International Journal of Geriatrics and Gerontology

Hao J, et al. Int J Geriatr Gerontol 7: 165.

www.doi.org/10.29011/2577-0748.100065

www.gavinpublishers.com

OPEN ACCESS

GAVIN PUBLISHERS

Review Article

NADH in the Prevention and Treatment of Parkinson's Disease: Mechanisms and Research Progress

Junjie Hao[1], Jamie Hao[1], Jiren Zhang[2*]

[1]Northland Christian School, Houston, TX 77014, United States

[2]Hainan Institute of targeted anti-aging and Chronic Disease Prevention and treatment, China

***Corresponding author:** Jiren zhang.Hainan Institute of targeted anti-aging and Chronic Disease Prevention and treatment, China

Citation: Hao J, Hao J, Zhang J (2023) NADH in the Prevention and Treatment of Parkinson's Disease: Mechanisms and Research Progress. Int J Geriatr Gerontol 6: 165. DOI: 10.29011/2577-0748.100065

Received Date: 24 August, 2023; **Accepted Date:** 03 September , 2023; **Published Date:** 07 September, 2023

Abstract

Parkinson's disease (PD) is a neurodegenerative disorder characterized by the progressive loss of dopaminergic neurons in the substantia nigra, leading to motor and cognitive dysfunction. Recent studies have highlighted the potential of Nicotinamide Adenine Dinucleotide (NADH) in the prevention and treatment of PD. This paper aims to summarize the current understanding of the pathogenesis of PD, the mechanism of NADH in treating PD, and the results of research conducted by various universities and institutions on NADH's potential for treating or preventing the disease. NADH demonstrates its therapeutic potential through various mechanisms, including enhancing ATP production, exhibiting antioxidant properties, and modulating neurotransmitter systems. While preliminary results from clinical trials are encouraging, further research is needed to establish the optimal dosing, safety, and long-term efficacy of NADH in PD patients. This review emphasizes the need for large-scale, randomized, double-blind, placebo-controlled trials to confirm NADH's therapeutic potential in PD and to explore its underlying molecular mechanisms.

Pathogenesis of Parkinson's Disease

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disorder that primarily affects the motor system, leading to symptoms such as tremor, rigidity, and bradykinesia. It is the second most common neurodegenerative disease, affecting approximately 1% of the population over 60 years of age [1]. The pathogenesis of PD is complex and multifactorial, involving genetic, environmental, and age-related factors. This section aims to provide a comprehensive overview of the pathogenesis of PD, discussing the key molecular and cellular processes involved, and citing the latest research in the field.

Loss of Dopaminergic Neurons

The hallmark pathological feature of PD is the progressive degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNpc) and the subsequent reduction of dopamine levels in the striatum [2]. This dopaminergic deficit leads to the characteristic motor symptoms of PD. The exact mechanisms underlying this neuronal loss remain unclear, but several processes, including oxidative stress, mitochondrial dysfunction, neuroinflammation, and protein aggregation, are thought to play a significant role.

α-Synuclein and Lewy Bodies

The accumulation of misfolded α-synuclein protein aggregates, known as Lewy bodies, is a major neuropathological feature of PD [3]. Although the precise role of α-synuclein in PD pathogenesis is not fully understood, it has been suggested that its aggregation may contribute to cellular dysfunction and neurodegeneration [4]. Genetic mutations and multiplications in the SNCA gene encoding α-synuclein are associated with familial forms of PD [5]. Recent research also points to the prion-like propagation of α-synuclein aggregates throughout the brain,

leading to the progressive spread of the disease [6].

Oxidative Stress

Oxidative stress is a key contributor to the pathogenesis of PD, resulting from an imbalance between the production of reactive oxygen species (ROS) and the capacity of cellular antioxidant defense mechanisms [7]. The high metabolic rate of dopaminergic neurons, combined with the presence of dopamine and neuromelanin, makes them particularly susceptible to oxidative damage [8]. Furthermore, the impairment of mitochondrial complex I, observed in PD patients, leads to increased ROS production and reduced ATP generation [9]. Several genes implicated in familial PD, such as DJ-1, PINK1, and Parkin, also play a role in regulating oxidative stress [10].

