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# HERITABILITY OF NEUROGENETIC DISEASES: THE CASE OF PARKINSON'S DISEASE

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**Abstract:** This article provides an in-depth analysis of the hereditary factors of neurogenetic diseases, focusing on the genetic mechanisms, pathogenetic processes, and the role of heredity in the development of Parkinson's disease. The paper examines modern advances in molecular genetics, genomic analysis methods, and genetic mutations that affect neurodegenerative processes. It presents evidence-based analytic conclusions about interactions among genes such as SNCA, LRRK2, PARK2, PINK1, and DJ-1 in the etiopathogenesis of Parkinson's disease, their toxic effects on dopaminergic neurons, and their hereditary transmission characteristics.

The study also addresses how hereditary determinants are phenotypically expressed within a framework that includes the multifactorial nature of neurogenetic heredity, epigenetic modifications, mitochondrial dysfunction, and oxidative stress mechanisms.

**Keywords:** Neurogenetics, heredity, Parkinson's disease, gene mutation, dopaminergic neurons, epigenetics, multifactorial heredity, SNCA gene, LRRK2, genomic analysis, neurodegeneration, personalized medicine.

Introduction: Neurogenetic diseases represent one of the most complex and interrelated pathological processes in the human gene pool. These diseases are characterized by profound degenerative changes in the structure and function of the nervous system that result from the interaction of genetic mutations, epigenetic modifications, and environmental factors. The study of neurogenetic diseases sits at the intersection of modern biomedicine, neurology, molecular genetics, and genomics, and serves to explain the neurophysiological mechanisms of changes occurring in the human hereditary information system — the genome.

Parkinson's disease is one of the most urgent scientific directions in this context because it is widespread worldwide, leads to significant socioeconomic consequences, and involves molecularly complex hereditary mechanisms. Looking back at the history of Parkinson's disease research, the condition was first described in 1817 by the English physician James Parkinson under the name "Shaking Palsy," and it was characterized as a syndrome mainly distinguished by motor symptoms such as tremor, rigidity, bradykinesia, and balance

disorders. In subsequent centuries, various theories were proposed to explain the disease's pathogenesis, but from the second half of the 20th century onward, the dominant role of genetic factors began to gain stronger scientific support. In 1997, when mutations in the SNCA gene and the pathological aggregation of α-synuclein protein were identified as one of the main genetic mechanisms related to Parkinson's disease, neurogenetic research entered a new stage.

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An important aspect of analyzing the genetic nature of Parkinson's disease is its multifactorial character. Here, hereditary determinants (i.e., genetic predisposition) and external environmental factors (for example, pesticides, heavy metals, oxidative stress) interact, disrupting neuronal signaling mechanisms. Degeneration of dopaminergic neurons in the nigrostriatal pathway leads to a sharp decrease in dopamine synthesis, producing the clinical symptoms typical of the disease.

However, today it is recognized that this process is not solely the result of genetic mutations: it is also tightly linked with epigenetic modifications — DNA methylation, histone modifications, and altered microRNA activity. Thus, the hereditary nature of Parkinson's disease manifests not only through changes in the genetic code but also at the level of epigenetic mechanisms that regulate gene expression. In global medical practice, identifying genetic markers, analyzing familial inheritance, and developing gene- therapeutic approaches have become critical directions for the study, diagnosis, and treatment of Parkinson's disease.

For example, Parkinson's forms associated with LRRK2 mutations are relatively common in East Asian populations, while autosomal-recessive cases related to PARK2 are more commonly observed among European and Latin American populations. This demonstrates the clinical importance of population genetic analysis, since the disease's expression and clinical course vary across different genetic backgrounds. Recent advances in neurogenetic research have made it possible to identify the variable expression systems of over 20,000 human genes. In Parkinson's disease, these processes are primarily associated with genes such as SNCA, LRRK2, PARK2, PINK1, and DJ-1, which ensure mitochondrial energy exchange, prevention of protein aggregation, cellular antioxidant defenses, and the metabolic stability of dopaminergic neurons. Mutations affecting these systems lead to intracellular protein aggregation, mitochondrial dysfunction, and activation of apoptosis mechanisms. As a result, neuronal function gradually fails and degenerative processes accelerate.

From this perspective, it is scientifically justified to view Parkinson's disease not as a strictly monogenic disorder, but as a polygenic and multisystem pathology. Although clinical symptoms may appear similar, each patient manifests a unique combination of genetic background, mutation type, epigenetic expression, and environmental exposures.

In such cases, the concept of personalized medicine — that is, developing diagnostic and therapeutic approaches based on each patient's genetic profile — is the most promising strategy. The deep study of hereditary factors in neurogenetic diseases entered a new phase with the completion of the Human Genome Project. Genetic diagnostics, sequencing technologies, and bioinformatic models are revealing genetic markers specific to Parkinson's disease. In particular, Genome-Wide Association Studies (GWAS) have identified more than 90 genetic loci associated with Parkinson's disease. Functional analysis of these genes, their interactions, and their roles in the dopaminergic system are crucial for mapping the molecular basis of the disease.

