronal injury underscores the critical interplay between oxidative stress, mitochondrial dysfunction, and inflammation in the pathophysiology of neurological disorders (Lee et al., 2021).

Oxidative stress exerts diverse effects on cellular function, underscoring the substantial therapeutic potential of targeting these processes. The body employs two primary defense

mechanisms: endogenous and exogenous antioxidants. Endogenous antioxidants include enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase, which neutralize ROS like superoxide anion radicals and hydrogen peroxide. Exogenous antioxidants, obtained from dietary sources, augment these intrinsic defenses. Compounds such as vitamin C, vitamin E, beta-carotene, and plant-derived flavonoids directly interact with ROS to neutralize them, which in turn preserves cell membrane integrity and mitigates inflammation (Kumar et al., 2015). Nutritional strategies aimed at enhancing the activities of antioxidant enzymes offer a promising approach to safeguarding cerebral cells against oxidative damage. Additionally, increasing the intake of dietary antioxidants further supports cellular defense mechanisms and helps to cope with oxidative stress (Vetrani et al., 2012).

2. THE CONCEPT OF NEUROLOGICAL PATHOLOGIES IN HUMANS AND MICE

Neurological disorders represent a significant global health burden, impacting millions of people around the world and creating huge challenges for effective prevention and treatment. These pathologies are medical conditions that affect the central and peripheral nervous systems and are especially common in the growing elderly population. They involve changes in the nervous system's structure, biochemical processes, and electrical activity, often leading to damage or loss of nerve cells and their connections (Dias-Carvalho et al., 2024). According to the 2021 study, stroke, Alzheimer's disease, Parkinson's disease, multiple sclerosis, and meningitis are among the top neurological conditions contributing to the loss of health study (Steinmetz et al., 2024). In addition to these, conditions like Posttraumatic stress disorder (PTSD) have a profound impact on mental health and quality of life, though not typically fatal (Davis & Hamner, 2024).

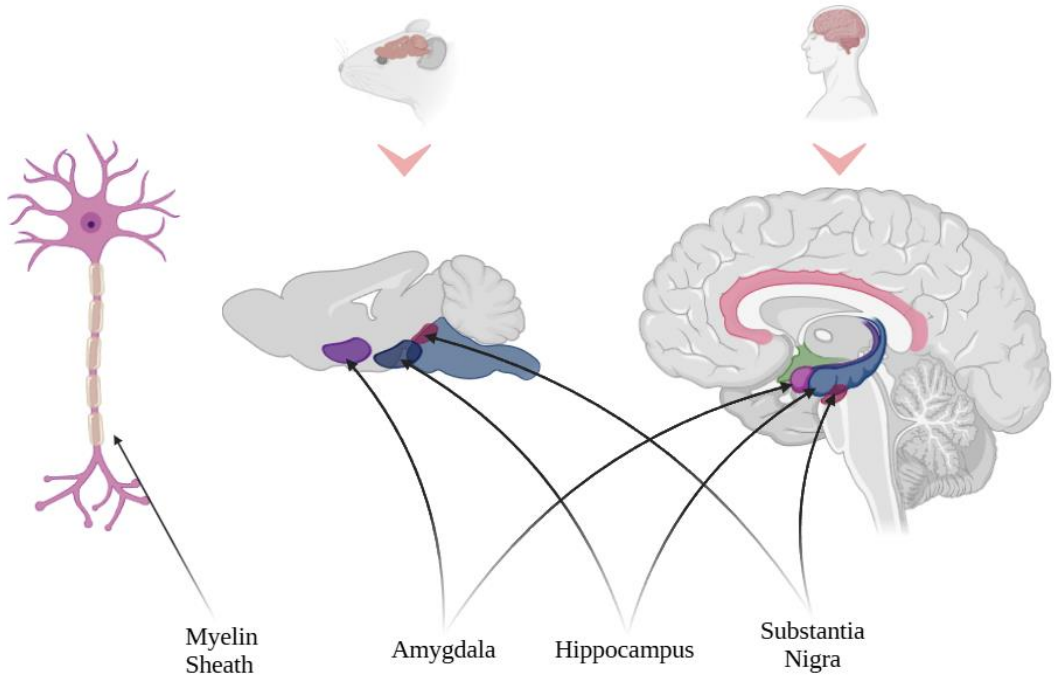


Fig. 1. Overview of key affected brain regions in mice and humans at neurological disorders. Illustrative representation of the brain parts affected by the most common neurological disorders - Hippocampus in Alzheimer's disease, Substantia Nigra in Parkinson's disease, Myelin Sheath in Multiple Sclerosis, and Amygdala in Posttraumatic stress disorder (PTSD). Created in BioRender. Divnych, A. (2025) https://BioRender.com/u89a631.

General knowledge to understand the causes of these disorders is greatly improved these days by using living models that mimic the specific disease. While many animal models are used to study

neurological and neurodegenerative disorders, mice and rats are among the most common because they share a closer similarity to humans than most other models. As shown in Fig.1, key brain regions such as the hippocampus, amygdala, and substantia nigra, along with the myelin sheath, are often affected by neurological disorders in both humans and mice. At the genomic level, the mouse and human genomes are approximately 85% identical, and mice, rats, and humans share about 95% of their genes (Tello et al., 2022). Human and mouse brains grow similarly at the structural and cellular levels, though at different speeds. As they grow, both also show similar age-related behaviors, like being more social, developing memory skills, and taking more risks (Semple et al., 2013). These facts make human neurological disorders with a mutant gene component – ideal candidates for modeling via manipulations of genes in mice.