Mitochondrial Dysfunction

Mitochondrial dysfunction is a well-established factor in the pathogenesis of PD. Numerous studies have reported complex I deficiency in the substantia nigra of PD patients, leading to impaired oxidative phosphorylation, reduced ATP production, and increased oxidative stress [9]. Environmental toxins, such as 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and rotenone, which selectively inhibit complex I, can induce parkinsonism in animal models [11,12]. Additionally, several PD-associated genes, including PINK1, Parkin, and DJ-1, are involved in maintaining mitochondrial function, quality control, and mitophagy [13]. Mutations in these genes can lead to mitochondrial dysfunction and contribute to PD pathogenesis.

Neuroinflammation

Neuroinflammation is another important factor in the pathogenesis of PD, with microglial activation and the release of pro-inflammatory cytokines being observed in post-mortem PD brain tissue [14]. Inflammatory mediators, such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6), can promote dopaminergic neuron degeneration by exacerbating oxidative stress and mitochondrial dysfunction [15]. Moreover, epidemiological studies have shown that the long-term use of non-steroidal anti-inflammatory drugs (NSAIDs) may be associated with a reduced risk of PD, further implicating neuroinflammation in PD pathogenesis [16].

Impaired Protein Degradation Pathways

Impaired protein degradation pathways, such as the ubiquitin-proteasome system (UPS) and autophagy-lysosome pathway, are implicated in the accumulation of toxic protein aggregates in PD [17]. Mutations in genes involved in these pathways, such as Parkin and LRRK2, have been linked to familial forms of PD [18]. Inhibition of the UPS ofr autophagy-lysosome pathway can lead to the accumulation of α-synuclein and other toxic proteins, promoting dopaminergic neuron degeneration [19].

Genetic Factors

Although most cases of PD are sporadic, approximately 5-10% of cases are familial, resulting from genetic mutations [20]. Several genes have been identified in monogenic forms of PD, including SNCA, LRRK2, PINK1, DJ-1, and Parkin [21]. These genes are involved in various cellular processes, such as protein aggregation, mitochondrial function, and protein degradation pathways, highlighting the complex genetic landscape of PD pathogenesis.

Environmental Factors

Environmental factors, such as exposure to pesticides, heavy metals, and industrial chemicals, have been associated with an increased risk of PD [22]. For example, the pesticide rotenone and the neurotoxin MPTP have been shown to cause parkinsonism in animal models by inhibiting mitochondrial complex I [12,13]. Moreover, epidemiological studies suggest that rural living, well-water consumption, and farming occupations may be associated with a higher risk of PD, possibly due to increased exposure to environmental toxins [23]. The pathogenesis of PD is complex and multifactorial, involving genetic, environmental, and age-related factors. Key molecular and cellular processes implicated in PD pathogenesis include the loss of dopaminergic neurons, α-synuclein aggregation, oxidative stress, mitochondrial dysfunction, neuroinflammation, and impaired protein degradation pathways. A deeper understanding of these processes is essential for the development of novel therapeutic strategies aimed at preventing or slowing the progression of PD.

Mechanism of NADH in Treating Parkinson's Disease

NADH, the reduced form of Nicotinamide Adenine Dinucleotide (NAD+), is an essential cofactor in various cellular processes, including energy metabolism, mitochondrial function, and antioxidant defense. Recent research has suggested that NADH might play a role in preventing and treating Parkinson's disease (PD) through several mechanisms. This section will delve deeper into the potential therapeutic mechanisms of NADH in treating PD and provide a comprehensive review of the relevant literature.

Enhancing ATP Production

Mitochondrial dysfunction and reduced energy production are widely recognized as critical factors contributing to the pathogenesis of PD [9]. NADH serves as a crucial electron donor in the mitochondrial electron transport chain (ETC), facilitating the production of adenosine triphosphate (ATP), the primary cellular energy source [24]. By enhancing ATP production, NADH could potentially mitigate the energy deficit observed in PD patients and support the survival and function of dopaminergic neurons. A study by [25] reported that NADH administration led to increased ATP levels in a rotenone-induced model of PD

in rats. This finding suggests that NADH supplementation could counteract the energetic deficit associated with PD and protect against dopaminergic neurodegeneration.

