



# An update on pathogenesis and clinical scenario for Parkinson's disease: diagnosis and treatment

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## Abstract

In severe cases, Parkinson's disease causes uncontrolled movements known as motor symptoms such as dystonia, rigidity, bradykinesia, and tremors. Parkinson's disease also causes non-motor symptoms such as insomnia, constipation, depression and hysteria. Disruption of dopaminergic and non-dopaminergic neural networks in the substantia nigra pars compacta is a major cause of motor symptoms in Parkinson's disease. Furthermore, due to the difficulty of clinical diagnosis of Parkinson's disease, it is often misdiagnosed, highlighting the need for better methods of detection. Treatment of Parkinson's disease is also complicated due to the difficulties of medications passing across the blood–brain barrier. Moreover, the conventional methods fail to solve the aforementioned issues. As a result, new methods are needed to detect and treat Parkinson's disease. Improved diagnosis and treatment of Parkinson's disease can help avoid some of its devastating symptoms. This review explores how nanotechnology platforms, such as nanobiosensors and nanomedicine, have improved Parkinson's disease detection and treatment. Nanobiosensors integrate science and engineering principles to detect Parkinson's disease. The main advantages are their low cost, portability, and quick and precise analysis. Moreover, nanotechnology can transport medications in the form of nanoparticles across the blood–brain barrier. However, because nanobiosensors are a novel technology, their use in biological systems is limited. Nanobiosensors have the potential to disrupt cell metabolism and homeostasis, changing cellular molecular profiles and making it difficult to distinguish sensor-induced artifacts from fundamental biological phenomena. In the treatment of Parkinson's disease, nanoparticles, on the other hand, produce neurotoxicity, which is a challenge in the treatment of Parkinson's disease. Techniques must be developed to distinguish sensor-induced artifacts from fundamental biological phenomena and to reduce the neurotoxicity caused by nanoparticles.

**Keywords** Parkinson's disease · Neurodegenerative disease · Diagnostics · Disease management · Nanobiosensor · Biomarker

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## Introduction

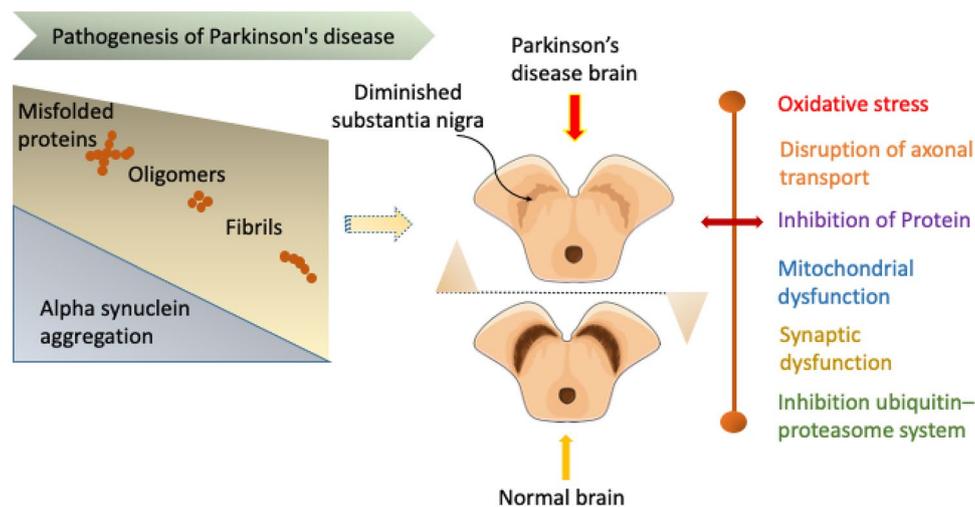
The human body's physiological state is regulated in large part by the central nervous system (Singh et al. 2022). Parkinson's disease is a central nervous system disorder that affects the brain, spinal cord, and the nerves that link the brain and spinal cord. Parkinson's disease primarily affects the elderly, although it can also affect young people. Parkinson's disease is also caused by neuroinflammation; several studies have shown an interaction between neuroinflammation and Parkinson's disease pathogenic pathways (Rai et al. 2022). Parkinson's disease is recognised as a crucially significant feature of the central nervous system (CNS) proteostasis because of dysregulation at multiple levels of the autophagic and endolysosomal pathways (Rai et al. 2021c).

Parkinson's disease (PD) is one of the most incapacitating neurological disorders. Despite the availability of symptomatic therapies, there has been little attention given to the health of Parkinson's disease patients (Rai et al. 2021b). Throughout the last few decades, researchers have attempted and succeeded in developing a preclinical model that has improved in the early-stage diagnosis of Parkinson's disease. However, researchers have had only limited success in the effective diagnosis of Parkinson's disease. Dopaminergic neurons produce dopamine, which is used to coordinate voluntary activities with the support of the motor cortex and other crucial structures (Rai and Singh 2020). Parkinson's disease is incurable, and current therapies merely alleviate symptoms. Because Parkinson's disease motor symptoms often appear late, the person may be unaware. As a result, people may not inform their doctor, delaying early detection and treatment of the disease. According to research, Parkinson's disease may be caused by brain injury, for example, Lewy bodies have been discovered in substantia nigra (Outeiro et al. 2019). In addition, dopamine deficiency was detected in the patient's body, paving the way for a better understanding of the pathogenesis of Parkinson's disease (Mahul-Mellier et al. 2020). Another study discovered a link between the loss of dopaminergic neurons in the striatum and the substantia nigra in Parkinson's patients (Ivanidze et al. 2020). This demonstrates that dopamine cell death in the stroma can lead to striatal dopamine deficiency. Therefore, levodopa and carbidopa have become the main drugs for the treatment of Parkinson's disease (You 2022). The combination of levodopa and carbidopa reduces nausea and vomiting caused by levodopa, allowing more levodopa to reach the brain. Parkinson's disease is also treated with catechol-O-methyltransferase inhibitors, which increase dopamine uptake and prolong the half-life of levodopa in the brain. MAOB inhibitors are also extensively used to treat Parkinson's disease. People with stiffness and tremors were treated with surgery prior to the development of levodopa as a medication for Parkinson's disease. Recent developments in basal ganglia physiology and the development of innovative techniques have aided in the development of alternative surgical approaches for Parkinson's disease treatment (Stoker et al. 2020). The most popular surgical techniques make use of deep brain stimulation for Parkinson's disease treatment (Hartmann et al. 2019). It is said to be more effective than earlier surgical therapies for Parkinson's disease. Deep brain stimulation is often used when conventional medications fail to treat the symptoms of Parkinson's disease. Overuse of Parkinson's disease medications, for example, can result in abnormal involuntary movements, cognitive impairment, autonomic dysfunction, drug-induced psychosis, and decreased mobility. Current Parkinson's disease treatments are unsuccessful in slowing down the breakdown of dopaminergic and non-dopaminergic pathways. Furthermore,

there are currently no drugs that can prevent or slow the progression of Parkinson's disease because the conventional drug delivery systems are not able to pass the blood–brain barrier for the treatment of Parkinson's disease. Parkinson's disease is difficult to diagnose, as there is presently no diagnostic test for the disease. A neurologist diagnoses Parkinson's disease based on the patient's medical history (Tolosa et al. 2022). Therefore, a more holistic approach is needed to treat and diagnose Parkinson's disease. This is where nanotechnology came into play. Nanotechnology can be used to diagnose and treat Parkinson's disease through the use of nanoparticles and modified nanotherapeutic drugs (Silva and Almeida 2021). Nanoparticles can pass through the BBB due to their nanosize and are a viable alternative to medication delivery and other approaches (Naqvi et al. 2020). Nanotechnology has the potential to enhance CNS disorder therapy and diagnostic tools, as well as to allow efficient medication transfer (Mittal et al. 2022). Drugs might be modified via nanoengineering to accomplish activities such as crossing the BBB, modifying signalling pathways, targeting specific cells, successful gene transfer, and boosting nerve cell regeneration and maintenance. This review explores the nanobiosensors as diagnostic tool for Parkinson's disease and role of a nanocarrier framework in the delivery of neurotherapeutic drugs used in the treatment of Parkinson's disease.