For instance, genetic modification and gene-targeting strategies are extensively utilized to generate null mutations or gene knockouts in mice, enabling the modeling of a variety of Alzheimer's disease-related pathologies (Elder et al., 2010). Transgenic mouse models, based on mutations in the amyloid precursor protein (APP) and presenilins, effectively replicate numerous pathological features of Alzheimer's disease. Although these models do not fully recapitulate the complexity of the human condition, they have provided critical insights into the mechanisms of β-amyloid toxicity and its role in disease progression (Elder et al., 2010). Rodent models can be widely used in gene mutation experiments to study Parkinson's disease (Magen & Chesselet, 2010). For instance, mouse models using mutated α-synuclein genes replicate some clinical features of Parkinson's disease, such as dopamine-induced neuron loss and motor impairments. Promising approaches combine genetic modifications with toxin exposure, as seen in the MitoPark mouse (an animal model of Parkinson's disease with impaired respiratory chain function in dopamine neurons (Ekstrand & Galter, 2009)). It mimics dopamine neuron degeneration and motor decline while highlighting the role of mitochondrial dysfunction in the disease (Potashkin et al., 2010).

Regarding multiple sclerosis, no single animal model can fully capture its diversity, including its clinical and radiological variations. Nevertheless, such models as experimental autoimmune encephalomyelitis (EAE) or toxin-induced models offer some investigation insights. But they often differ from human multiple sclerosis in terms of disease onset, progression, and treatment timing, and may not reflect the full complexity of the human immune system. Nevertheless, genetically modified mice, like the 2D2 TCR transgenic (express a MOG-specific T cell receptor) and IgH MOG models (B cell heavy chain knock-in mouse strain), have helped scientists to understand how certain T cells and B cells contribute to EAE, used to study multiple sclerosis. These models have also shown that specific immune cells, especially Th1/Th17 cells, and CD4+ T cells, play a key role in the disease's development (Procaccini et al., 2015).

Genetically modified animal models provide a good platform for investigating the impact of targeting general biological pathways and systems. These models allow us to explore how interventions aimed at broad cellular processes, such as metabolic pathways or neuronal signaling, may influence the progression of neurological disorders. They also allow to test various strategies that could potentially slow down or prevent disease development, which is the primary topic of this review.

3. INVOLVEMENT OF OXIDATIVE STRESS ON NEUROLOGICAL DISORDERS AND EFFECTS OF NUTRITION

The brain is especially susceptible to oxidative damage due to its high metabolic activity, substantial ROS production, weak antioxidant defenses, abundant polyunsaturated lipid content, very high energy demands, non-replicating neurons, and high membrane surface area relative to the cytoplasm (Lee et al., 2020). While oxygen is essential for cellular function and survival, an imbalance caused by excessive ROS or a weakened antioxidant system can lead to oxidative injury (Chiurchiù et al., 2016). This vulnerability makes the brain more susceptible to neurodegenerative

diseases driven by oxidative stress. To maintain a healthy balance, cells have intricate antioxidant mechanisms to regulate oxygen intake and utilization. These mechanisms include non-enzymatic antioxidants like glutathione, taurine, creatine, zinc, vitamins E, C, and A, as well as antioxidant enzymes such as SOD, catalase, and glutathione peroxidase (Alkadi, 2020). Exogenic ROS sources such as diverse chemicals and radiation may substantially increase ROS levels in the cellular milieu (Juan et al., 2021). Mitochondria provides oxidative phosphorylation, a process that relies on the mitochondrial respiratory chain to generate ATP. During this process, around 10% of the oxygen consumed is converted into ROS which serves as natural byproducts and key contributors to oxidative stress (Lushchak, 2014; Sousa et al., 2018). The mitochondrial DNA, responsible for coding essential proteins involved in oxidative phosphorylation, is particularly vulnerable. Mutations in mitochondrial DNA can impair the synthesis of these components, disrupting ATP production, increasing ROS levels, and leading to system-wide imbalances (Lushchak, 2014).