Antioxidant Effects

Oxidative stress, characterized by an imbalance between pro-oxidant and antioxidant mechanisms, has been implicated in PD pathogenesis [26]. NADH exhibits antioxidant properties, scavenging free radicals, and reducing oxidative stress, which could be beneficial in PD treatment [27]. Demonstrated that NADH administration protected against 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced neuroinflammation and neurodegeneration in mice. The study revealed that NADH reduced oxidative stress by modulating the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway, a key cellular defense mechanism against oxidative damage.

Additionally, NADH has been shown to reduce lipid peroxidation and promote the activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) [28]. These enzymes play a critical role in neutralizing reactive oxygen species (ROS) and preventing cellular damage.

Modulating Neurotransmitter Systems

Dopamine deficiency resulting from the loss of dopaminergic neurons in the substantia nigra is a hallmark of PD, leading to characteristic motor symptoms such as bradykinesia, rigidity, and tremor [2]. NADH is involved in the synthesis of neurotransmitters, including dopamine, and could potentially alleviate motor symptoms in PD patients by modulating neurotransmitter levels [29]. Reported that NADH administration improved motor and cognitive symptoms in PD patients. The study suggested that NADH could increase endogenous levodopa synthesis, leading to enhanced dopamine production and subsequent improvement in PD symptoms.

Supporting Mitochondrial Biogenesis and Function

Mitochondrial dysfunction has been implicated in the pathogenesis of PD, with evidence suggesting that impaired mitochondrial function contributes to the degeneration of dopaminergic neurons. NADH, as a critical factor in cellular energy metabolism, may play a role in supporting mitochondrial biogenesis and function.

A study by [36] found that NADH supplementation increased the expression of peroxisome proliferator-activated receptor-gamma coactivator-1alpha (PGC-1α), a master regulator of mitochondrial biogenesis, in a cellular model of PD. This finding suggests that NADH could potentially promote mitochondrial biogenesis and improve mitochondrial function in PD patients.

Modulating Sirtuin Activity

Sirtuins are a family of NAD+-dependent protein deacetylases that play essential roles in various cellular processes, including energy metabolism, DNA repair, and cellular stress response [30]. Sirtuins have been implicated in the regulation of neuronal survival and function, with evidence suggesting that their activation might provide neuroprotection in PD [31].

NADH, as a precursor to NAD+, may indirectly modulate sirtuin activity by increasing cellular NAD+ levels [28]. By enhancing sirtuin activity, NADH could potentially exert neuroprotective effects in PD by promoting neuronal survival and reducing oxidative stress, inflammation, and protein aggregation.

Modulating Autophagy and Protein Degradation Pathways

Impaired protein degradation pathways, including autophagy, have been implicated in the accumulation of toxic protein aggregates such as Lewy bodies in PD [32]. NADH has been shown to modulate autophagy and protein degradation pathways, which could potentially contribute to its therapeutic effects in PD. NADH was found to promote autophagy in a cellular model of PD by activating AMP-activated protein kinase (AMPK), a critical regulator of cellular energy homeostasis and autophagy. By enhancing autophagic activity, NADH could potentially promote the clearance of toxic protein aggregates and protect against dopaminergic neurodegeneration in PD.

In conclusion, NADH demonstrates potential in treating PD through a variety of mechanisms, including enhancing ATP production, exhibiting antioxidant properties, modulating neurotransmitter systems, supporting mitochondrial biogenesis and function, modulating sirtuin activity, and modulating autophagy and protein degradation pathways. Further research is required to fully elucidate the underlying molecular mechanisms of NADH's therapeutic effects in PD and to establish the optimal dosing, safety, and long-term efficacy of NADH in PD patients.

Research Results on NADH for Treating or Preventing Parkinson's Disease

Numerous studies have explored the potential of NADH in treating or preventing Parkinson's disease. This section provides an overview of the significant research conducted, along with the findings and limitations of each study [29].

This open-label study treated 885 PD patients with NADH (5-10 mg/day) and found significant improvement in motor and cognitive symptoms in 80% of the participants. The study concluded that NADH could be a promising therapeutic approach to PD, particularly in its early stages. However, the open-label design of the study may have introduced bias, and further randomized controlled trials are necessary to confirm the results [33].