## Parkinson's disease pathogenesis

Parkinson's disease has a number of pathophysiological characteristics, one of which is the development of Lewy bodies in the substantia nigra (Menšíková et al. 2022). Neurofilaments make up Lewy bodies, which are generally found in areas of severe neuronal loss (Deture and Dickson 2019). Parkinson's disease is a neurodegenerative disorder characterised by dopaminergic cell loss in the substantia nigra compacta nigra pars (Muddapu and Chakravarthy 2021). Lewy bodies are made up of alpha-synuclein oligomers that have misfolded into aggregates to form Lewy bodies. Lewy bodies impair dopamine production by causing oxidative stress, axonal dysfunction, protein inhibition, mitochondrial dysfunction, synaptic dysfunction, and ubiquitin–proteasome system disruption in the brain (Fig. 1) (Gómez-Benito et al. 2020). Furthermore, dopamine deficiency has been associated with motor symptoms of Parkinson's disease (Jankovic and Tan 2020a). Mitochondrial dysfunction has been found to be detrimental in Parkinson's disease, with a link between mitochondrial complex I dysfunction and neuronal degeneration caused by striatal substantia nigra ATP deficiency (Chen et al. 2019). Several genes have been linked to mitochondrial malfunction and increased oxidative stress, and the neurotoxic effects of MPTP were



**Fig. 1** Aggregation of alpha-synuclein and Lewy bodies in Parkinson's disease. Parkinson's disease is characterized by loss of dopaminergic neurons in the substantia nigra pars compacta and affects the brain, spinal cord, and nerves connecting the brain and spinal cord. The presence of Lewy bodies is a symptom of Parkinson's disease. Lewy bodies are an intracellular aggregation of alpha-synuclein in the brain. Pathological oligomers and higher-order aggregates of

misfolded alpha-synuclein proteins form fibrils and aggregates in Parkinson's disease brain neurons as Lewy bodies. The presence of Lewy bodies in the brainstem impairs the production of dopamine. This leads to oxidative stress, axonal dysfunction, protein sequestration, mitochondrial dysfunction, synaptic dysfunction, and suppression of the ubiquitin–proteasome system

sensitive to alpha-synuclein transgenic mice (Minakaki et al. 2020). Numerous studies have shown that genetic factors may play a role in the aetiology of Parkinson's disease (Day and Mullin 2021). Extensive Lewy body formation is one of the pathophysiological characteristics associated with mutant synuclein, and the A53T mutation causes early Parkinson's disease and the LRRK2 variation causes late Parkinson's disease with Lewy body dementia (Rivero-ríos et al. 2020). Additionally, the ubiquitin–proteasome system's autophagy pathway is involved in lysosomal and proteasome dysfunction. Impaired iron metabolism is linked to a variety of genetic and environmental variables (Blasiak et al.). Despite advances in molecular and cellular research, Parkinson's disease remains unclear. Toxins such as rotenone, paraquat, maneb, and epoxomicin have also been linked to the onset of Parkinson's disease in studies on animals. Mutations in the PARK7 gene cause a rare form of Parkinson's disease (Kin et al. 2019). In a related population-based study, loci that may contribute to the onset of sporadic Parkinson's disease were found (Wang et al. 2021). In addition, a single genetic mutation led to symptoms that were similar to sporadic Parkinson's disease (Selvaraj and Piramanayagam 2019). The identification of new biomarkers for Parkinson's disease diagnosis may lead to an understanding of the mechanisms by which specific genetic abnormalities cause Parkinson's disease (Krokidis 2019). Future studies and treatments for Parkinson's disease should concentrate on additional dysfunctional brain systems because the disorder is plainly more complex than a dopamine dysfunction.

Additionally, the finding of substances that cause Parkinson's disease in both human and animal models lends credence to the idea that environmental factors may be a contributing factor in the onset of the disease (Lee and Yankee 2021). People with Parkinson's disease have a shorter life expectancy and are 2.56 times more likely to die than those who do not have the disease (Russillo et al. 2022). Furthermore, medical therapy cannot slow or stop the progression of Parkinson's disease. Furthermore, according to the Michael. Fox Foundation for Parkinson's Research, people often acquire Parkinson's symptoms around the age of 60, and many live for 10–20 years following diagnosis (Raccagni et al. 2020). Late-onset Parkinson's disease is associated with rapid disease progression and cognitive impairment in Parkinson's disease patients. Only a few research have studied the long-term effects of Parkinson's disease. Parkinson's disease linked to an increased chance of dementia as well as the likelihood of death (Szeto et al.). Understanding the mechanism and aetiology of Parkinson's disease is crucial for creating effective diagnostic and therapeutic approaches. However, further research is required to truly understand the pathogenesis of Parkinson's disease.

## Clinical diagnosis of Parkinson's disease

Parkinson's disease is a neurological disorder that is clinically characterised as Parkinsonism (Akkaoui et al. 2020). Parkinson's disease results in the death of dopaminergic

neurons in the substantia nigra pars compacta as well as the formation of intraneuronal Lewy bodies in the brain (Wal et al. 2022). Parkinson's disease is clinically diagnosed by reviewing the medical history of the patient (Peterson et al. 2020). In addition, poor sleep, a loss of smell, and constipation all play a role in the clinical diagnosis of Parkinson's disease (Mou et al. 2020). Moreover, any environmental exposure as well as a person's current and previous information are used to make a clinical diagnosis of Parkinson's disease (Ball et al. 2019). A family history and ethnicity are also clinically examined to diagnose Parkinson's disease. Parkinson's disease is treated using drugs that are taken orally to increase the levels of dopamine in the brain because dopamine cannot be administered directly into the bloodstream (Güneş 2022). People with advanced Parkinson's disease often die or become dependent on others for care. Parkinson's disease remains a clinical diagnosis, dependent on the clinician's ability to detect its characteristic symptoms, particularly in the early stages. Although complex interactions between hereditary and environmental factors are thought to be involved, the specific cause of Parkinson's disease remains unknown (Pang et al. 2019). Many risk factors for sporadic Parkinson's disease have been identified, including pesticide and other toxin exposure, a family history, and oophorectomy, however, age is still the most crucial factor (Ball et al. 2019). The expectation that Parkinson's disease pharmacotherapy would be beneficial is based on an appropriate clinical diagnosis (Association 2020). Early Parkinson's disease detection, for example, employing cutting-edge technology such as nanobiosensors, is critical for assisting clinicians in precisely diagnosing the disease before permanent damage occurs.