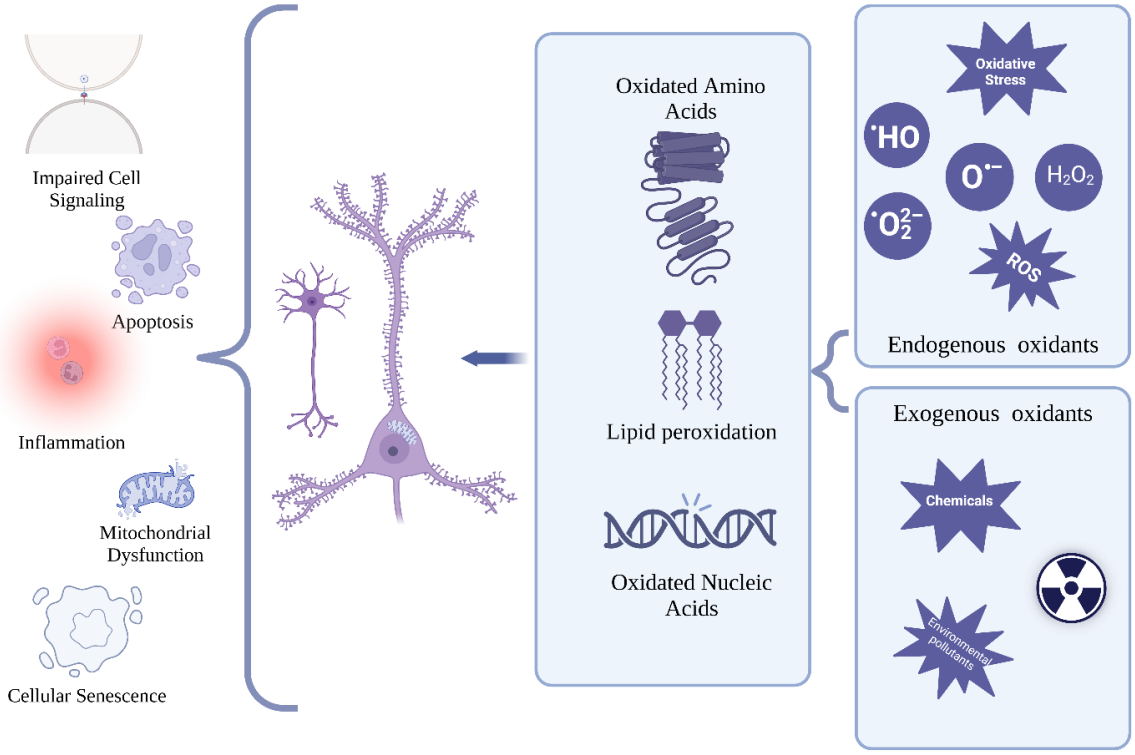


Fig. 2. Cellular damage induced by reactive oxygen species. Illustrative representation of the common ROS targets of damage causing various cellular consequences in pyramidal neurons. Created in BioRender. Divnych, A. (2025) https://BioRender.com/f02s325 by modifying the original idea (Santibáñez-Andrade et al., 2023).

Increased levels of ROS and reactive nitrogen species (RNS) along with altered antioxidant defense systems are common in the case of many neurodegenerative diseases (Domanskyi & Parlato, 2022). Figure 2 shows the destructive effects of reactive nitrogen species can lead to completely different outcomes. These effects, along with mitochondrial dysfunction, cellular senescence, and apoptosis, contribute to genomic instability, protein degradation, and impaired cell signalling. Collectively they play a role in ageing and the development of diseases like neurodegenerative disorders, cardiovascular diseases, and cancer.

Neurodegenerative diseases are primarily marked by the apoptosis or necrosis of neuronal cells, resulting in significant damage to the nervous system. As the most metabolically active organ in the body, the brain is particularly susceptible to oxidative stress. The brain has a high oxygen demand, utilizing approximately 20% of the body's total oxygen consumption (Tavares et al., 2023).

Additionally, the brain contains high levels of redox-active metals, such as copper and iron, which contribute to producing ROS (Gao et al., 2023). Neurons, in particular, require a substantial amount of energy. They consume up to 80% of the energy produced in the brain (Hyder et al., 2013). Their ability to handle oxidative stress appears limited, possibly due to the low expression of antioxidant defence regulators like nuclear factor erythroid 2-related factor 2 (Nrf2), even during inflammation (Levings et al., 2023). Mitochondrial gene deletions, often found in neuronal cell bodies, seem to arise from oxidatively damaged axons in white matter plaques and then multiply within affected cells. Oxidized lipids accumulate in active cortical lesions of multiple sclerosis patients, correlating with dendritic and axonal fragmentation or signs of apoptosis. Mitochondrial damage leads to energy deficits, hindering neuronal impulse conduction. Severe damage can cause axonal and neuronal degeneration via ionic imbalances and calcium buildup (Lassmann & van Horssen, 2016). Therefore, oxidative injury and mitochondrial damage, leading to energy failure, appear crucial in neuronal dysfunction and death.

As we already established, neuronal activity relies on a constant supply of energy, primarily from glucose with the utilization of oxygen. Metabolites are delivered to the brain from blood through the blood-brain barrier (BBB). Energy metabolism in the brain involves complex processes, where glucose is transported into cells primarily by the glucose transporter 1 (GLUT1) transporter on endothelial cells, and subsequently taken up by astrocytes. These cells use glucose for glycolysis, producing lactate, which is then transferred into neurons to fuel their activity. Sufficient energy levels in neurons are critically important for synaptic function and neurotransmitter release (Lushchak et al., 2021). However, numerous studies demonstrate that excessive glucose levels and the associated overactivity of the mitochondrial electron transport chain can lead to increased generation of ROS and the development of oxidative stress. For example, consumption of a high-carbohydrate diet resulted in lower plasma Total Antioxidant Status (TAS), suggesting an intensification of oxidative stress associated with hyperglycemia, whereas expression of Cu/Zn-SOD was reduced (Gregersen et al., 2012). Consumption of a high-fat (energy-dense) diet also triggered oxidative stress (Devaraj et al., 2008). Bioactive peptides from various sources, including marine organisms, milk, and plants, have antioxidant properties. They can neutralize free radicals and reduce metal ions, potentially protecting cells from oxidative stress by enhancing the activity of antioxidant enzymes (Chakrabarti et al., 2014). Excessive consumption of protein can have a negative impact on the homeostasis of neuron cells in rodents (Camiletti-Moirón et al., 2015; Żebrowska et al., 2019). On the opposite side, the reduction of caloric intake without malnutrition is one of the most consistent experimental interventions that increases mean and maximum lifespans in different species. Calorie restriction (CR) can significantly influence brain metabolism, primarily by altering glucose utilization and mitochondrial function (Ribeiro et al., 2012). This metabolic shift can impact levels of oxidative stress markers, as CR has been shown to reduce ROS production and enhance antioxidant defenses in the brain (Rattan, 2008). Mitochondrial activity can be regulated through various mechanisms, including mitochondrial dynamics, fusion, and fission, which play key roles in energy production, apoptosis, and cellular signaling. Modulating mitochondrial shape and function offers potential therapeutic opportunities, especially in conditions like cancer and neurological disorders

In conclusion, proper regulation of energy metabolism in the brain is essential for maintaining optimal neuronal function, as both excessive nutrient intake and caloric restriction affect oxidative stress and cellular balance. Effective control of energy supply and mitochondrial activity is vital for supporting brain health and minimizing oxidative damage.

4. NEUROINFLAMMATION AND THE ROLE OF NUTRITION

Inflammation is a complex biological response to how the body deals with injury and infection to eliminate the initial cause of cell injury and affect repair (Skaper et al., 2018). This process is initiated by danger signals, which activate pathways involving signal transmission, the production of inflammatory mediators, and the activation of cellular effectors such as immune cells (Medzhitov, 2008). Even though inflammation is one of the tools of human's immune defense, it also promotes the generation of ROS, which can extend oxidative stress and lead to the oxidation of lipids, nucleic acids, and proteins, leading to the formation of DAMPs. These oxidative modifications can further amplify inflammation leading to apoptosis or necrosis, contributing to tissue damage (Fig. 3) (Ávila-Escalante et al., 2020).