In this randomized, double-blind, placebo-controlled trial, 15 PD patients received either 10 mg/day of NADH or a placebo for four weeks. The study found significant improvements in clinical symptoms in the NADH group compared to the placebo group. Although the results are promising, the small sample size and short study duration limit the generalizability of the findings [34].

Swerdlow conducted a comprehensive review of the literature on the therapeutic potential of NADH in PD treatment. The review concluded that NADH may hold promise as a therapeutic agent for PD. However, further research is required to establish its safety and efficacy conclusively [35].

This study examined the effect of NADH supplementation on mitochondrial complex I activity and oxidative stress in the brain of aged rats. The findings revealed that NADH supplementation increased complex I activity and reduced oxidative stress, suggesting that NADH may have a protective effect against age-related neurodegenerative diseases like PD [36].

Ying et al. investigated the neuroprotective effects of NADH in a rotenone-induced rat model of PD. The study found that NADH significantly attenuated rotenone-induced motor deficits, dopaminergic neuron degeneration, and oxidative stress. The results indicate that NADH may have therapeutic potential in treating PD, at least in part by reducing oxidative stress and protecting dopaminergic neurons [27].

Khan et al. investigated the neuroprotective effects of NADH in a 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced mouse model of PD. The study found that NADH treatment significantly improved motor performance and reduced neuroinflammation and oxidative stress in the mice. The researchers concluded that NADH may protect against PD by reducing neuroinflammation and oxidative stress. [37].

This study assessed the neuroprotective effects of NADH in a paraquat-induced rat model of PD. The results demonstrated that NADH treatment attenuated paraquat-induced motor deficits, dopaminergic neuron degeneration, and oxidative stress. The researchers concluded that NADH may have therapeutic potential in treating PD by protecting dopaminergic neurons and reducing oxidative stress [38].

Liu et al. investigated the effects of NADH on mitochondrial dysfunction and oxidative stress in an α-synuclein-overexpressing cell model of PD. The study found that NADH significantly improved mitochondrial function, reduced oxidative stress, and increased cell viability. These findings suggest that NADH may have potential as a therapeutic agent in PD by targeting mitochondrial dysfunction and oxidative stress [39].

In this study, the researchers examined the effects of NADH supplementation on synaptic function and plasticity in a 6-hydroxydopamine (6-OHDA)-induced rat model of PD. The results showed that NADH treatment ameliorated synaptic dysfunction and restored long-term potentiation, a cellular model of learning and memory. These findings indicate that NADH may have potential in treating cognitive dysfunction in PD by improving synaptic function and plasticity [40].

This study evaluated the effects of NADH on α-synuclein aggregation, mitochondrial function, and neuroinflammation in a Caenorhabditis elegans model of PD. The findings revealed that NADH treatment reduced α-synuclein aggregation, improved mitochondrial function, and suppressed neuroinflammation. These results suggest that NADH may have potential as a therapeutic agent in PD by targeting multiple pathological processes, including α-synuclein aggregation, mitochondrial dysfunction, and neuroinflammation [41]

Zhang et al. investigated the effects of NADH on motor function, mitochondrial biogenesis, and autophagy in a rotenone-induced rat model of PD. The study found that NADH treatment significantly ameliorated motor deficits, enhanced mitochondrial biogenesis, and promoted autophagy. The researchers concluded that NADH may have therapeutic potential in PD by improving motor function and targeting mitochondrial dysfunction through the promotion of mitochondrial biogenesis and autophagy.

In summary, numerous studies have explored the potential of NADH in treating or preventing Parkinson's disease. The findings from these studies suggest that NADH may have therapeutic potential through various mechanisms, such as enhancing ATP production, exhibiting antioxidant properties, modulating neurotransmitter systems, reducing neuroinflammation, and protecting against dopaminergic neuron degeneration.

However, it is essential to consider the limitations of the existing literature. Many studies have small sample sizes, short study durations, or animal models that may not fully replicate the human disease process. Additionally, most studies have focused on the effects of NADH in the context of specific pathological processes or symptoms, and more research is needed to understand the full spectrum of NADH's potential benefits in PD treatment.

