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Parkinson's Disease

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Abstract: This article is devoted to methods of identifying and correcting problems related to attention and memory. The article analyzes the role of attention and memory in human mental development, how they are interrelated, and the factors affecting these processes. The authors also suggest ways to improve attention and memory through psychocorrective methods, including games, exercises, relaxation techniques, and cognitive therapy methods. The article is of practical importance for children who have difficulty concentrating during education and people with memory loss, and includes recommendations for psychologists, pedagogues, and parents.

Keywords: *Attention, Memory, Psychocorrection, Psychological methods, Memory development, Concentration, Stress reduction, Cognitive therapy, Psychological exercises. Game techniques, amnesia.*

Introduction

Parkinson's disease (PD), or simply Parkinson's, is a neurodegenerative disease primarily of the central nervous system, affecting both motor and non-motor systems. Symptoms typically develop gradually, with non-motor issues becoming more prevalent as the disease progresses. Common motor symptoms include tremors, bradykinesia (slowness of movement), rigidity, and balance difficulties, collectively termed parkinsonism. In later stages, Parkinson's disease dementia, falls, and neuropsychiatric problems such as sleep abnormalities, psychosis, mood swings, or behavioral changes may arise.

Most cases of Parkinson's disease are sporadic, though contributing factors have been identified. Pathophysiology involves progressive degeneration of nerve cells in the substantia nigra, a midbrain region that provides dopamine to the basal ganglia, a system involved in voluntary motor control. The cause of this cell death is poorly understood but involves the aggregation of alpha-synuclein into Lewy bodies within neurons. Other potential factors involve genetic and environmental influences, medications, lifestyle, and prior health conditions.

Diagnosis is primarily based on signs and symptoms, typically motor-related, identified through neurological examination. Medical imaging techniques like positron emission tomography can support the diagnosis. Parkinson's typically manifests in individuals over 60, with about one percent affected. In those younger than 50, it is termed "early-onset PD".

Methodology

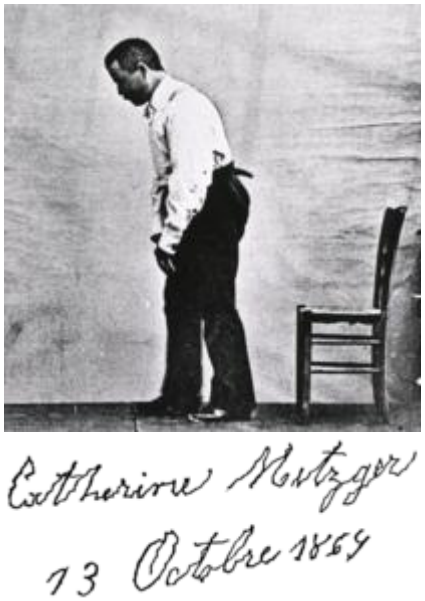
No cure for Parkinson's is known, and treatment focuses on alleviating symptoms. Initial treatment typically includes L-DOPA, MAO-B inhibitors, or dopamine agonists. As the disease progresses, these medications become less effective and may cause involuntary muscle movements. Diet and rehabilitation therapies can help improve symptoms. Deep brain stimulation is used to manage severe motor symptoms when drugs are ineffective. There is little evidence for treatments addressing non-motor symptoms, such as sleep disturbances and mood instability. Life expectancy for those with PD is near-normal but is decreased for early-onset.

Classification and terminology.Parkinsonism and Parkinson-plus syndrome. Parkinson's disease (PD) is a neurodegenerative disease affecting both the central and peripheral nervous systems, characterized by the loss of dopamine-producing neurons in the substantia nigra region of the brain. It is classified as a synucleinopathy due to the abnormal accumulation of the protein alpha-synuclein, which aggregates into Lewy bodies within affected neurons.

The loss of dopamine-producing neurons in the substantia nigra initially presents as movement abnormalities, leading to Parkinson's further categorization as a movement disorder. In 30% of cases, disease progression leads to the cognitive decline known as Parkinson's disease dementia (PDD). Alongside dementia with Lewy bodies, PDD is one of the two subtypes of Lewy body dementia.