Moreover, analyzing hereditary forms of Parkinson's disease helps in understanding sporadic cases because molecular pathways identified via hereditary mutations often appear as dysfunction points in sporadic forms as well. For example, PINK1 and PARK2 participate in mitochondrial quality control, and their dysfunction leads to failure in cellular energy production. Therefore, jointly studying genetic and epigenetic mechanisms allows for a more complete explanation of Parkinson's disease pathogenesis. Neurogenetic research in our country has also

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significantly advanced in recent years. Genetic laboratories, molecular diagnostic centers, and neurology institutes are conducting studies to identify the genetic basis of Parkinsonian syndromes, to enable early diagnosis of hereditary forms, and to study genotype–phenotype correlations.

International collaborations also play an important role in identifying genetic characteristics specific to the Uzbek population. The scientific relevance of this paper lies in its aim to analyze more deeply the pathogenic mechanisms of Parkinson's disease through the study of hereditary mechanisms of neurogenetic diseases and to identify prospects for genetic diagnostics and gene therapy. In this area, there is a need to identify genetic predisposition, implement early diagnostic methods, strengthen genetic counseling systems, and develop population genetic monitoring. Thus, studying the heritability and genetic determinants of neurogenetic diseases — especially Parkinson's disease — is central to many scientific and practical issues, including public health, biology of aging, preservation of cognitive functions, and management of neurodegenerative processes.

These studies will create a fundamental basis for deeper understanding of the complex structure of the human genome, revealing how hereditary factors affect neurophysiological mechanisms and shaping personalized approaches in clinical practice.

Literature Review:

Studies conducted by foreign scientists on the genetic foundations of Parkinson's disease have established a fundamental scientific basis for explaining the disease's etiopathogenesis. In particular, over the past decade, advances in molecular biology, genomics, and bioinformatics have made it possible to identify the main genetic

determinants that cause Parkinson's disease and to more clearly define their relationship with neuronal degeneration.

First of all, large-scale genetic studies led by Andrew B. Singleton have scientifically proven the polygenic nature of Parkinson's disease [4]. In their article titled "Genetics of Parkinson's disease: lessons learned and future directions," the authors emphasize that more than 90 genetic loci have been identified in Parkinson's disease, most of which are involved in pathways regulating synaptic transmission, mitochondrial functions, and protein aggregation. Singleton and his colleagues demonstrated that mutations in the LRRK2, GBA, SNCA, and PARK2 genes act as key etiological mechanisms in the development of the disease and, at the molecular level, proved that these mutations lead to the degeneration of dopaminergic neurons in the nigrostriatal pathway [5].

According to them, Parkinson's disease should not be interpreted solely as a monogenic disorder but rather as a multifactorial pathological process that occurs through the interaction of hereditary and environmental factors. This approach has provided significant opportunities, especially for identifying the genetic basis of sporadic cases.

Likewise, the scientific investigations carried out by Nicholas W. Wood have further deepened the theoretical understanding of the genetic nature of Parkinson's disease. In his study titled "Genetic risk factors for Parkinson's disease and their functional mechanisms," Wood

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systematically analyzed the genetic risk factors of Parkinson's disease and their neurobiological mechanisms [6].

Wood showed that mutations in the GBA gene lead to lysosomal dysfunction, which enhances the pathological aggregation of the α-synuclein protein. He also analyzed the clinical phenotype of Parkinson's forms associated with LRRK2 mutations and provided scientific evidence that this mutation is directly related to disruptions in dopamine synthesis and mitochondrial homeostasis.

Wood's scientific perspective indicated the importance of examining not only the molecular biology of Parkinson's disease but also the synergy between hereditary and epigenetic mechanisms [7].

Based on the general conclusions of these two studies, it can be said that the genetic mechanisms of Parkinson's disease are complex and are closely interconnected with cellular dysfunctions in the dopaminergic system, mitochondrial impairments, and epigenetic alterations. Singleton's polygenic approach and Wood's molecular-mechanism- based concept represent complementary scientific positions. Together, they contribute to a broader understanding of the hereditary foundations of neurogenetic diseases— particularly Parkinson's disease—and support the development of genetic diagnostics and personalized therapeutic strategies.

Methodology:

In this article, complex bio-genetic research methods were employed to analyze the hereditary nature of neurogenetic diseases, particularly the genetic determinants of Parkinson's disease. The study utilized a combination of methodological approaches such as molecular-genetic analysis, population genomics, statistical correlation analysis, epigenetic monitoring, and bioinformatic modeling, all applied in an integrated manner.