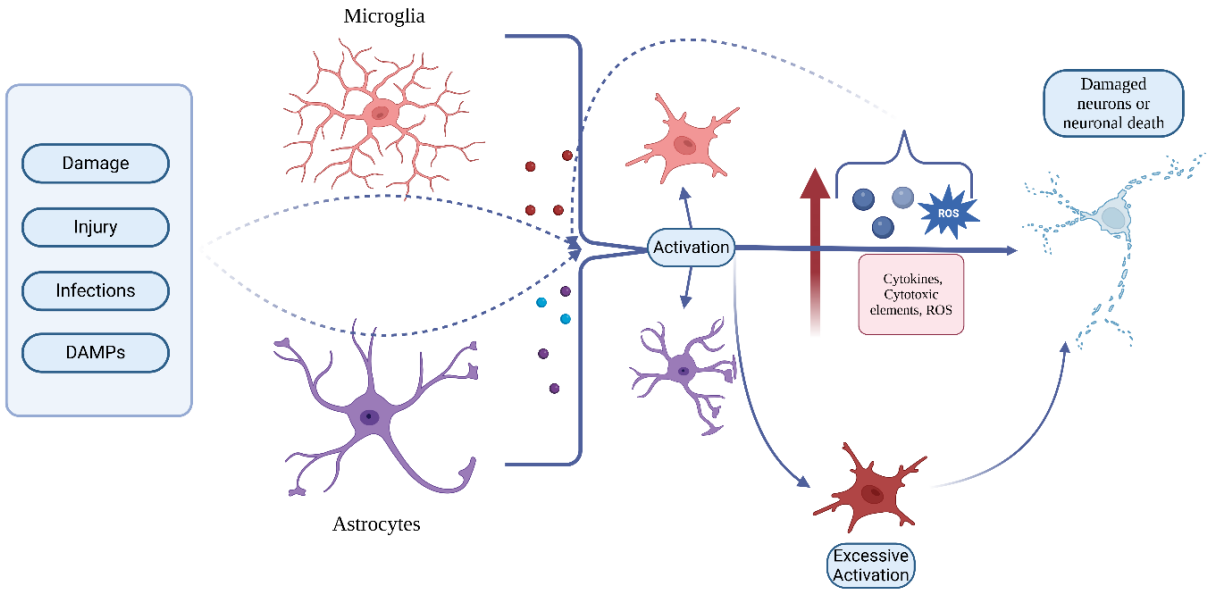


Fig. 3. The neuroinflammatory process. When exposed to signals of damage, injury, infections, or DAMPs, astrocytes and microglia undergo progressive activation, characterized by morphological changes and the release of pro-inflammatory factors such as cytokines, cytotoxic elements, and ROS. This activation is often triggered by signals from stressed or damaged neurons. Persistent activation creates a feedback loop not only between astrocytes and microglia but also involving neurons, amplifying neuroinflammatory responses. Over time, this sustained neuroinflammation leads to neuronal dysfunction, synaptic loss, and excitotoxicity, ultimately contributing to neuronal death and the progression of neurodegenerative conditions. Created in BioRender. Divnych, A. (2025) https://BioRender.com/r90s996 by modifying the original idea (Morales et al., 2014).

Inflammation significantly contributes to Alzheimer's disease progression by activating microglia and astrocytes in response to amyloid-β (Aβ) deposits. This leads to increased production of pro-inflammatory cytokines, reactive oxygen species, and complement components. Often found near Aβ plaques, mast cells can amplify neuroinflammatory responses through degranulation, histamine release, and crosstalk with glial cells, further exacerbating blood-brain barrier breakdown

and neuronal damage (Skaper et al., 2018). Activated microglia adopt a pro-inflammatory state, releasing cytokines like TNF-α, IL-1β, and IL-6, which damage dopaminergic neurons. Misfolded α-synuclein also triggers microglial activation, promoting oxidative stress and a cycle of neuroinflammation and neuronal death. Additionally, inflammation disrupts the blood-brain barrier, allowing peripheral immune cells to infiltrate the brain and exacerbate local immune responses. That also contributes to the development of Parkinson`s disease (Pajares et al., 2020). Inflammation also plays a critical role in the pathology of PTSD by driving immune system dysregulation and mitochondrial dysfunction. Elevated levels of pro-inflammatory cytokines, such as IL-1β, IL-6, and TNFα, promote mitochondrial dysfunction by triggering excessive ROS production, which in turn activates inflammatory pathways, leading to neuroinflammation. This inflammatory response disrupts normal neuronal function, particularly in areas like the amygdala, further contributing to the emotional and cognitive symptoms of PTSD (O. Lushchak et al., 2023).

Nutritional strategies for managing neuroinflammation involve modulating inflammatory pathways and oxidative stress within the brain, offering potential avenues for preventing and controlling neurodegenerative diseases. Omega-3 fatty acids, especially docosahexaenoic acid, have demonstrated anti-inflammatory effects by reducing pro-inflammatory cytokine production and enhancing neuronal membrane integrity (Swaminathan & Jicha, 2014). A high-fat diet also induces neuroinflammation and mitochondrial impairment in mice's cerebral cortex and synaptic fraction (Cavaliere et al., 2019). Polyphenols, found abundantly in fruits and vegetables, exhibit antioxidant and anti-inflammatory properties by scavenging free radicals and modulating signaling pathways such as NF-κB (Barber et al., 2023). Caloric restriction and intermittent fasting have shown promise in reducing neuroinflammation through mechanisms like promoting autophagy and decreasing oxidative stress intensity (Kurowska et al., 2023). Specific micronutrients, including vitamin D and zinc, play essential roles in immune regulation and neuronal protection (Quarantelli, 2015). Moreover, the gut-brain axis represents a crucial target for nutritional interventions, as modulation of gut microbiota composition and function can influence neuroinflammation (Fornari Laurindo et al., 2024). Multiple animal studies have shown that the ketogenic diet (KD) reduces excessive immune activation and regulates inflammation pathways, such as adenosine signaling, NLRP3 inflammasome, and gut microbiota. By modulating these mechanisms, KD helps decrease neuroinflammation, which plays a key role in the progression of neurological disorders like epilepsy and epileptic encephalopathies (Koh et al., 2020).

