American Journal of
Biomedical Science & Research

www.biomedgrid.com
ISSN: 2642-1747

Review Article

Pathogenesis and Molecular Mechanisms of Parkinson's Disease

Burcu Boz, Emine Diraman and Fatma Gönül Sezgin*

Faculty of Science and Art, Department of Biology, Ondokuz Mayıs Üniversity, Samsun, Turkey.

***Corresponding author:** Fatma Gonul Sezgin, Department of Biology, Ondokuz Mayıs Üniversity, Samsun, Turkey.

To Cite This Article: *Burcu Boz, Emine Diraman and Fatma Gönül Sezgin*. Pathogenesis and Molecular Mechanisms of Parkinson's Disease. Am J Biomed Sci & Res. 2024 24(3) AJBSR.MS.ID.003203,* DOI: 10.34297/AJBSR.2024.24.003203

Received: October 15, 2024; **Published:** October 18, 2024

Abstract

Parkinson's Disease (PD) is frequently encountered nowadays, after Alzheimer's disease, the second most common neurodegenerative diseases an in an increased incidence of disease with aging. This disease does not only occur in older people and can be seen in early ages. Although the etiology of the disease is uncertain, many factors such as genetic, environmental, and toxic causes were thought to cause this disease. Molecular mechanisms such as mitochondrial dysfunction, oxidative stress, ubiquitin proteosome system degradation, excitotoxicity, microglial activation and inflammation are responsible for Parkinson's disease. There are four main findings of Parkinson's disease characterized by rest tremor, rigidity, bradykinesia and deterioration of postural reflexes. The combinations of symptoms and findings are different in each patient. Studies on the course and treatment of Parkinson's Disease in recent years can be compiled and ideas can be gathered to improve the patients' quality of life and improvement.

Keywords: Parkinson, Parkinson's Disease, Neurodegeneration, Motor Nervous System

Introduction

Parkinson's Disease and Parkinsonism

Parkinson's Disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease [1]. It is a chronic, progressive disease characterized by both motor and nonmotor features. The disease has a significant clinical impact on patients, families, and caregivers through its progressive degenerative effects on mobility and muscle control. PD is primarily associated with the gradual loss of cells in the substantia nigra of the brain. This area is responsible for the production of dopamine. Dopamine is a chemical messenger that transmits signals between two regions of the brain to coordinate activity (Figure 1). For example, it connects the substantia nigra and the corpus striatum to regulate muscle activity [2]. The motor symptoms of PD are attributed to the loss of striatal dopaminergic neurons (Figure 2), although the presence of nonmotor symptoms supports neuronal loss in nondopaminergic areas as well [3]. PD is the most common form of Parkinsonism [4]. The term parkinsonism is a symptom complex used to describe the motor features of PD, which include resting tremor, bradykinesia and muscular rigidity [3]. People are usually more familiar with the motor symptoms of PD, because these are the signs of the disease that are noticeable from the outside.

These symptoms are "cardinal" symptoms of PD, include:

1. Tremor - a shaking of the hands, arms, or legs, especially when the limb is at rest
2. Rigidity - an abnormal stiffness in a limb or part of the body
3. Postural instability - impaired balance or difficulty standing or walking
4. Bradykinesia - gradual loss and slowing down of spontaneous movement [5].

PD is highly variable, and not every patient with PD will experience all the symptoms. Different patients will have different combinations of symptoms as well as severity of symptoms, and each case of PD progresses on an individual level [6].

What are some of the non-motor symptoms of Parkinson's?

Because PD is a type of movement disorder, the associated non-motor symptoms can often be overlooked. However, there are several common symptoms of PD that do not primarily involve movement [7].