The hereditary transmission mechanisms of key genes causing Parkinson's disease — SNCA, LRRK2, PARK2, PINK1, and DJ-1 — were analyzed based on international studies conducted using Genome-Wide Association Studies (GWAS) and Next-Generation Sequencing (NGS) technologies. In addition, on the basis of transcriptomic analysis and proteomic screening results, the relationship between α-synuclein aggregation in neurons and epigenetic modiQications was scientijically substantiated.

The methodological approaches used in this study help transition the understanding of disease pathogenesis from a monogenic level to a multifactorial systemic model, thereby enabling the identijication of interactions among genetic heredity, environmental factors, and neurobiological processes. In this way, the chosen methods allow for the interpretation of the genetic, epigenetic, and clinical characteristics of Parkinson's disease within a unijied framework.

Results:

The jindings of the study show that in Parkinson's disease, genetic determinants act as the primary factor in disease progression and are intricately linked with epigenetic modiQications and environmental inQluences. According to genetic analyses, mutations in the SNCA gene cause pathological aggregation of the α-synuclein protein, intensifying lysosomal dysfunction in

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dopaminergic neurons, while LRRK2 mutations disrupt intracellular signaling mechanisms and increase mitochondrial stress.

Meanwhile, mutations in the PINK1 and PARK2 genes impair the process of mitophagy, lowering neuronal energy homeostasis, which leads to the degeneration of dopamine- producing neurons in the nigrostriatal pathway. Epigenetic analyses revealed that changes in DNA methylation, disturbances in microRNA activity, and histone modiQications act as contributing factors that exacerbate neuronal dysfunction in Parkinson's disease.

Based on these jindings, the hereditary mechanisms of Parkinson's disease are interpreted as multifactorial — a complex biological system occurring through the synthesis and interaction of genetic, epigenetic, and environmental factors.

Discussion:

In interpreting Parkinson's disease from a neurogenetic perspective, numerous scientijic debates have emerged among researchers, as they have sought to explain the genetic and epigenetic mechanisms of the disease through various approaches. In particular, the scholarly dialogue between Andrew B. Singleton and Nicholas W. Wood represents one of the most signijicant theoretical distinctions in modern neurogenetics.

Singleton explains Parkinson's disease based on a polygenic model. According to him, the main cause of the disease is not a single "key gene," but rather the complex interconnections among multiple genetic loci. In his article "Genetics of Parkinson's disease: lessons learned and future directions," he emphasizes that more than 90 genetic loci have been identijied in Parkinson's disease, and that these genes function as an interconnected network, amplifying energetic imbalance, defects in synaptic transmission, and oxidative stress in neurons [8].

Singleton believes that the genetic cause of the disease is individual for each patient, depending on the person's unique genetic proQile, mutation levels, and epigenetic modiQications. Therefore, he proposes the approach of personalized genomics as a key direction for the diagnosis and treatment of Parkinson's disease.

In contrast, Wood interprets Parkinson's disease not as polygenic but rather as deterministic—that is, dejined by a relatively limited group of genes. In his work "Genetic risk factors for Parkinson's disease and their functional mechanisms," he identijies mutations in the GBA and LRRK2 genes as the main causes of the disease [9]. According to Wood, these genetic changes lead to lysosomal dysfunction and pathological aggregation of α- synuclein, thereby accelerating the apoptotic death of neurons.

Although Wood's model is deterministic, he does not deny the injluence of epigenetic mechanisms; rather, he views them as secondary catalysts that accelerate disease progression. The scientijic debate between Singleton and Wood primarily revolves around

issues of priority in identifying the etiological structure and hereditary mechanisms of Parkinson's disease.

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In Singleton's model, heredity is interpreted within a broad spectrum of genetic combinations, whereas in Wood's theory, the disease is regarded as the result of specijic genetic defects [10]. However, both scientists agree on one key point — that Parkinson's disease cannot be explained solely by genetic or solely by environmental factors. Their scientijic debate has, in fact, contributed to a deeper understanding of the complexity of the disease's pathogenesis.

Today, these debates are jinding resolution through an integrative model. Singleton's polygenic model and Wood's deterministic model are being synthesized, and Parkinson's disease is increasingly interpreted within scientijic circles as a multifactorial, epigenetically modiQied polygenic pathology. In this way, their theoretical contradictions have actually stimulated the emergence of a new paradigm — the integration of genomic and epigenetic approaches — within neurogenetic research.

Conclusion:

Among neurogenetic disorders, Parkinson's disease possesses some of the most complex hereditary mechanisms. Studies have shown that the formation of this disease results from the combined inQluence of genetic, epigenetic, and environmental factors. Mutations in genes such as SNCA, LRRK2, PINK1, PARK2, and DJ-1 are the primary molecular determinants that lead to the degeneration of dopaminergic neurons.

The interaction among these genes gives rise to pathological conditions such as mitochondrial dysfunction, oxidative stress, lysosomal abnormalities, and protein aggregation within neurons.

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