Both human and mouse models exhibit neuroinflammation characterized by activation of microglia and astrocytes, release of pro-inflammatory cytokines, and disruption of the blood-brain barrier. However, differences exist in specific inflammatory mediators, the temporal dynamics of the response, and the extent of neuronal damage (Tamura et al., 2022).

5. CONCLUSIONS

As the human population ages, the prevalence of aging-related diseases increases, placing an ever-increasing burden on healthcare systems around the world. Neurodegenerative diseases stand out due to the lack of effective therapies. The burden of these diseases is expected to grow at an increasing rate unless more effective treatments are developed, or cures are discovered. While neurological pathologies vary in their nature, they often share common underlying mechanisms, such as oxidative stress and inflammation (Ozgen et al., 2022). Neurons and microglia are both affected by the interconnected mechanisms of oxidative stress, mitochondrial damage, and inflammation, leading to neuronal dysfunction and death (Koellhoffer et al., 2017). Therefore, understanding these mechanisms, particularly their interplay, is crucial for developing effective preventative and therapeutic strategies.

This review demonstrates that targeting these shared pathways, especially through dietary interventions, is promising for therapeutic interventions. While dietary changes alone may not cure

neurological disorders, they have the potential to slow disease progression and support brain health (Barber et al., 2023). Further research should focus on refining these approaches and exploring complementary strategies, such as antioxidant therapies and mitochondrial support, to improve outcomes and enhance the quality of life for those affected by these debilitating conditions.

Acknowledgements

The authors thank Professor Maria Bayliak and M. Sc. Leading Specialist Tetiana Dmytriv of the Department of Biochemistry and Biotechnology for their critical review reading of the article.

This work was supported by a grant from the Ministry of Education and Science of Ukraine (grant number 0123U101790).

Conflict of interests

The authors declare that they have no conflict of interest.

REFERENCES

Alkadi, H. (2020). A Review on Free Radicals and Antioxidants. *Infectious Disorders - Drug Targets*, *20*(1), 16–26. https://doi.org/10.2174/1871526518666180628124323

Ávila-Escalante, M. L., Coop-Gamas, F., Cervantes-Rodríguez, M., Méndez-Iturbide, D., & Aranda-González, I. I. (2020). The effect of diet on oxidative stress and metabolic diseases—Clinically controlled trials. *Journal of Food Biochemistry*, *44*(5). https://doi.org/10.1111/jfbc.13191

Barber, K., Mendonca, P., Evans, J. A., & Soliman, K. F. A. (2023). Antioxidant and Anti-Inflammatory Mechanisms of Cardamonin through Nrf2 Activation and NF-kB Suppression in LPS-Activated BV-2 Microglial Cells. *International Journal of Molecular Sciences*, *24*(13), 10872. https://doi.org/10.3390/ijms241310872

Camiletti-Moirón, D., Aparicio, V., Nebot, E., Medina, G., Martínez, R., Kapravelou, G., Andrade, A., Porres, J., López-Jurado, M., & Aranda, P. (2015). High-intensity Exercise Modifies the Effects of Stanozolol on Brain Oxidative Stress in Rats. *International Journal of Sports Medicine*, *36*(12), 984–991. https://doi.org/10.1055/s-0035-1548941

Cavaliere, G., Trinchese, G., Penna, E., Cimmino, F., Pirozzi, C., Lama, A., Annunziata, C., Catapano, A., Mattace Raso, G., Meli, R., Monda, M., Messina, G., Zammit, C., Crispino, M., & Mollica, M. P. (2019). High-Fat Diet Induces Neuroinflammation and Mitochondrial Impairment in Mice Cerebral Cortex and Synaptic Fraction. *Frontiers in Cellular Neuroscience*, *13*, 509. https://doi.org/10.3389/fncel.2019.00509

Chakrabarti, S., Jahandideh, F., & Wu, J. (2014). Food-derived bioactive peptides on inflammation and oxidative stress. *BioMed Research International*, *2014*, 608979. https://doi.org/10.1155/2014/608979

Chiurchiù, V., Orlacchio, A., & Maccarrone, M. (2016). Is Modulation of Oxidative Stress an Answer? The State of the Art of Redox Therapeutic Actions in Neurodegenerative Diseases. *Oxidative Medicine and Cellular Longevity*, *2016*, 7909380. https://doi.org/10.1155/2016/7909380

Davis, L. L., & Hamner, M. B. (2024). Post-traumatic stress disorder: the role of the amygdala and potential therapeutic interventions - a review. *Frontiers in Psychiatry*, *15*, 1356563. https://doi.org/10.3389/fpsyt.2024.1356563

Degan, D., Ornello, R., Tiseo, C., Carolei, A., Sacco, S., & Pistoia, F. (2018). The Role of Inflammation in Neurological Disorders. *Current Pharmaceutical Design*, *24*(14), 1485–1501. https://doi.org/10.2174/1381612824666180327170632

Devaraj, S., Wang-Polagruto, J., Polagruto, J., Keen, C. L., & Jialal, I. (2008). High-fat, energy-dense, fast-food-style breakfast results in an increase in oxidative stress in metabolic syndrome. *Metabolism: Clinical and Experimental*, *57*(6), 867–870. https://doi.org/10.1016/j.metabol.2008.02.016