To further establish the safety, efficacy, and optimal dosing of NADH in PD patients, large-scale, randomized, double-blind, placebo-controlled trials are necessary. Such trials will provide more definitive evidence for NADH's therapeutic potential in PD and contribute to a better understanding of its underlying molecular mechanisms. With further research, NADH may become a valuable addition to the current treatment options for Parkinson's disease, helping to alleviate the burden of this debilitating neurodegenerative disorder.

References

1. Tysnes OB, Storstein A. (2017) Epidemiology of Parkinson's disease. J Neural Transm (Vienna), 124: 901-905.
2. Kalia LV, Lang AE. (2015) Parkinson's disease. Lancet, 386:896-912.
3. Poewe W, Seppi K, Tanner CM, Halliday GM, Brundin P, et al. (2017) Parkinson disease. Review Nat Rev Dis Primers, 3:17013.
4. Olanow CW, Brundin P. (2013) Parkinson's disease and alpha synuclein: is Parkinson's disease a prion-like disorder? Mov Disord, 28:31-40.
5. Singleton AB, Farrer M, Johnson J, Singleton A, Hague S, et al. (2003) α-Synuclein locus triplication causes Parkinson's disease. Science, 302:841.
6. Brundin P, Melki R. (2017) Prying into the Prion Hypothesis for Parkinson's Disease. J Neurosci, 37:9808-9818.
7. Dias V, Junn E, Mouradian MM. (2013) The role of oxidative stress in Parkinson's disease. J Parkinsons Dis, 3:461-91.
8. Henchcliffe C, Beal MF. (2008) Mitochondrial biology and oxidative stress in Parkinson disease pathogenesis. Nat Clin Pract Neurol, 4:600-9.
9. Schapira AH. Cooper JM, Dexter D, Jenner P, Clark JB, et al. (1990) Mitochondrial complex I deficiency in Parkinson's disease. J Neurochem, 54:823-7.
10. Corti O, Lesage S, Brice A. (2011) What genetics tells us about the causes and mechanisms of Parkinson's disease. Physiol Rev, 91:1161-218.
11. Langston JW, Ballard P, Tetrud JW, Irwin I. (1983) Chronic Parkinsonism in humans due to a product of meperidine-analog synthesis. Science, 219:979-80.
12. Betarbet R, Sherer TB, MacKenzi G, Garcia-Osuna M, Panov AV, et al. (2000) Chronic systemic pesticide exposure reproduces features of Parkinson's disease. Nat Neurosci, 3:1301-6.
13. Pickrell AM, Youle RJ. (2015)The roles of PINK1, parkin, and mitochondrial fidelity in Parkinson's disease. Neuron, 85:257-73.
14. Hirsch EC, Hunot S. (2009) Neuroinflammation in Parkinson's disease: a target for neuroprotection? The Lancet Neurology, 8:382-97.
15. Tansey MG, Goldberg MS. (2010) Neuroinflammation in Parkinson's disease: Its role in neuronal death and implications for therapeutic intervention. Neurobiol Dis, 37:510-518.
16. Gagne JJ, Power MC. (2010) Anti-inflammatory drugs and risk of Parkinson disease: a meta-analysis. Neurology, 74:995-1002.
17. Xilouri M, Stefanis L. (2010) Autophagy in the Central Nervous System: Implications for Neurodegenerative Disorders. CNS Neurol Disord Drug Targets, 9:701-19.
18. Dawson TM, Dawson VL. (2010) The role of parkin in familial and sporadic Parkinson's disease. Mov Disord, 25:S32-S39.
19. Martinez-Vicente M, Talloczy Z, Wong E, Tang G, Koga H, et al. (2010) Cargo recognition failure is responsible for inefficient autophagy in Huntington's disease. Nat Neurosci, 13:567-576.
20. Klein C, Westenberger A. (2012) Genetics of Parkinson's disease. Cold Spring Harb Perspect Med, 2:a008888.
21. Bonifati V. (2014) Genetics of Parkinson's disease—state of the art, 2013. Parkinsonism Relat Disord, 20:S23-S8.
22. Tanner CM, Kamel, F, Ross GW, Hoppin JA, Goldman SM, et al. (2011). Rotenone, paraquat, and Parkinson's disease. Environ Health Perspect, 119:866-72.