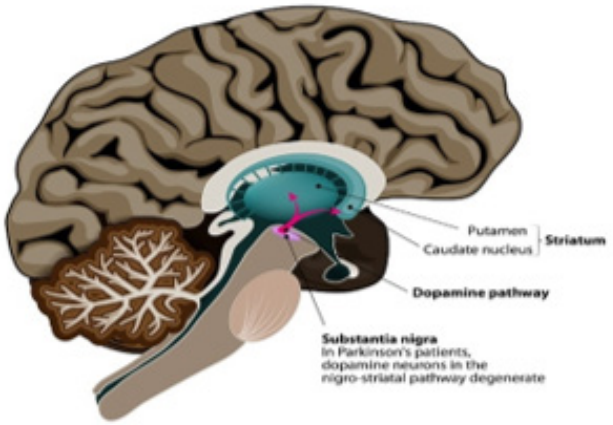

Figure 1: Parkinson's disease and loss of neurons [2].

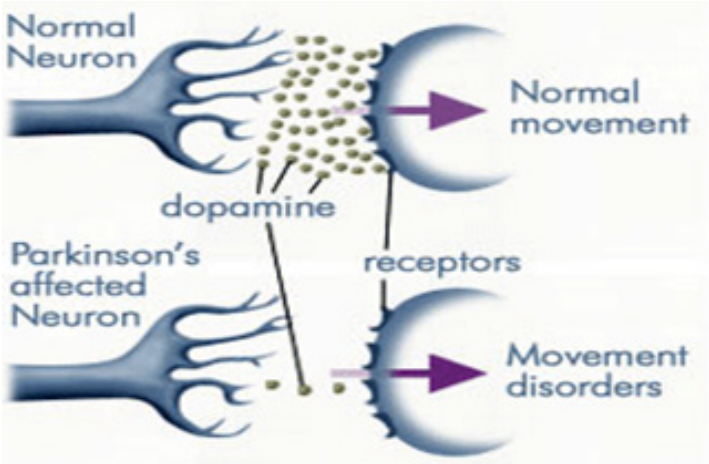

Figure 2: Dopamine levels in a normal and a Parkinson's affected neuron [15].

a. Disturbances in the Sense of Smell
b. Sleep Problems
c. Depression and Anxiety
d. Psychosis
e. Fatigue
f. Cognitive Changes
g. Weight Loss
h. Gastrointestinal Issues
i. Lightheadedness
j. Urinary Issues
k. Sexual Concerns
l. Sweating
m. Melanoma
n. Personality Changes
o. Eye & Vision Issues

Prevelance

The onset of the disease is usually at an age of 65 to 70 years. Earlier onset is seen in genetic variants. Males were 1.5 times more affected by PD in a majority of the studies [8]. The prevalence of the disease is generally accepted to range from 100 to 200 per 100,000 people and the annual incidence is thought to be 15 per 100,000 [9].

Risk Factors of Parkinson's

Risk factors for PD include [10].

a. Age
b. Gender
c. Ethnicity
d. Family history and genetics
e. Head Trauma
f. Pesticides
g. carbon monoxide
h. metals
i. industrial wastes
j. well water

Suggested Physiological Processes Related to Pathogenesis of Parkinson's Disease

Different pathways and their dysfunctions resulting from genetic modifications in PD-related genes and lead to an increased oxidative stress. Mutations or altered expression of these proteins result in mitochondrial impairment, oxidative stress, and protein misfolding. Also, dopamine metabolism may be oxidized to reactive dopamine quinones contributing to increased levels of reactive oxygen species. α-Synuclein becomes modified and accelerate its aggregation. Increased oxidative stress provokes impaired function of the UPS that degrades misfolded or damaged proteins and hereby further affecting cell survival. Environmental toxins impair mitochondrial function, increase the generation of free radicals, and lead to aggregation of proteins, including α-synuclein. Mitochondrial dysfunction by complex I inhibition affects by adding an increase in oxidative stress and a decline in ATP production, leading to damage of intracellular components and to cell death. Also, neuroinflammatory mechanisms might contribute to thecascade of consequences leading to cell death. In summary, all these several cellular mechanisms attributed to oxidative stress are implicated in the selective degeneration of dopaminergic neurons (Figure 3), [11].