Dias-Carvalho, A., Sá, S. I., Carvalho, F., Fernandes, E., & Costa, V. M. (2024). Inflammation as common link to progressive neurological diseases. *Archives of Toxicology*, *98*(1), 95–119. https://doi.org/10.1007/s00204-023-03628-8

Divnych, A. (2025). Graphical overview of the review targets. Created in BioRender. https://BioRender.com/y65k654

Divnych, A. (2025). Overview of key affected brain regions in mice and humans at neurological disorders. Created in *BioRender*. https://BioRender.com/u89a631

Divnych, A. (2025). Cellular damage induced by reactive oxygen species. Created in *BioRender*. https://BioRender.com/f02s325

Divnych, A. (2025). The neuroinflammatory process. Created in *BioRender*. https://BioRender.com/r90s996

Dmytriv, T. R., Tsiumpala, S. A., Semchyshyn, H. M., Storey, K. B., & Lushchak, V. I. (2023). Mitochondrial dysfunction as a possible trigger of neuroinflammation at post-traumatic stress disorder (PTSD). *Frontiers in Physiology*, *14*, 1222826. https://doi.org/10.3389/fphys.2023.1222826

Domanskyi, A., & Parlato, R. (2022). Oxidative Stress in Neurodegenerative Diseases. *Antioxidants (Basel, Switzerland)*, *11*(3), 504. https://doi.org/10.3390/antiox11030504

Ekstrand, M. I., & Galter, D. (2009). The MitoPark Mouse – An animal model of Parkinson's disease with impaired respiratory chain function in dopamine neurons. *Parkinsonism & Related Disorders*, *15*, S185–S188. https://doi.org/10.1016/s1353-8020(09)70811-9

Elder, G. A., Gama Sosa, M. A., & de Gasperi, R. (2010). Transgenic mouse models of Alzheimer's disease. *The Mount Sinai Journal of Medicine, New York*, *77*(1), 69–81. https://doi.org/10.1002/msj.20159

Fornari Laurindo, L., Aparecido Dias, J., Cressoni Araújo, A., Torres Pomini, K., Machado Galhardi, C., Rucco Penteado Detregiachi, C., Santos de Argollo Haber, L., Donizeti Roque, D., Dib Bechara, M., Vialogo Marques de Castro, M., de Souza Bastos Mazuqueli Pereira, E., José Tofano, R., Jasmin Santos German Borgo, I., & Maria Barbalho, S. (2024). Immunological dimensions of neuroinflammation and microglial activation: exploring innovative immunomodulatory approaches to mitigate neuroinflammatory progression. *Frontiers in Immunology*, *14*, 1305933. https://doi.org/10.3389/fimmu.2023.1305933

Gao, G., You, L., Zhang, J., Chang, Y.-Z., & Yu, P. (2023). Brain Iron Metabolism, Redox Balance and Neurological Diseases. *Antioxidants (Basel, Switzerland)*, *12*(6), 1289. https://doi.org/10.3390/antiox12061289

Gregersen, S., Samocha-Bonet, D., Heilbronn, L. K., & Campbell, L. v. (2012). Inflammatory and oxidative stress responses to high-carbohydrate and high-fat meals in healthy humans. *Journal of Nutrition and Metabolism*, *2012*, 238056. https://doi.org/10.1155/2012/238056

Hassan, W., Noreen, H., Rehman, S., Kamal, M. A., & da Rocha, J. B. T. (2022). Association of Oxidative Stress with Neurological Disorders. *Current Neuropharmacology*, *20*(6), 1046–1072. https://doi.org/10.2174/1570159X19666211111141246

Hyder, F., Rothman, D. L., & Bennett, M. R. (2013). Cortical energy demands of signaling and nonsignaling components in brain are conserved across mammalian species and activity levels. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(9), 3549–3554. https://doi.org/10.1073/pnas.1214912110

Juan, C. A., Pérez de la Lastra, J. M., Plou, F. J., & Pérez-Lebeña, E. (2021). The Chemistry of Reactive Oxygen Species (ROS) Revisited: Outlining Their Role in Biological Macromolecules (DNA, Lipids and Proteins) and Induced Pathologies. *International Journal of Molecular Sciences*, *22*(9), 4642. https://doi.org/10.3390/ijms22094642

Koellhoffer, E. C., McCullough, L. D., & Ritzel, R. M. (2017). Old Maids: Aging and Its Impact on Microglia Function. *International Journal of Molecular Sciences*, *18*(4), 769. https://doi.org/10.3390/ijms18040769

Koh, S., Dupuis, N., & Auvin, S. (2020). Ketogenic diet and Neuroinflammation. *Epilepsy Research*, *167*, 106454. https://doi.org/10.1016/j.eplepsyres.2020.106454

Kumar, V., Khan, A. A., Tripathi, A., Dixit, P. K., & Bajaj, U. K. (2015). Role of oxidative stress in various diseases: Relevance of dietary antioxidants. *The Journal of Phytopharmacology*, *4*(2), 126–132. https://doi.org/10.31254/phyto.2015.4213

Kurowska, A., Ziemichód, W., Herbet, M., & Piątkowska-Chmiel, I. (2023). The Role of Diet as a Modulator of the Inflammatory Process in the Neurological Diseases. *Nutrients*, *15*(6), 1436. https://doi.org/10.3390/nu15061436

Lassmann, H., & van Horssen, J. (2016). Oxidative stress and its impact on neurons and glia in multiple sclerosis lesions. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease*, *1862*(3), 506–510. https://doi.org/10.1016/j.bbadis.2015.09.018

Lee, K. H., Cha, M., & Lee, B. H. (2020). Neuroprotective Effect of Antioxidants in the Brain. *International Journal of Molecular Sciences*, *21*(19), 7152. https://doi.org/10.3390/ijms21197152