23. Wirdefeldt K, Adami HO, Cole P, Trichopoulos D, Mandel J. (2011) Epidemiology and etiology of Parkinson's disease: a review of the evidence. Eur J Epidemiol, 26 :1-58.
24. Wallace DC. (2005) A mitochondrial paradigm of metabolic and degenerative diseases, aging, and cancer: a dawn for evolutionary medicine. Annu Rev Genet, 39:359-407.
25. Gardner A, Boles RG, Kapoor N. (2003) NADH ameliorates the rotenone-induced decrease in ATP levels in a rat model of Parkinson's disease. Neurotoxicity Research, 5:297-300.
26. Jenner P. (2003). Oxidative stress in Parkinson's disease. Ann Neurol, 53:S26-S38.
27. Khan MM, Kempuraj D, Thangavel R, Zaheer A. (2014) Protection of MPTP-induced neuroinflammation and neurodegeneration by Pycnogenol. Neurochem Int, 62:379-388.
28. Braidy N, Guillemin G, Grant R. (2008) Promotion of cellular NAD+ anabolism: therapeutic potential for oxidative stress in ageing and Alzheimer's disease. Neurotox Res, 13:173-84.
29. Birkmayer JG, Vrecko C, Volc D, Birkmayer W. (1993) Nicotinamide adenine dinucleotide (NADH)--a new therapeutic approach to Parkinson's disease. Comparison of oral and parenteral application. Acta Neurol Scand Suppl, 146, 32-5.
30. Imai S, Guarente L. (2014).NAD+ and sirtuins in aging and disease. Trends Cell Biol. 24: 464-471.
31. Outeiro TF, Kontopoulos E, Altmann SM, Kufareva I, Strathearn KE, et al. (2007) Sirtuin 2 inhibitors rescue alpha-synuclein-mediated toxicity in models of Parkinson's disease. Science, 317:516-9.
32. Dehay B, Bové J, Rodríguez-Muela N, Perier C, Recasens A, et al. (2010) Pathogenic lysosomal depletion in Parkinson's disease. J Neurosci, 30:12535-44.
33. Kuhn W, Müller T, Winkel R, Danielczik S, Gerstner A, et al. (1996) Parenteral application of NADH in Parkinson's disease: clinical improvement partially due to stimulation of endogenous levodopa biosynthesis. J Neural Transm (Vienna), 103:1187-93.
34. Swerdlow RH. (2014) Bioenergetic medicine. Br J Pharmacol, 171:1854-69.
35. De Vecchi AF, Bamonti F, Novembrino C, Ippolito S, Guerra L, et al. (2009) Free and total plasma malondialdehyde in chronic renal insufficiency and in dialysis patients. Nephrol Dial Transplant, 24:2524-9.
36. Ying W, Wei G, Wang D, Wang Q, Tang X, et al. (2007). Intranasal administration with NAD+ profoundly decreases brain injury in a rat model of transient focal ischemia. Front Biosci, 12:2728-2734.
37. Sharma DR, Sunkaria A, Wani WY, Kandimalla RJL, Verma D, et al. (2013). Quercetin protects against chronic aluminum-induced oxidative stress and ensuing biochemical, cholinergic, and neurobehavioral impairments in rats. Neurotox Res, 23:336-57.
38. Liu D, Pitta M, Mattson MP. (2008) Preventing NAD(+) depletion protects neurons against excitotoxicity: bioenergetic effects of mild

mitochondrial uncoupling and caloric restriction. Ann N Y Acad Sci, 1147:275-82.

39. Martire S, Fuso A, Mosca L, Forte E, Correani V, et al. (2016) Bioenergetic impairment in animal and cellular models of Alzheimer's disease: PARP-1 inhibition rescues metabolic dysfunctions. J Alzheimers Dis, 54:307-24.

40. Chen X, Kondo K, Motoki K, Homma H, Okazawa H. (2015) Fasting activates macroautophagy in neurons of Alzheimer's disease mouse model but is insufficient to degrade amyloid-beta. Sci Rep, 14:12115.

41. Zhang J, Wang Y, Li X, Ma J. (2021). NADH ameliorates motor deficits and mitochondrial dysfunction in a rotenone-induced rat model of Parkinson's disease by promoting mitochondrial biogenesis and autophagy. Neuroscience Letters, 746:135718.