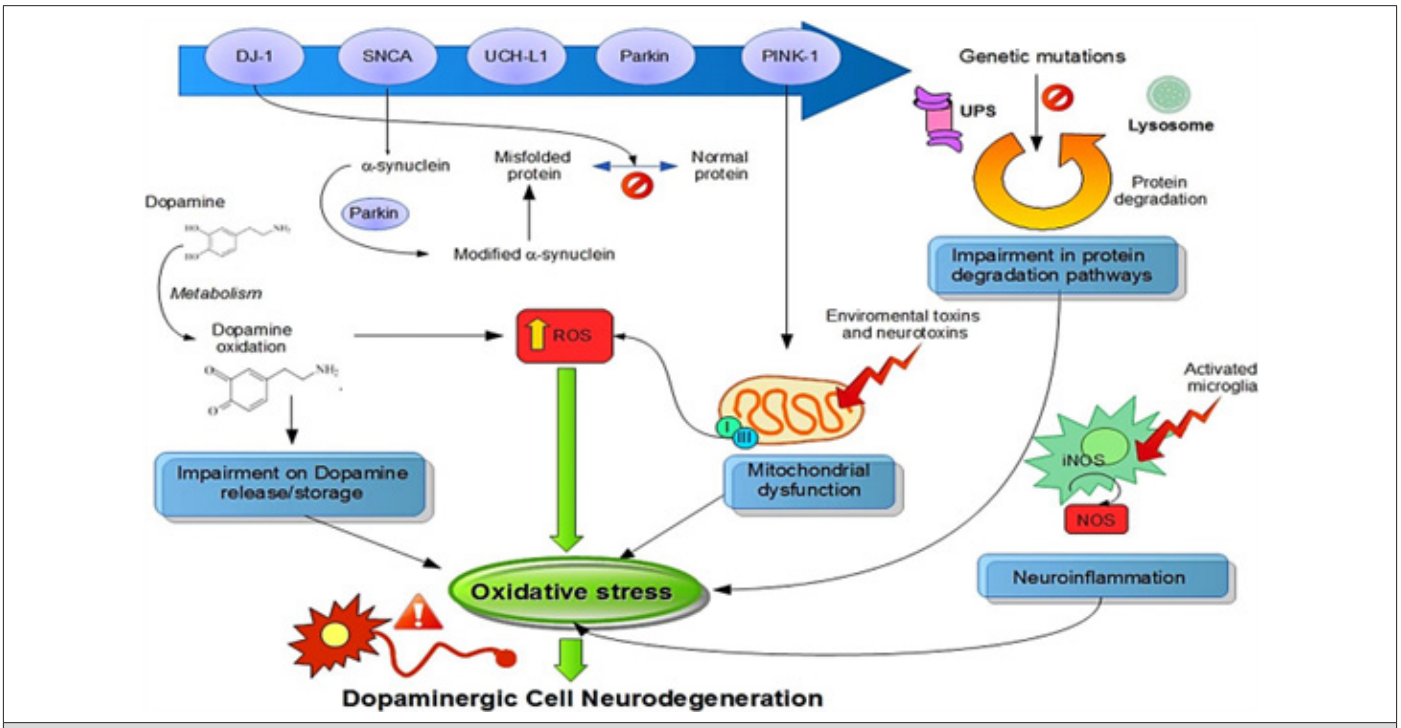

Figure 3: Molecular mechanisms of PD [11].

Treatment of Parkinson Disease

The purpose of treatment in PD is to alleviate the symptoms that disrupt the patient's daily life and activities, and to slow or eliminate the progression of the disease. However, treatment can help to limit and prevent complications that develop when disease progresses (Medical News Today, 2018). These treatments include:

a. supportive therapies - such as physiotherapy

b. medications

c. surgical treatments such as

d. Pallidotomy, Thalamotomy,

e. Deep brain stimulation,

f. Cell-based treatment,

g. Stem cells and gene therapy Transplantation of Human Fetal Dopamine Cells (Medical News Today, 2018).