The four cardinal motor symptoms of Parkinson's—bradykinesia (slowed movements), postural instability, rigidity, and tremor—are called parkinsonism. These four symptoms are not exclusive to Parkinson's and can occur in many other conditions, including HIV infection and recreational drug use. Neurodegenerative diseases that feature parkinsonism but have distinct differences are grouped under the umbrella of Parkinson-plus syndromes or, alternatively, atypical parkinsonian disorders. Parkinson's disease can be attributed to genetic factors or be idiopathic, in which there is no clearly identifiable cause. The latter, also called sporadic Parkinson's, makes up some 85–90% of cases.

Parkinsonism.



Motor symptoms include a stooping posture, the "Parkinsonian gait", and micrographia—jagged, diminutive handwriting.

Although a wide spectrum of motor and non-motor symptoms appear in Parkinson's, the cardinal features remain tremor, bradykinesia, rigidity, and postural instability, collectively termed parkinsonism. Appearing in 70–75 percent of PD patients, tremor is often the predominant motor

symptom. Resting tremor is the most common, but kinetic tremors—occurring during voluntary movements—and postural tremor—preventing upright, stable posture—also occur. Tremor largely affects the hands and feet: a classic parkinsonian tremor is "pill-rolling", a resting tremor in which the thumb and index finger make contact in a circular motion at 4–6 Hz frequency.

Bradykinesia describes difficulties in motor planning, beginning, and executing, resulting in overall slowed movement with reduced amplitude that affects sequential and simultaneous tasks. Bradykinesia can also lead to hypomimia, reduced facial expressions. Rigidity, also called rigor, refers to a feeling of stiffness and resistance to passive stretching of muscles that occurs in up to 89 percent of cases. Postural instability typically appears in later stages, leading to impaired balance and falls. Postural instability also leads to a forward stooping posture.

Beyond the cardinal four, other motor deficits, termed secondary motor symptoms, commonly occur. Notably, gait disturbances result in the Parkinsonian gait, which includes shuffling and paroxysmal deficits, where a normal gait is interrupted by rapid footsteps—known as festination—or sudden stops, impairing balance and causing falls. Most PD patients experience speech problems, including stuttering, hypophonic, "soft" speech, slurring, and festinating speech (rapid and poorly intelligible) Handwriting is commonly altered in Parkinson's, decreasing in size—known as micrographia—and becoming jagged and sharply fluctuating. Grip and dexterity are also impaired.

Results and discussion

Neuropsychiatric and cognitive

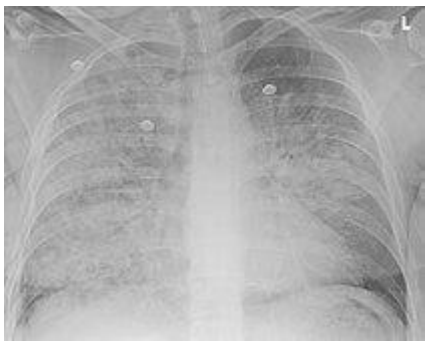
Neuropsychiatric symptom prevalence in Parkinson's disease

Symptom	Prevalence (%)
Anxiety	40–50
Apathy	40
Depression	20–40
Impulse control disorders	36–60
Psychosis	15–30

Neuropsychiatric symptoms like anxiety, apathy, depression, hallucinations, and impulse control disorders occur in up to 60% of those with Parkinson's. They often precede motor symptoms and vary with disease progression. Non-motor fluctuations, including dysphoria, fatigue, and slowness of thought, are also common. Some neuropsychiatric symptoms are not directly caused by neurodegeneration but rather by its pharmacological management.

Cognitive impairments rank among the most prevalent and debilitating non-motor symptoms. These deficits may emerge in the early stages or before diagnosis, and their prevalence and severity tend to increase with disease progression. Ranging from mild cognitive impairment to severe Parkinson's disease dementia, these impairments include executive dysfunction, slowed cognitive processing speed, and disruptions in time perception and estimation.