### Anti-Parkinsonian activities

Parkinson's disease treatment can be done with *Mucuna pruriens* (Mp) (Rai et al. 2020). Mp is an annual and perennial legume of the Fabaceae family with a variety of medicinal properties. Although *mucuna pruriens*, like any other source of levodopa, can help lessen the motor symptoms of Parkinson's disease, the amount of levodopa in a supply of *mucuna pruriens* is unreliable and unregulated. Several key bioactive components, such as Ursolic acid (UA) and Betulinic acid (BA), have similar neuroprotective properties as L-DOPA. Ursolic acid has been shown to reduce oxidative stress in nigrostriatal tissue and enhance neurobehavioral activity in an MPTP-induced Parkinsonian animal model (Rai et al. 2019). The findings demonstrated that UA reduces behavioural impairments, restores altered dopamine levels and protects dopaminergic neurons in MPTP-intoxicated mouse. Chlorogenic acid (CA) found in MPTP-Intoxicated Mouse, such as UA, has strong anti-Parkinsonian efficacy

in a toxin-induced Parkinsonian mouse model (Singh et al. 2018). Via the signalling pathway, chlorogenic acid reduces MPTP-induced apoptosis in a Parkinson's disease mouse model (Singh et al. 2020). A study investigates the neuroprotective effects of *Withania somnifera* (Ws) root extract in Parkinsonian mice (Ayaz et al. 2022). The mice were separated into three groups: control, maneb (MB) and paraquat (PQ), and MB-PQ with Ws root extract for 3, 6, and 9 weeks. Behavioral tests revealed a considerable improvement in the motor activity patterns and gripping ability of Parkinsonian mice exposed to Ws root extract. Anti-Parkinsonian activity of *Mucuna pruriens*, ursolic acid, and chlorogenic acid in MPTP intoxicated mouse model, as well as anti-apoptotic activity of *Withania somnifera* in Paraquat and Maneb induced mouse model, were reported; however, there is a strong need to test the efficacy of these anti-Parkinsonian activities in some other neurodegenerative diseases, in addition to Parkinson's disease.

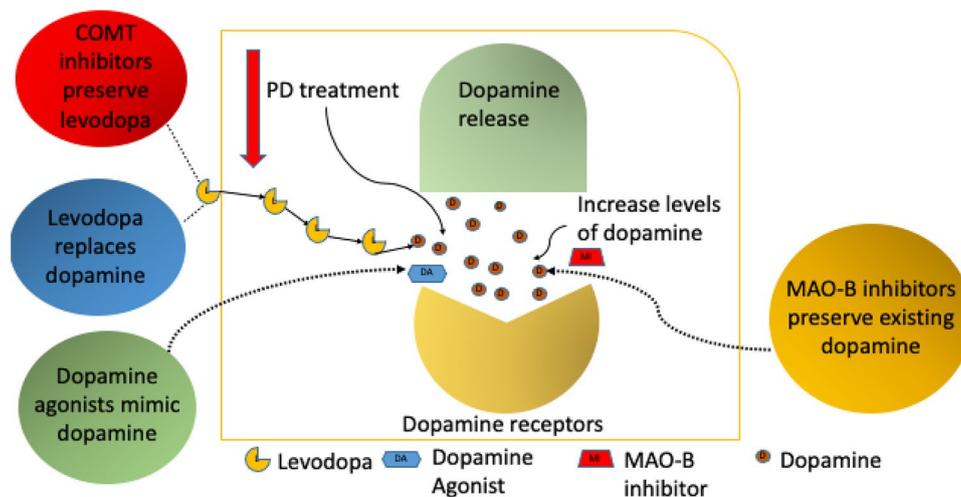
### Management of Parkinson's disease

Carbidopa and levodopa are medications that doctors can administer to Parkinson's disease patients (Hauser et al. 2021). However, levodopa is more effective than other Parkinson's disease medications. Levodopa is a natural substance that can be easily absorbed in the brain and converted to dopamine, which acts as a dopamine replacement therapy for Parkinson's disease treatment (Aradi and Hauser 2020). Carbidopa binds to levodopa and inhibits it from being converted to dopamine outside the brain regions. These medicines are not capable of reducing the damage caused by Parkinson's disease. Also, high doses of levodopa can cause uncontrolled movements. Carbidopa and levodopa are the active components of the brand-name medication Duopa. It is, however, given as a gel through a feeding tube, which distributes the medication directly into the small intestine. Duopa is given to patients with Parkinson's disease who are resistant to carbidopa-levodopa. Dopamine agonists, unlike levodopa, are not converted to dopamine and instead act in the brain to imitate dopamine. Dopamine agonists are not as successful as levodopa in treating the symptoms of Parkinson's disease (Müller 2021). They have a longer half-life and can be used in conjunction with levodopa to decrease the risk of irregular levodopa side effects. Apomorphine is a dopamine agonist that is used to treat Parkinson's disease symptoms as well. Some dopamine agonists have similar side effects to carbidopa-levodopa (Carbone et al. 2019). MAO-B inhibitors also work by inhibiting the enzyme monoamine oxidase B, which aids in the breakdown of dopamine in the brain. MAO-B metabolises dopamine in the brain (Tan et al. 2022b).

Dopamine agonists stimulate neurons in the brain like dopamine and are used instead of dopamine to treat Parkinson's disease movement symptoms. When a dopamine agonist and an MAO-B inhibitor are combined, the breakdown of levodopa and dopamine in the brain is inhibited (Cho et al. 2021). This procedure has the potential to improve the efficacy of levodopa treatment in Parkinson's disease. Catechol-O-methyltransferase degrades DOPA and other neurotransmitters (COMT). The combination of levodopa medications and COMT inhibitors lowers levodopa and dopamine breakdown (Zahoor et al. 2018). This can improve levodopa efficacy by increasing levodopa availability in the brain (Fig. 2). For several years, these medications have been used to treat tremors associated with Parkinson's disease. Benztropine and trihexypenidyl are two anticholinergics used for the treatment of Parkinson's disease (Barrett et al. 2021). However, these medications have various side effects, such as memory problems, disorientation, hallucinations, constipation, dry mouth, and urinary problems. In most cases, amantadine is prescribed to patients for the treatment of early-stage Parkinson's disease. Parkinson's disease is a progressive disorder in which the patient's response to pharmacotherapy declines over time, resulting in various motor complications. Because medications are given to patients after the disease has progressed, Parkinson's disease must be prevented by early detection before the multiple uses of medications that may cause many side effects.

## Surgical procedures for Parkinson's disease treatment

Deep brain stimulation treatment (DBS) is a surgical method used to treat Parkinson's disease by stimulating patients' brains (Krauss et al. 2021). During this surgery, electrodes are implanted in particular parts of the brain to treat the symptoms of Parkinson's disease. DBS is a treatment that employs nanotechnology-based electrodes to treat Parkinson's disease. These electrodes create electrical impulses in the brains to regulate the abnormal impulses induced by Parkinson's disease. This technique has been approved by the Food and Drug Administration as a viable therapy for severe Parkinson's disease cases (Mahajan et al. 2021). Deep brain stimulation surgery is more effective than drug therapy for Parkinson's disease (Lozano et al. 2019). Some people experience problems with their DBS operation, which requires surgeons to address the problem. Deep brain stimulation is often used in individuals with severe Parkinson's disease who are unresponsive to medication therapy. DBS is advantageous for dyskinesias that do not improve with medication adjustments, as well as for inconsistent and fluctuating responses to levodopa. Parkinson's disease-related involuntary movements are surgically treated in deep brain regions involved in motor regulation. A neurosurgeon may install a metal framework in the skull while under local anaesthetic in this type of surgery (Özlu 2018). Diagnostic imaging is used by surgeons to identify target locations in the brain