Lee, K. H., Cha, M., & Lee, B. H. (2021). Crosstalk between Neuron and Glial Cells in Oxidative Injury and Neuroprotection. *International Journal of Molecular Sciences*, *22*(24), 13315. https://doi.org/10.3390/ijms222413315

Levings, D. C., Pathak, S. S., Yang, Y.-M., & Slattery, M. (2023). Limited Expression of Nrf2 in Neurons Across the Central Nervous System. *BioRxiv : The Preprint Server for Biology*, 2023.05.09.540014. https://doi.org/10.1101/2023.05.09.540014

Lushchak, O., Strilbytska, O., Koliada, A., & Storey, K. B. (2023). An orchestrating role of mitochondria in the origin and development of post-traumatic stress disorder. *Frontiers in Physiology*, *13*, 1094076. https://doi.org/10.3389/fphys.2022.1094076

Lushchak, V. I. (2014). Free radicals, reactive oxygen species, oxidative stress and its classification. *Chemico-Biological Interactions*, *224*, 164–175. https://doi.org/10.1016/j.cbi.2014.10.016

Lushchak, V. I., Duszenko, M., Gospodaryov, D. v, & Garaschuk, O. (2021). Oxidative Stress and Energy Metabolism in the Brain: Midlife as a Turning Point. *Antioxidants (Basel, Switzerland)*, *10*(11), 1715. https://doi.org/10.3390/antiox10111715

Magen, I., & Chesselet, M.-F. (2010). *Genetic mouse models of Parkinson's disease* (pp. 53–87). https://doi.org/10.1016/S0079-6123(10)84004-X

Medzhitov, R. (2008). Origin and physiological roles of inflammation. *Nature*, *454*(7203), 428–435. https://doi.org/10.1038/nature07201

Morales, I., Guzmán-Martínez, L., Cerda-Troncoso, C., Farías, G. A., & Maccioni, R. B. (2014). Neuroinflammation in the pathogenesis of Alzheimer's disease. A rational framework for the search of novel therapeutic approaches. *Frontiers in Cellular Neuroscience*, *8*, 112. https://doi.org/10.3389/fncel.2014.00112

Mukherjee, S., Ali, S., Hashmi, S., & Jahan, S. (2023). History, Origin and Types of Neurological Disorders. In *Applications of Stem Cells and derived Exosomes in Neurodegenerative Disorders* (pp. 1–32). Springer Nature Singapore. https://doi.org/10.1007/978-981-99-3848-3_1

Ozgen, S., Krigman, J., Zhang, R., & Sun, N. (2022). Significance of mitochondrial activity in neurogenesis and neurodegenerative diseases. *Neural Regeneration Research*, *17*(4), 741. https://doi.org/10.4103/1673-5374.322429

Pajares, M., I Rojo, A., Manda, G., Boscá, L., & Cuadrado, A. (2020). Inflammation in Parkinson's Disease: Mechanisms and Therapeutic Implications. *Cells*, *9*(7), 1687. https://doi.org/10.3390/cells9071687

Potashkin, J. A., Blume, S. R., & Runkle, N. K. (2010). Limitations of animal models of Parkinson's disease. *Parkinson's Disease*, *2011*, 658083. https://doi.org/10.4061/2011/658083

Procaccini, C., de Rosa, V., Pucino, V., Formisano, L., & Matarese, G. (2015). Animal models of Multiple Sclerosis. *European Journal of Pharmacology*, *759*, 182–191. https://doi.org/10.1016/j.ejphar.2015.03.042

Quarantelli, M. (2015). MRI/MRS in neuroinflammation: methodology and applications. *Clinical and Translational Imaging*, *3*(6), 475–489. https://doi.org/10.1007/s40336-015-0142-y

Rattan, S. I. S. (2008). Hormesis in aging. *Ageing Research Reviews*, *7*(1), 63–78. https://doi.org/10.1016/j.arr.2007.03.002

Ribeiro, L. C., Rodrigues, L., Quincozes-Santos, A., Tramontina, A. C., Bambini-Junior, V., Zanotto, C., Diehl, L. A., Biasibetti, R., Kleinkauf-Rocha, J., Dalmaz, C., Goncalves, C.-A., & Gottfried, C. (2012). Caloric restriction improves basal redox parameters in hippocampus and cerebral cortex of Wistar rats. *Brain Research*, *1472*, 11–19. https://doi.org/10.1016/j.brainres.2012.07.021

Salganik, R. I. (2001). The Benefits and Hazards of Antioxidants: Controlling Apoptosis and Other Protective Mechanisms in Cancer Patients and the Human Population. *Journal of the American College of Nutrition*, *20*(sup5), 464S-472S. https://doi.org/10.1080/07315724.2001.10719185

Santibáñez-Andrade, M., Quezada-Maldonado, E. M., Rivera-Pineda, A., Chirino, Y. I., García-Cuellar, C. M., & Sánchez-Pérez, Y. (2023). The Road to Malignant Cell Transformation after Particulate Matter Exposure: From Oxidative Stress to Genotoxicity. *International Journal of Molecular Sciences*, *24*(2), 1782. https://doi.org/10.3390/ijms24021782

Semple, B. D., Blomgren, K., Gimlin, K., Ferriero, D. M., & Noble-Haeusslein, L. J. (2013). Brain development in rodents and humans: Identifying benchmarks of maturation and vulnerability to injury across species. *Progress in Neurobiology*, *106–107*, 1–16. https://doi.org/10.1016/j.pneurobio.2013.04.001

Skaper, S. D., Facci, L., Zusso, M., & Giusti, P. (2018). An Inflammation-Centric View of Neurological Disease: Beyond the Neuron. *Frontiers in Cellular Neuroscience*, *12*, 72. https://doi.org/10.3389/fncel.2018.00072