Autonomic



Dysphagia—an autonomic failure—can lead to aspiration pneumonia (pictured).

Autonomic nervous system failures, known as dysautonomia, can appear at any stage of Parkinson's. They are among the most debilitating symptoms and greatly reduce quality of life. Although almost all PD patients suffer cardiovascular autonomic dysfunction, only some are symptomatic Chiefly, orthostatic hypotension—a sustained blood pressure drop of at least 20 mmHg systolic or 10 mmHg diastolic after standing—occurs in 30–50 percent of cases. This can result in lightheadedness or fainting: subsequent falls are associated with higher morbidity and mortality.

Other autonomic failures include gastrointestinal issues like chronic constipation, impaired stomach emptying and subsequent nausea, excessive salivation, and dysphagia (difficulty swallowing): all greatly reduce quality of life. Dysphagia, for instance, can prevent pill swallowing and lead to aspiration pneumonia. Urinary incontinence, sexual dysfunction, and thermoregulatory dysfunction—including heat and cold intolerance and excessive sweating—also frequently occur.

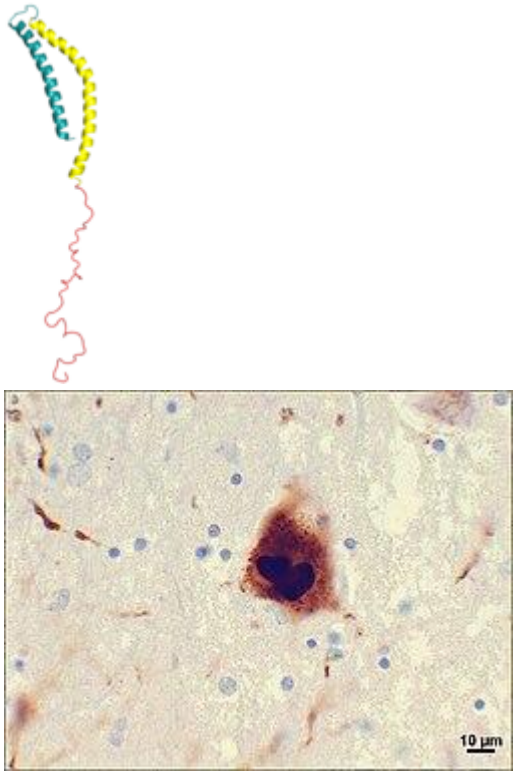
Literature review

Other non-motor symptoms. Sensory deficits appear in up to 90 percent of patients and are usually present at early stages. Nociceptive and neuropathic pain are common, with peripheral neuropathy affecting up to 55 percent of individuals. Visual impairments are also frequently observed, including deficits in visual acuity, color vision, eye coordination, and visual hallucinations. An impaired sense of smell is also prevalent. PD patients often struggle with spatial awareness, recognizing faces and emotions, and may experience challenges with reading and double vision

Sleep disorders are highly prevalent in PD, affecting up to 98%. These disorders include insomnia, excessive daytime sleepiness, restless legs syndrome, REM sleep behavior disorder (RBD), and sleep-disordered breathing, many of which can be worsened by medication. RBD may begin years before the initial motor symptoms. Individual presentation of symptoms varies, although most people affected by PD show an altered circadian rhythm at some point of disease progression.

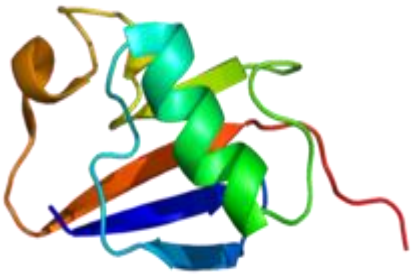
PD is also associated with a variety of skin disorders that include melanoma, seborrheic dermatitis, bullous pemphigoid, and rosacea. Seborrheic dermatitis is recognized as a premotor feature that indicates dysautonomia and demonstrates that PD can be detected not only by changes of nervous tissue, but tissue abnormalities outside the nervous system as well.