**Fig. 2** Clinical Management of Parkinson's disease. Dopamine is the chemical messenger responsible for smooth and purposeful movements. Dopamine agonists act in the brain in the same way as dopamine. This causes neurons in the brain to use dopamine agonists to relieve the symptoms of Parkinson's disease movement disorder. When an MAO-B inhibitor is taken at the same time, the breakdown of levodopa and dopamine in the brain is slowed. This improves

the effect of levodopa. Catechol-O-methyltransferase (COMT) is a neurotransmitter-degrading enzyme that breaks down dopamine and other neurotransmitters. The breakdown of levodopa and dopamine is reduced when levodopa medications are combined with a COMT inhibitor. This enhances the effect of levodopa by increasing its availability in the brain

and create small nickel-sized holes. Surgeons can employ high-frequency radio waves to create tiny lesions in these structures to treat the symptoms of Parkinson's disease. This technique may aid patients with severe Parkinson's disease or those that do not respond to medication treatments. Despite DBS's effectiveness and widespread acceptance, critical problems remain, such as which brain regions should be targeted and in which patients.

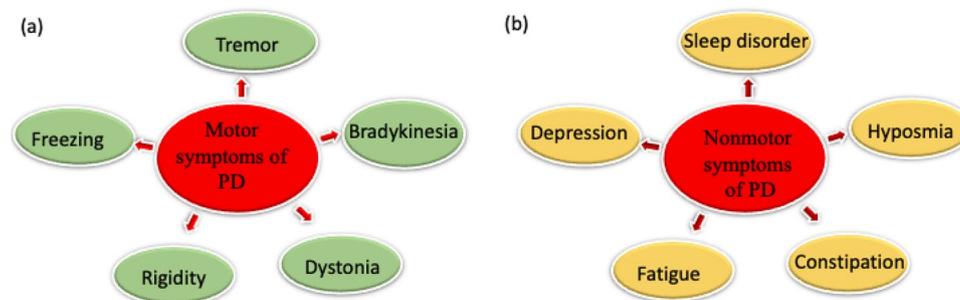
### Clinical manifestation of Parkinson's disease

Parkinson's disease is characterised by both motor and non-motor symptoms. Tremor is one of Parkinson's disease's motor symptoms. Rigidity, sluggishness, and unsteadiness are also symptoms of Parkinson's disease (Zahoor et al. 2018). Non-motor symptoms can have a wide range of effects on the cardiovascular and genitourinary systems (Bonnet et al. 2012). Nonmotor symptoms of Parkinson's disease include insomnia, REM sleep behavior disorder, and loss of smell; constipation, insomnia, and depression (Dahbour et al. 2022). Multiple imaging studies have found that rapid eye movement (REM) sleep impairments are substantially linked to an elevated risk of late-stage Parkinson's disease (Long et al. 2020). Patients with Parkinson's disease often have tremor, rigidity, cerebral dyskinesia, dystonia, and other motor disorders (Fig. 3a) (Lubomski et al. 2021). As Parkinson's disease progresses, nonmotor symptoms such as depression, hypotension, sleep disturbances, irritability, and constipation become more common and may precede motor symptoms (Fig. 3b) (Yu et al. 2018). Parkinson's disease is a progressive ailment that affects the neurological system and the nerve-controlled areas of the body. The symptoms appear gradually. The initial sign might be a little tremor in only one hand. While tremors are prevalent, the disease can also induce stiffness or slowness of movement.

Therefore it is important to diagnose the disease early using nanobiosensors.

### Molecular mechanisms of Parkinson's disease

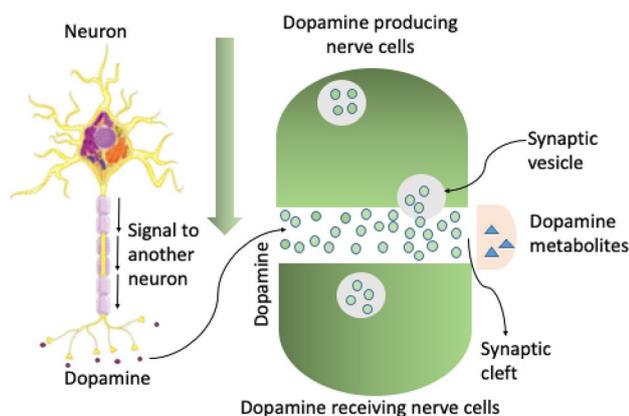
The primary pathogenic feature of this condition is a significant loss of dopamine-producing neurons in the substantia nigra pars compacta, resulting in a severe depletion of dopamine in the striatum, to which these neurons project (Pamies et al. 2022). Parkinson's disease causes up to 70% of the dopaminergic neurons in the SNc to die, although symptoms are seldom noticed because the striatum, which is located directly below the SNc, may partially compensate (Gcwensa et al. 2021). Yet, the striatum's large neurons also begin to progressively die. The death of dopaminergic neurons is thought to be influenced by a number of factors, including dopamine metabolism, oxidative stress, mitochondrial dysfunction, endoplasmic reticulum stress, protein degradation system impairment, and neuroinflammation (Picca et al. 2020). Dopamine oxidation can cause oxidative stress and damage to dopaminergic neurons (Chang and Chen 2020). Mitochondrial oxidative stress causes the formation of oxidised dopamine, which eventually leads to decreased glucocerebrosidase activity, lysosomal dysfunction, and alpha-synuclein accumulation in normal and Parkinson's disease neurons (Ghiglieri 2023). Mitochondrial dysfunction has been linked to practically every neurodegenerative disease, including Parkinson's disease (Rey et al. 2022). Mutations associated with Parkinson's disease may cause mitochondrial malfunction. Endoplasmic reticulum stress is seen in the SNc of Parkinson's disease patients' brains, resulting in the death of dopaminergic neurons (Li et al. 2021b). Experiment after experiment has shown that the buildup



**Fig. 3** Motor and non-motor symptoms of Parkinson's disease. Parkinson's disease is characterized by various motor and non-motor symptoms. Tremor, rigidity, freezing, bradykinesia, dystonia, and other motor abnormalities are common in patients with Parkinson's disease. Despite its status as a paradigmatic movement disorder, Parkinson's disease is accompanied by a wide range of non-motor symp-

toms in addition to motor symptoms. As the disease progresses, non-motor symptoms become more common. The common symptoms are depression, hyposmia, sleep disturbances, fatigue, and constipation, may manifest before motor symptoms. The specific clinicopathologic correlates for most of these nonmotor features are still unclear

of misfolded or unfolded proteins causes endoplasmic reticulum stress, which contributes to neuronal death or apoptosis (Shi et al. 2022). The first autophagy, which resembles endoplasmic reticulum stress, is largely thought to be cytoprotective. Overexpression of autophagy-related gene 5 prevents dopaminergic neuron death in an MPTP-induced zebrafish model of Parkinson's disease (Lindholm and Saarma 2022). Growing evidence suggests that the immune system has a role in the development of Parkinson's disease. Numerous earlier research has shown that pro-inflammatory cytokines including TNF-, IL-1, IL-6, and IFN- are increased in both CSF and post-mortem brain of Parkinson's disease patients (Tansey et al. 2022). To summarise, the pathophysiology of Parkinson's disease is compositive and caused by a combination of hereditary and environmental factors. Mutations in single or several genes may exacerbate the effects of environmental neurotoxins (Tran et al. 2020). Mutations related to Parkinson's disease cause mitochondrial and endoplasmic reticulum malfunction, autophagy impairment, and immune dysregulation (Abais et al. 2015). Alpha-synuclein aggregation, oxidative stress, ferroptosis, mitochondrial failure, neuroinflammation, and gut dysbiosis have all been identified as PD mechanisms (Dong-Chen et al. 2023). The interactions between all these molecular mechanisms complicate the pathogenesis of Parkinson's disease and pose significant challenges to treatment development. However, further research is needed, to understand the specific molecular mechanisms underlying Parkinson's disease (Fig. 4).