Sousa, J. S., D'Imprima, E., & Vonck, J. (2018). *Mitochondrial Respiratory Chain Complexes* (pp. 167–227). https://doi.org/10.1007/978-981-10-7757-9_7

Steinmetz, J. D., Seeher, K. M., Schiess, N., Nichols, E., Cao, B., Servili, C., Cavallera, V., Cousin, E., Hagins, H., Moberg, M. E., Mehlman, M. L., Abate, Y. H., Abbas, J., Abbasi, M. A., Abbasian, M., Abbastabar, H., Abdelmasseh, M., Abdollahi, M., Abdollahi, M., … Dua, T. (2024). Global, regional, and national burden of disorders affecting the nervous system, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *The Lancet Neurology*, *23*(4), 344–381. https://doi.org/10.1016/S1474-4422(24)00038-3

Swaminathan, A., & Jicha, G. A. (2014). Nutrition and prevention of Alzheimer's dementia. *Frontiers in Aging Neuroscience*, *6*, 282. https://doi.org/10.3389/fnagi.2014.00282

Tamura, Y., Yamato, M., & Kataoka, Y. (2022). Animal Models for Neuroinflammation and Potential Treatment Methods. *Frontiers in Neurology*, *13*, 890217. https://doi.org/10.3389/fneur.2022.890217

Tavares, W. M., Araujo de França, S., Paiva, W. S., & Teixeira, M. J. (2023). Early tracheostomy versus late tracheostomy in severe traumatic brain injury or stroke: A systematic review and meta-analysis. *Australian Critical Care*, *36*(6), 1110–1116. https://doi.org/10.1016/j.aucc.2022.12.012

Tello, J. A., Williams, H. E., Eppler, R. M., Steinhilb, M. L., & Khanna, M. (2022). Animal Models of Neurodegenerative Disease: Recent Advances in Fly Highlight Innovative Approaches to Drug Discovery. *Frontiers in Molecular Neuroscience*, *15*, 883358. https://doi.org/10.3389/fnmol.2022.883358

Uttara, B., Singh, A. v, Zamboni, P., & Mahajan, R. T. (2009). Oxidative stress and neurodegenerative diseases: a review of upstream and downstream antioxidant therapeutic options. *Current Neuropharmacology*, *7*(1), 65–74. https://doi.org/10.2174/157015909787602823

Vetrani, C., Costabile, G., di Marino, L., & Rivellese, A. A. (2012). Nutrition and oxidative stress: a systematic review of human studies. *International Journal of Food Sciences and Nutrition*, *64*(3), 312–326. https://doi.org/10.3109/09637486.2012.738651

Żebrowska, E., Maciejczyk, M., Żendzian-Piotrowska, M., Zalewska, A., & Chabowski, A. (2019). High Protein Diet Induces Oxidative Stress in Rat Cerebral Cortex and Hypothalamus. *International Journal of Molecular Sciences*, *20*(7), 1547. https://doi.org/10.3390/ijms20071547

Andrii Divnych*, Ph.D. student, Department of Biochemistry and Biotechnology, Vasyl Stefanyk Precarpathian National University, Ivano-Frankivsk, Ukraine.
ORCID ID: https://orcid.org/0009-0005-7790-9508
Volodymyr Lushchak, Professor, Doctor of Sciences, Department of Biochemistry and Biotechnology, Vasyl Stefanyk Precarpathian National University, Ivano-Frankivsk, Ukraine.
ORCID ID: https://orcid.org/0000-0001-5602-3330
E-mails: andrii.divnych.24@pnu.edu.ua, volodymyr.lushchak@pnu.edu.ua
*Corresponding author

Received: 18 November 2024; **Revised:** 14 December 2024; **Accepted:** 17 December 2024; **Published:** 29 December 2024

Дівнич Андрій, Лущак Володимир. Харчові підходи у протидії неврологічним захворюванням: акцент на запаленні та оксидативному стресі. *Журнал Прикарпатського університету імені Василя Стефаника. Біологія*, Том 11 (2024), С.44-С.56.

Неврологічні розлади охоплюють широкий спектр відхилень, які впливають як на центральну, так і на периферійну нервову систему, виникаючи внаслідок структурних, біохімічних або електричних аномалій у головному мозку, спинному мозку та периферійних нервах. Ці патології проявляються через різноманітні симптоми, включаючи оніміння, когнітивні розлади, порушення моторної координації, судоми та змінені стани свідомості. За даними Всесвітньої організації охорони здоров'я, неврологічні розлади вражають людей усіх вікових груп і географічних регіонів, і на сьогодні майже один мільярд осіб у світі страждає від цих захворювань. Дослідження свідчать, що етіологія неврологічних розладів є мультифакторною, включаючи генетичні мутації, порушення в системах і

шляхах клітин, що призводять до пошкодження нейронів, а також багато зовнішніх чинників, які сприяють прогресуванню захворювання.

У цьому огляді розглядаються природа впливу запалення та оксидативного стресу на розвиток неврологічних розладів, а також можливі харчові дієтичні втручання для модулювання цих процесів. Спочатку визначено та описано концепцію неврологічних розладів, акцентовано увагу на важливості використання тваринних моделей для прогресу в дослідженнях цієї галузі. Далі проаналізовані окислювальний стрес і запалення, їхній вплив на нейрони, а також розглянуто науково-обґрунтовані харчові стратегії, які можуть впливати на описані процеси. Основна мета полягає в підкресленні потенціалу дієтичних підходів у зниженні ризику розвитку неврологічних розладів шляхом впливу на ключові механізми, такі як окислювальний стрес та запалення. Передбачається, що ретельно розроблений харчовий режим може покращити баланс між клітинним пошкодженням і відновленням, зменшити ймовірність незворотного пошкодження нейронів, подовжити тривалість життя та покращити загальну якість життя.

Ключові слова: Неврологічні розлади, антиоксидантна система, запалення, оксидативний стрес.