Causes of Parkinson's disease



The protein alpha-synuclein aggregates into Lewy bodies and neurites. Structural model of alpha-synuclein (left), photomicrograph of Lewy bodies (right).

As of 2024, the cause of neurodegeneration in Parkinson's remains unclear, though it is believed to result from the interplay of genetic and environmental factors. The majority of cases are sporadic with no clearly identifiable cause, while approximately 5–10 percent are familial. Around a third of familial cases can be attributed to a single monogenic cause. Molecularly, abnormal aggregation of alpha-synuclein is considered a key contributor to PD pathogenesis, although the trigger for this aggregation remains debated. Proteostasis disruption and the dysfunction of cell organelles, including endosomes, lysosomes, and mitochondria, are implicated in pathogenesis. Additionally, maladaptive immune and inflammatory responses are potential contributors. The substantial heterogeneity in PD presentation and progression suggests the involvement of multiple interacting triggers and pathogenic pathways.



Ribbon diagram of parkin

Parkinson's can be narrowly defined as a genetic disease, as rare inherited gene variants have been firmly linked to monogenic PD, and the majority of sporadic cases carry variants that increase PD risk. PD heritability is estimated to range from 22 to 40 percent. Around 15 percent of diagnosed individuals have a family history, of which 5–10 percent can be attributed to a causative risk gene mutation. However, carrying one of these mutations may not lead to disease. Rates of familial PD vary by ethnicity: monogenic PD occurs in up to 40% of Arab-Berber patients and 20% of Ashkenazi Jewish patients.

As of 2024, around 90 genetic risk variants across 78 genomic loci have been identified. Notable risk variants include SNCA (which encodes alpha-synuclein), LRRK2, and VPS35 for autosomal dominant inheritance, and PRKN, PINK1, and DJ1 for autosomal recessive inheritance. LRRK2 is the most common autosomal dominant variant, responsible for 1–2 percent of all PD cases and 40 percent of familial cases. Parkin variants are associated with nearly half of recessive, early-onset monogenic PD. Mutations in the GBA1 gene, linked to Gaucher's disease, are found in 5–15 percent of PD cases. The GBA1 variant frequently leads to cognitive decline.

Environmental health and Exposome

Laboratory Diagnostics of Viral Hepatitis

Serological Assays: ELISA-based tests remain the cornerstone of hepatitis diagnostics, detecting antigens (e.g., HBsAg, HCV antigen) and antibodies (e.g., anti-HAV, anti-HCV).

Molecular Diagnostics: PCR and nucleic acid amplification techniques (NAAT) are highly sensitive for detecting and quantifying HBV DNA and HCV RNA, as reported by Pawlotsky et al. (2002).

Genotyping and Resistance Testing: Genotypic assays aid in tailoring antiviral therapy, especially for HCV and HBV.

Environmental toxicants like pesticides are believed to be a trigger for Parkinson's.

The limited heritability of Parkinson's strongly suggests environmental factors are involved, though identifying these risk factors and establishing causality is challenging due to PD's decade-long prodromal period. However, environmental toxicants such as air pollution, pesticides, and industrial solvents like trichloroethylene are strongly linked to Parkinson's.

Certain pesticides—like paraquat, glyphosate, and rotenone—are the most established environmental toxicants for Parkinson's and are likely causal. PD prevalence is strongly associated with local pesticide use, and many pesticides are mitochondrial toxins. Paraquat, for instance, structurally resembles metabolized MPTP which selectively kills dopaminergic neurons by inhibiting mitochondrial complex 1 and is widely used to model PD. Pesticide exposure after diagnosis may also accelerate disease progression. Without pesticide exposure, an estimated 20 percent of all PD cases would be prevented.