**Fig. 4** Dopamine neuron function. Dopamine is a neurotransmitter in the brain, a chemical released by neurons to transmit messages to other neurons. There are several different dopamine pathways in the brain, one of which is critical for the motivational component of reward-motivated behavior

## Imaging approaches for Parkinson's disease diagnosis

Computed tomography, magnetic resonance imaging (MRI), positron emission tomography (PET), and single photon emission tomography (SPECT) are used as imaging methods to diagnose Parkinson's disease (Verger et al. 2021). However, these techniques are only available in modern and high-cost hospitals. Several experimental techniques have been studied to understand how they can be used to diagnose Parkinson's disease. For example, 1018 g of iron in a cell structure with a diameter of 100 nm was determined using a synchrotron X-ray fluorescent nanoprobe for in vitro chemotaxis for iron metabolism in Parkinson's disease (Griffin 2018). They found that Parkinson's disease was associated with elevated levels of iron in the northern fat nigra pars compacta. In addition, in serological testing, neurotrophic factors derived from glial cell lines were used as neuroprotective agents using ultra-sensitive microscopic marbles. Simultaneous use of such particles for imaging and therapy paves the way for serological approaches to the treatment of Parkinson's disease (Ntetsika et al. 2021). Similar techniques for treating cancer have been developed. Furthermore, a technique for detecting cell loss was developed in 1999 (Kamath et al. 2022). Using this method, they discovered 60% of dopamine-producing neurons in the substantia nigra pars compacta with increased substantia nigra in postmortem samples, as well as 40% in the Nigral matrix. When compared to controls, they detected more than half the total number of dopamine-containing neurons. This study assessed the extent to which the loss of dopamine-containing brain cells has been linked to the development of Parkinson's disease. Despite these technological advancements, Parkinson's disease is still commonly diagnosed by clinical examination. Because of the uncertainty involved with this approach, and the emergence of noticeable motor-related symptoms occurring after a large degree of neurodegeneration, it is not possible to diagnose Parkinson's disease in its early stages.

## Nanotechnology for Parkinson's disease treatment

To treat disorders such as Parkinson's disease, nanotechnology can deliver neurotherapeutic drugs to precise sites via specific channels (Shabani et al. 2023). For example, certain ligands for receptors and transporters expressed on the blood–brain barrier are functionalized or modified on the surface of nanoparticles (Pinheiro et al. 2021). This

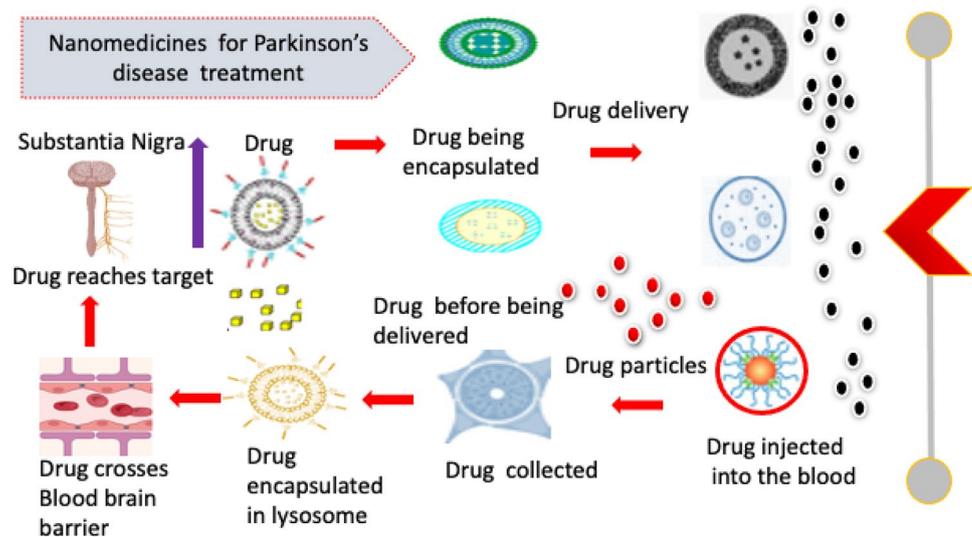
enables improved bioavailability in the brain via receptor-mediated endocytosis for the treatment of Parkinson's disease. Nanoparticles modified with a peptide-mimetic antibody function as a molecular Trojan horse (Pardridge 2020). This allows large molecules such as drugs and genes to pass through the blood–brain barrier and enter the brain for the treatment of Parkinson's disease. A more invasive approach that can pass through the blood–brain barrier is based on a hyperosmotic solution, and a less invasive approach targets specific endogenous transport systems within the blood–brain barrier (Teleanu et al. 2022). For example, the transferrin receptor contributes to the transport of iron to the brain via receptor-mediated endocytosis (Pulgar 2019). This method acts as a Trojan horse that transfers genes via the blood–brain barrier. This procedure has been shown to regulate striatal tyrosine hydroxylase (TH) activity (Boado 2022). It was discovered that PLGA nanoparticles loaded with antioxidants bound to the transferrin receptor antibody (OX26) induce strong antioxidant stress in Parkinson's disease (Riccardi et al. 2021). In an *in vitro* study, they observed that targeted nanoparticles enhanced cell absorption and reduced cell survival in RG2 rat glioma cells through receptor-mediated endocytosis compared to non-targeted nanoparticles (Li et al. 2020). These findings imply that transferrin receptors might be exploited to treat a range of neurodegenerative diseases, particularly Parkinson's disease, by modifying medication transport across the cell membrane. *In vivo* pharmacokinetic studies with lactoferrin-bound nanoparticles showed a 2.49-fold increase in AUC over 24 h compared to unbound nanoparticles. *In vitro* biological experiments on immortalised mouse endothelial cell lines also showed that bound nanoparticles were absorbed via clathrin-mediated endocytosis without affecting cell viability (Kim et al. 2023). In addition, nanoparticles significantly reduced striatal lesions in the 6-hydroxydopamine (6-OHDA)-induced rat Parkinson's disease model (Acidic 2021). These findings imply that lactoferrin might be a viable targeting ligand for improving active targeting and accumulation in the brain. Lactoferrin-coated nanoparticles may aid in the delivery of medications to the brain in the treatment of Parkinson's disease (Tang et al. 2019). Lactoferrin was used to demonstrate long-term non-invasive target gene therapy in a rotenone-induced model of chronic Parkinson's disease. They found that intravenous administration of nanoparticles decorated with lactoferrin efficiently transports genes to the brains of experimental mice, inducing stronger and longer-lasting glial cell line-derived neurotrophic factor (GDNF) expression than single doses. Due to their unique properties, nanoparticles can accumulate in specific organs even if there is no active target entity on their surface. For example, increased permeability and retention effects result in the