Vitamins in Parkinson's Disease

Vitamin E intake reduces the risk of PD regardless of gender. There is also a strong relationship between high homocysteine levels and PD pathogenesis. Therefore, regulating homocysteine levels may prevent PD progression. It has been suggested that homocysteine levels are directly related to vitamin B (VitB) levels. Supplemental VitB has been shown to reduce homocysteine levels in blood plasma. PD symptoms have been reduced in treatments with VitB1, VitB6, VitB9 and VitB12 [12,13]. Vitamin C is important for PD patients due to its ability to increase the absorption of levodopa, one of the drugs used in PD treatment. There is an inverse relationship between vitamin D levels and PD risk and severity. Coenzyme Q10 has a protective effect in PD by improving abnormalities in the electron transport chain and exhibiting anti-apoptotic activity [14-16].

Conclusion

The disease symptoms and findings are different in each patient. Many patients experience some symptoms and not others. The pace at which the disease worsens varies on an individual basis. Therefore, the same treatment is not applied to each patient. Appropriate and correct treatment methods should be chosen ac-

cording to the main cause of the disease. PD risk may be reduced by consuming nuts.

Acknowledgement

None.

Conflict of Interest

None.

References

1. Lebouvier T, Chaumette T, Paillusson S, Duyckaerts C, Bruley des Varannes S, et al. (2018) Treatment options for Parkinson's disease. Medical News Today, Available at: *https://www.medicalnewstoday.com/articles/323462.php. [Accessed 18.11.2018].*
2. (2018) News-Medical Net Parkinson's Disease Pathophysiology. Available at: *https://www.news-medical.net/health/Parkinsons-Disease-Pathophysiology.aspx [Accessed 08.12.2018].*
3. Great Britain (2006) National Collaborating Centre for Chronic Conditions. Parkinson's disease: national clinical guideline for diagnosis and management in primary and secondary care. Royal College of Physicians.
4. Adams RD, Victor M, Ropper A H (1997) Principles of Neurology. 6th ed. New York, NY, McGraw-Hill, 1067-1078.
5. (2014) National Institute of Neurological Disorders and Stroke, National Institutes of Health. Parkinson's Disease. NIH Publication No. 15: 139.
6. (2018) The Michael J Fox Foundation for Parkinson's Re. Parkinson's Disease Symptoms Available at: *https://www.michaeljfox.org/understanding-parkinsons/living-with-pd/topic.php [Accessed18.11.2018].*
7. (2018) Amerıcan Parkınson Dısease Associatıon Avaible at: *https://www.apdaparkinson.org/what-is-parkinsons/symptoms/ [Accessed 08.12.18]*.
8. Von Campenhausen S, Bornschein B, Wick R, Kai Bötzel, Cristina Sampaio, et al. (2005) Prevalence andincidence of Parkinson's disease in Europe. Eur Neuropsychopharmacol 15: 473-490.
9. Tysnes O B, Storstein A (2017) Epidemiology of Parkinson's disease. Journal of Neural Transmission 124(8): 901-905.
10. Jankovic J, Tolosa E (2007) Parkinsons‟s disease and movement disorders, Lipincott Williams& Wilkins, Philadelphia.
11. Blesa J, Trigo Damas I, Quiroga Varela A, Jackson Lewis V R (2015) Oxidative stress and Parkinson's disease. Frontiers in neuroanatomy 9: 91.
12. Kennedy D O (2016) B vitamins and the brain: Mechanisms, dose and efficacy-A review. Nutrients 8(2): 68.
13. Markisic M, Pavlovic A M, Pavlovic DM (2017) The impact of homocysteine, vitamin b12, and vitamin d levels on functional outcome after first-ever ischaemic stroke. BioMed Res Int 5489057.
14. Rai SN, Singh P, Steinbusch HWM, Vamanu E, Ashraf G, et al. (2021) The Role of Vitamins in Neurodegenerative Disease: An Update. Biomedicines. 9(10): 1284.
15. (2016) Dopamine levels in a normal and parkinson's affected neuron. Aging Science.
16. Derkinderen P, Thibaud Lebouvier, Tanguy Chaumette, Sébastien Paillusson, Charles Duyckaerts, et al. (2009) The second brain and Parkinson's disease. European Journal of Neuroscience 30(5) 735:741.