Dietary Factors. Emerging research suggests that diet may influence the risk of developing Parkinson's. A 2023 study found that adherence to a Western dietary pattern—characterized by high consumption of red and processed meats, fried foods, high-fat dairy products, and refined grains—is associated with an increased risk of Parkinson's. Individuals with the highest adherence to this dietary pattern had significantly higher odds—approximately seven times—of developing the disease. Conversely, diets rich in fruits, vegetables, whole grains, and lean proteins have been associated with a reduced risk of Parkinson's, potentially offering protective benefits. Further research is needed to establish causality and better understand the mechanisms underlying these associations.

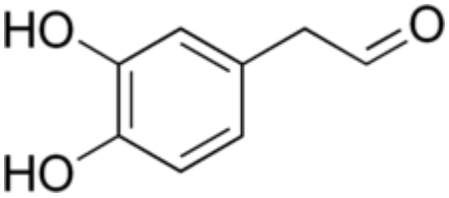
Hypotheses. Prionic hypothesis. The hallmark of Parkinson's is the formation of protein aggregates, beginning with alpha-synuclein fibrils and followed by Lewy bodies and Lewy neurites. The prion hypothesis suggests that alpha-synuclein aggregates are pathogenic and can spread to neighboring, healthy neurons and seed new aggregates. Some propose that the heterogeneity of PD may stem from different "strains" of alpha-synuclein aggregates and varying anatomical sites of origin. Alpha-synuclein propagation has been demonstrated in cell and animal models and is the most popular explanation for the progressive spread through specific neuronal systems However, therapeutic efforts to clear alpha-synuclein have failed. Additionally, postmortem brain tissue analysis shows that alpha-synuclein pathology does not clearly progress through the nearest neural connections.

Braak's hypothesis. Main article: Parkinson's disease and gut-brain axis § Braak's hypothesis

In 2002, Heiko Braak and colleagues proposed that Parkinson's disease begins outside the brain and is triggered by a "neuroinvasion" of some unknown pathogen. The pathogen enters through the nasal cavity and is swallowed into the digestive tract, initiating Lewy pathology in both areas. This alpha-synuclein pathology may then travel from the gut to the central nervous system through the vagus nerve. This theory could explain the presence of Lewy pathology in both the enteric nervous system and olfactory tract neurons, as well as clinical symptoms like loss of smell and gastrointestinal problems. It has also been suggested that environmental toxicants might be ingested in a similar manner to trigger PD.

Catecholaldehyde hypothesis

Main article: Catecholaldehyde hypothesis



The catecholaldehyde hypothesis argues that the dopamine metabolite DOPAL (pictured) triggers alpha-synuclein aggregation.

The enzyme monoamine oxidase (MAO) plays a central role in the metabolism of the neurotransmitter dopamine and other catecholamines. The catecholaldehyde hypothesis argues that the oxidation of dopamine by MAO into 3,4-dihydroxyphenylacetaldehyde (DOPAL) and hydrogen peroxide and the subsequent abnormal accumulation thereof leads to neurodegeneration. The theory posits that DOPAL interacts with alpha-synuclein and causes it to aggregate.

Conclusion

Mitochondrial dysfunction. Whether mitochondrial dysfunction is a cause or consequence of PD pathology remains unclear. Impaired ATP production, increased oxidative stress, and reduced calcium buffering may contribute to neurodegeneration. The finding that MPP^+—a respiratory complex I inhibitor and MPTP metabolite—caused parkinsonian symptoms strongly implied that mitochondria contributed to PD pathogenesis. Alpha-synuclein and toxicants like rotenone similarly disrupt respiratory complex I. Additionally, faulty gene variants involved in familial Parkinson's—including PINK1 and Parkin—prevent the elimination of dysfunctional mitochondria through mitophagy.

Neuroinflammation.Some hypothesize that neurodegeneration arises from a chronic neuroinflammatory state created by local activated microglia and infiltrating immune cells. Mitochondrial dysfunction may also drive immune activation, particularly in monogenic PD. Some autoimmune disorders increase the risk of developing PD, supporting an autoimmune contribution. Additionally, influenza and herpes simplex virus infections increase the risk of PD, possibly due to a viral protein resembling alpha-synuclein. Parkinson's risk is also decreased with immunosuppressants.

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