preferential accumulation of nanoparticles at the tumour site (Mitchell et al. 2021). Therefore, BBB is a serious obstacle to overcome for the treatment of Parkinson's disease. As a result, macrophages can be used as drug carriers to deliver a variety of therapeutic agents. In addition, bone marrow-derived macrophages were used in animal models to transport catalase to Parkinson's disease-affected brain regions (Haney et al. 2020). Furthermore, the self-assembled catalase/polymer complex was absorbed by the BMM and showed a continuous release for approximately 24 h (Alothman et al. 2021). It affects the breakdown of microglial hydrogen peroxide and may reduce the oxidative stress of Parkinson's disease. Nanoenzymes loaded into (1E, 2E)-1,2-bis((6-bromo-2H-chromen-3-yl) methylene) hydrazine (BMM) increased labelled enzyme deposition in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-treated animal tissues. MPTP causes Parkinsonism in primates, including humans (Niu et al. 2022). The production of nanoparticles loaded into macrophages may facilitate drug delivery to the brain. Nanoparticles can be manufactured and modified to have different properties (Yetisgin et al. 2020). Artificial nanoparticles have a variety of physicochemical properties, including their ability to pass through the blood brain barrier. Nanomedicine as a new method can significantly improve the current treatment of Parkinson's disease. Several nanoengineering solutions have been shown to be effective in maintaining drug concentrations on the market (Cheng et al. 2022). This improves half-life, bioavailability, and therapeutic effect. Studies have shown that nanodrugs can alleviate L-dopa-induced dyskinesias. Nanomedicines can be used to treat Parkinson's disease after being delivered to the body via the bloodstream (Padilla-Godínez et al. 2022). This allows nanomedicine to enter the bloodstream and penetrate the BBB to reach therapeutic targets. For example, in the treatment of Parkinson's disease, the medicine is encapsulated in lysosomes, penetrates the blood–brain barrier, and enters the brain (Fig. 5) (Cheng et al. 2022). Therefore, nanotechnology has the potential for the treatment of Parkinson's disease.

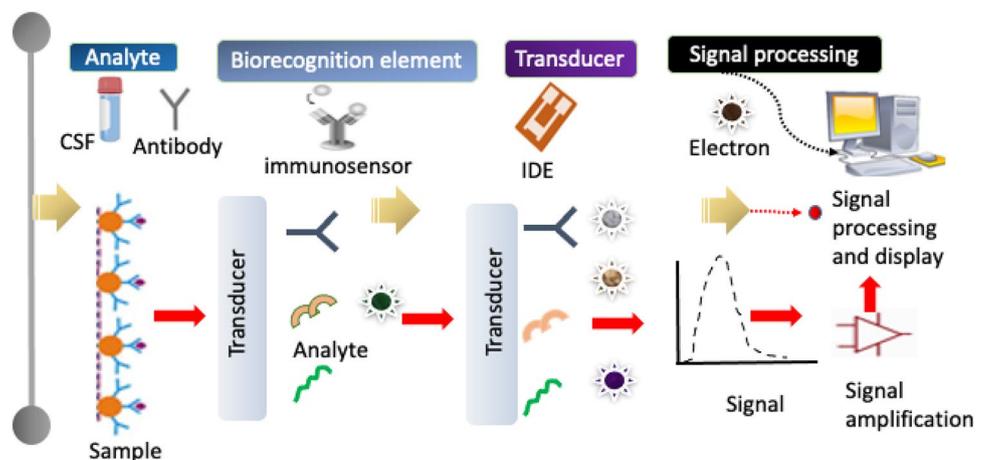
## Nanobiosensor

A biosensor is a device that provides a surface for probe-target interactions and converts the interactions into quantifiable signals (Nava et al. 2022). Optical, cantilever deflection, electrical, and electrochemical signals are examples of signal output. The basic operating principle of a nanobiosensor is to bind the bioanalyte of interest to a bioreceptor. This process then controls the physicochemical signals associated with the bond. For example, in nanobiosensors, chemical signals are converted into electrical signals by electrodes.

**Fig. 5** Treatment for Parkinson's disease using nanotechnology. Nanoparticles can be synthesized and manipulated to obtain various properties. Due to their physicochemical properties, engineered nanomaterials have a number of characteristics, including the ability to cross the blood–brain barrier. Nanomedicine can significantly improve the treatment of Parkinson's disease. Nanomedicines can improve half-life, bioavailability, and therapeutic benefit. In addition, nanomedicines can help alleviate L- DOPA-induced dyskinesia



**Fig. 6** Nanobiosensor. Signal transduction is used to fuel biosensors, with the transducer detecting the interaction and generating a signal. The primary concept of how a nanobiosensor works is to bind bioanalytes of interest to bioreceptors, which then drive the physicochemical signal associated with the binding. The chemical signal is converted to an electrical signal via electrodes in nanobiosensors. Nanobiosensors could also detect analytes such as CSF, antibodies, and other molecules of interest



Nanobiosensors can detect analytes such as cerebrospinal fluid (CSF), antibodies, and other molecules of interest (Fig. 6). The nanostructures of nanobiosensors act as a bridge between biological agents and physicochemical or biological agents (Singh et al. 2023). Nanosensors are mechanical or chemical sensors that may be utilised for temperature monitoring or chemical imbalance detection on the nanoscale (Sharma et al. 2021). Nanobiosensors are appealing development modalities due to a variety of benefits over traditional biosensor systems. When nano-sized components are used in the development of nanobiosensors, detection sensitivity may be dramatically increased (Attaallah et al. 2020). Nanobiosensor technologies are being developed for cancer diagnosis Electrochemical nanobiosensors, for example, as portable devices for quick detection of cancer biomarkers, have found significant applications in clinical medicine for diagnosis, treatment, and cancer screening (Gajdosova et al. 2020). Furthermore, nanobiosensors are an effective tool against COVID-19 because they are

designed to act directly on the infection, improve the efficacy of current antiviral drugs (Rai et al. 2021a). For example, a biosensor was used to identify COVID-19. The developed immunosensor had a very high sensitivity with a detection limit of 0.4 pg/mL, a much lower value, and a good linear response from 0.001 to 100 ng/mL (Antiochia 2020). In addition, nanobiosensors, which combine the benefits of nanomaterials and biosensing technologies, have been used for sensitive, selective, and quick disease detection and have received a lot of attention in the chemical, biology, and medical fields (2020). For sample-to-answer nucleic acid detection, an integrated paper-based biosensor paired with loop-mediated isothermal amplification (LAMP) was developed (Wang et al. 2022). A visible signal was then generated for the detection of target bacteria (Pandey et al. 2022). To monitor the interaction between the antigen, amyloid- $\beta$  derived diffusible ligands (ADDLs), and particular anti-ADDL antibodies, a nanoscale optical biosensor based on localised surface plasmon resonance (LSPR) spectroscopy

was developed (Asghari et al. 2021). This nanosensor, which employs the sandwich assay format, offers a unique analysis of the aggregation mechanisms of this putative Alzheimer's disease pathogen at physiologically relevant monomer concentrations. It also provides quantitative binding information for both antigen and second antibody detection, allowing the determination of ADDL concentration. A near-infrared optical nanosensor that can detect A $\beta$  intracellularly in living cells and intracranially in vivo was developed (Antman-Passig et al. 2022). This method allows researchers to investigate the molecular pathways behind A $\beta$  neurotoxicity in the progression of Alzheimer's disease. A biosensor is an analytical tool that combines a biological component that detects a biological response with an electrical signal transducer to create an electrical signal. Bacteriophages, proteins, antibodies, whole bacterial cells, enzymes, and others. To detect the analyte in a given sample, biosensors effectively mimic the highly specific interactions between molecules in biomolecules (Zambry et al. 2022). An amperometric fructose biosensor based on fructose dehydrogenase (FDH) was developed (Bollella et al. 2018). The biosensor demonstrated linearity in the range of 0.1–5.0 mM with a quick reaction time of 4 s and a limit of detection of 1 M. A malate quinone oxidoreductase enzyme-based biosensor for the detection of malic acid was created. The detection limit was 2.0 M  $\mu$ M. Malic acid concentrations in white, rose, and red wine samples were successfully detected by the biosensor (Gajek et al. 2021). A biosensor that detects hydroquinone and other polyphenolic antioxidant capacity using tyrosinase (TYN) enzyme encapsulated on a Nafion film on a carbon paste electrode was reported (Liu et al. 2019). The biosensor performed effectively at hydroquinone concentrations up to 120  $\mu$ M., with a detection limit of 1.6  $\mu$ M. Biosensors were used to study oxidative stress in Huntington's disease neurons (Malankhanova et al. 2022). The cells acquired might be utilised to investigate the redox potential of glutathione in HD neurons as well as to screen for novel therapeutic molecules that reduce oxidative stress. Nanobiosensors are fast emerging as an alternative to conventional methods of various detection methods, with growing simplicity and mobility, as well as improved sensitivity and reproducibility.

### Diagnosis of Parkinson's disease using nanobiosensors

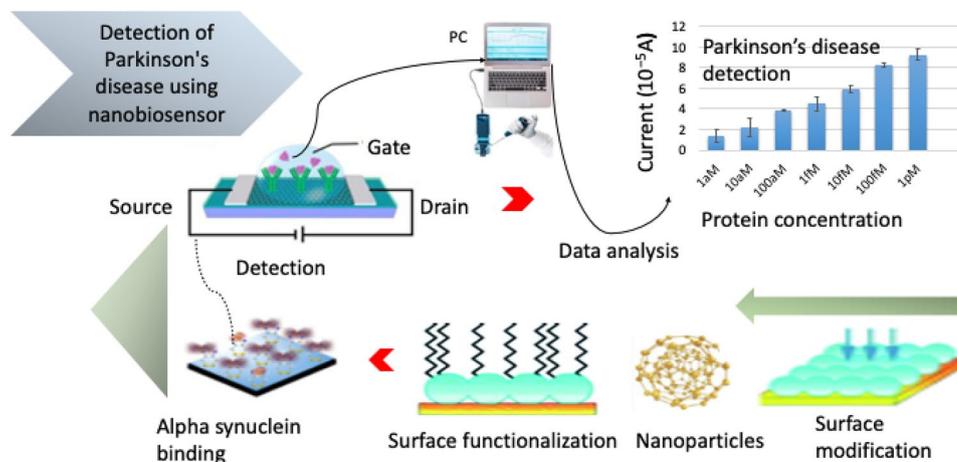
Improved laboratory equipment has enabled researchers to identify a wide spectrum of compounds with high sensitivity (Naresh and Lee 2021). Techniques such as 2-D gel electrophoresis, 6 mass spectroscopy, and isotope-coded affinity tags are sensitive but must be treated prior to detection. These treatments involve purification and concentration processes, which are typically carried out by chromatography (Punetha and Kotiya 2023). Additionally, the experimental

technique must be carried out by trained professionals with an extensive understanding of the topic at hand. These techniques are essential for fundamental research studies, but may not provide an attractive choice for routine diagnosis or research that needs extensive screening of several samples. It is important to develop new devices for detecting specific chemicals or components in patients, but also novel sensing methodologies that will allow researchers to conduct studies to better or produce knowledge about the disease or miss function. Therefore, nanobiosensors are used in a variety of sensing applications. The detection surface of the nanobiosensor is used to capture the electrical signal generated by the detection material (Banigo et al. 2020). Nanobiosensors are also widely used in a variety of applications, especially as components of sensor processes in the medical field (Huang et al. 2021a). For example, photolithography is used to manufacture nanobiosensors and microstructures (Fruntillo et al. 2021). Understanding the concept of biosensing forms the basis of research and development of nanobiosensors. A biosensor is an analytical device that combines biological detection elements such as sensor systems and transducers into a single device. In terms of selectivity and sensitivity, these sensors outperform all other diagnostic devices currently available. The most interesting use of nanobiosensors is in the diagnosis of Parkinson's disease and other clinical abnormalities (Perspectives 2022). For example, wearable devices based on silicon nanomembranes have been used to detect clinical abnormalities (Cheng et al. 2023). Nanofabrication enables the development of such sensors that can be used to improve the diagnostic accuracy of Parkinson's disease (Dixit et al. 2023). Several nanotechnology-based methods have been used to detect dopamine for the diagnosis of Parkinson's disease. For example, a carbon paste electrode that can detect dopamine and ascorbic acid simultaneously was developed (Moradpour and Beitollahi 2022). Both silver nanoparticles and carbon nanotubes are used to reinforce the electrodes, resulting in more efficient electrochemical catalysis with excellent selectivity, sensitivity, and detection limits in the micromolar range of both molecules. Also, a three-dimensional graphene foam zinc oxide (ZnO) nanowire array was developed. Using differential pulse voltammetry, the array detected dopamine, uric acid, and ascorbic acid in Parkinson's disease (Li et al. 2021a). The use of nanowires improved the electrical conductivity and sensitivity of nanobiosensors and reduced the detection limit of dopamine and uric acid to 1 nanomol. They discovered that Parkinson's disease patients had lower levels of UA than healthy people. This suggests that uric acid can be used to diagnose Parkinson's disease using a biomarker. Parkinson's disease is also linked to mitochondrial malfunction and complex I inhibition, which includes NADH (Curtis et al. 2022). Furthermore, ubiquinone oxidoreductase has been linked to dopaminergic neuronal death

in Parkinson's disease (Wen et al. 2020). In several studies, alpha-synuclein has been identified as a key neuronal protein in the diagnosis of Parkinson's disease (Gómez-Benito et al. 2020). NMR spectroscopy, fluorescence measurement, western blotting, and size exclusion chromatography were used to identify Parkinson's disease (Strohäker et al. 2019). A highly ordered microfabricated array for the photoelectrochemical detection of alpha synuclein has been developed using gold-doped TiO<sub>2</sub> nanotubes (Jang et al. 2020). The array enabled the primary antibody to be immobilised while retaining the stability and binding of -synuclein. The use of secondary antibodies in combination with gold nanoparticle-bound glucose oxidase significantly increases signal amplification. The detection of new compounds using carbon nanotubes and gold nanoparticles was conducted (Hannon et al. 2022). They created an electrochemical nanobiosensor that can help identify Parkinson's disease early. They measured the circulating biomarker miR-195 in Parkinson's disease patients. They also altered the surface of the carbon electrode, which had been screen-printed with exfoliated graphene oxide and gold nanowires. For differential pulse voltammetry experiments, they prepared single-stranded thiolized probes for selective hybridization to target miRNAs (Erdem and Eksin 2023). In this study, doxorubicin was used as an electrochemical biomarker. They found high sensitivity, a detection limit of 2.9 femtomols, and a dynamic range of 10.0–900.0 femtomols. They also found the selectivity of target miRNAs over non-specific oligonucleotides. They discovered the development of a new signal-on-biosensor for the selective and sensitive detection of miR 133b for the diagnosis of Parkinson's disease. The linear concentration range of the sensor was 10 fM to 520 pM. Under ideal conditions, they achieved a detection limit of 168 aM and a sensitivity of 0.3 nApM1. Furthermore, the sensor distinguishes between matched and mismatched miR sequences. For the electrochemical detection of synuclein as a biomarker for Parkinson's disease, a nanobiosensor with a

detection limit of 10 aM and a sensitivity of 1 aM was used (Ganguly et al. 2021). These findings imply that nanobiosensors can be utilised to correctly identify Parkinson's disease (Fig. 7). Electrochemical nanobiosensors have low detection limits, good selectivity, and outstanding performance. Furthermore, electrochemical nanobiosensors are great candidates for detecting biomarkers for early Parkinson's disease diagnosis. Nanobiosensors have the potential to enhance the lives of Parkinson's disease patients and are great for laboratories and physicians utilized for Parkinson's disease early detection (Hyun et al. 2021). This will spark the attention of researchers in conducting more study on nanobiosensors for disease diagnosis and treatment. Parkinson's disease is challenging to diagnose since the cause is unknown, however protein aggregation, such as alpha synuclein, is considered to be one of the causes. Furthermore, Parkinson's disease treatment is challenging since drugs must penetrate the brain. For example, crossing the blood–brain barrier is difficult with current therapeutic approaches. As a result, nanotechnology may be useful for the detection and treatment of Parkinson's disease. Furthermore, nanotechnology is being used to treat Parkinson's disease by creating particles that are attracted to disease cells, allowing for direct therapy of specific cells. Biosensors, for example, are used to detect Parkinson's disease by immobilizing the target biomarker and detecting abnormalities in the form of signals to identify disease stages (Hyun et al. 2021). Based on the measurement of circulating biomarker, miR-195, an electrochemical nanobiosensor for early diagnosis of Parkinson's disease was developed. Based on the findings, the miR-195 electrochemical nanobiosensor could be recommended to physicians for the medical diagnosis of Parkinson's disease (Aghili et al. 2018). For the detection of late stage Parkinson's disease, deep learning algorithms were used to identify Parkinson's disease from multi-modal and in-the-wild sensor data (Papadopoulos et al. 2020). The findings suggest that the proposed method can be used as a stepping stone towards the

**Fig. 7** Detection of Parkinson's disease using nanobiosensor. Biosensors are devices that provide a solid surface for probe-target interaction and then convert that interaction into a measurable signal. Optical, cantilever deflections, electrical, and electrochemical signals are examples of signal output. For example, nanobiosensors could be used as electrochemical sensors to detect Parkinson's disease based on alpha-synuclein aggregation after partitioning into different concentrations



development of an accessible Parkinson's disease screening tool that will passively monitor the subject-smartphone interaction for signs of PD and could be used to reduce the critical gap between disease onset and treatment initiation. Moreover, data shows that early Parkinson's disease intervention has the potential to halt symptom development and enhance overall quality of life in the longterm (Jankovic and Tan 2020b). Unfortunately, the initial motor symptoms are usually very subtle, and as a result, patients seek medical attention only when their condition has significantly worsened, missing out on a better clinical outcome. To enhance the electrochemical signal for dopamine detection, a spin-coated silver encapsulated MoS<sub>2</sub> hybrid nanoparticle was developed and attached to the indium tin oxide electrode [68]. At low dopamine concentrations, the sensor exhibits a good repeatability and sensitivity. For dopamine electrochemical sensing, screen-printed molybdenum disulfide working electrodes were developed (Lin et al. 2021). The results revealed a broad linear detection range of dopamine from 1 to 300 M. For the detection of dopamine, a modified electrode with silver nanoparticles and graphene oxide was developed (Lindholm and Saarma 2022). In current clinical practice, assessment of motor symptoms in PD patients involves capture of patient history, use of patient diaries, and neurological evaluations. The Unified Parkinson's Disease Rating Scale (UPDRS) is time-consuming and subjective, and the brevity of routine in-clinic examinations may not accurately reflect motor impairments and fluctuations experienced in everyday life (Stathis and Papadopoulos 2022). Tools are needed to provide objective, quantitative, continuous, and real-world assessment of PD. Parkinson's disease, a dangerous neurological condition, is best treated if diagnosed early. Parkinson's disease detection with nanobiosensors (Table 1). Based on nanobiosensors, the methods for detecting Parkinson's disease are successful for both early and late stages of the disease, however, because nanosensors are a relatively new technology, their application in biological systems is limited because they can disrupt cell metabolism and homeostasis, altering cellular molecular profiles and making it difficult to distinguish sensor-induced

artefacts from fundamental biological phenomena. Further, nanoparticles can cause neurotoxicity in the treatment of Parkinson's disease, which cause a difficulty, therefore, research is needed to address such limitations.

### Limitations of nanobiosensor as a diagnostic tool

Nanotechnology has numerous advantages, for example, nanotechnology has the potential to enable new and faster computer types, more efficient power sources, and life-saving medical treatments. Nanotechnology has the potential to change the way we obtain and use energy. Nanotechnology, in particular, is likely to make solar power more affordable by lowering the cost of building solar panels and related equipment. As a result, energy storage devices will become more efficient. Nanotechnology will also enable new methods of energy generation and storage. However, nanotechnology has numerous disadvantages, for example, economic disruption and potential threats to security, privacy, health, and the environment are among the potential drawbacks. To begin, each biosensor is designed with a specific aim in mind. The mode of operation of a biosensor is determined by its bioreceptor and sensing technique. The electrical signal from the transducer is often quite small and overlaid on a very high baseline. Signal processing typically begins with the generation of a signal showing the baseline position from a similar transducer that is not coated with any bio-catalyst. The biosensor's relatively slow reaction rate considerably reduces the challenge of electrical noise filtering. At this point, the direct output is an analogue signal. The signal, on the other hand, might be transformed to digital form and delivered to a microprocessor unit, which would then analyse the data, transmit it to certain units, and export it to data storage. The distinctive parameter being monitored or detected by the instrument, on the other hand, is typically derived from the environment or creature. A biosensor can function both within and outside of a biological organism. Unlike optical biosensors, which include an optical transducer system and a biorecognition sensing component, electrochemical biosensors have an electrochemical transducer and are

**Table 1** Detection of Parkinson's disease using nanobiosensors

Electrode materials	Method	Linear range	LOD	References
{HRP-Ab2-GNPs}/Ab1/- SYN/Th/PAMAMAu/o-ABA/GCE	CV	1.6 pM–16 nM	1 pM	Jang et al. (2020)
Apt-CS/ $\alpha$ -Syn oligomer/Exo $\alpha$ -Syn oli	DPV	60 pM–150 nM	10 pM	Pontarollo et al. (2021)
Cystamine/GO/Au	EIS	5 pM–1 nM	1.2 pM	Ionescu (2022)
{TiO <sub>2</sub> /Au/Ab1/ $\alpha$ -Syn/{Ab2-Au-GOx}	PEC	4.2 pM–8.3 nM	1.3 pM	Erkmen et al. (2022)
AuNPs/PGA/EDC-NHS/Anti- $\alpha$ -Synalpha/BSA/ITO	SWV	0.3 pM–0.2 nM	9.3 fM	Štukovnik and Bren (2022)
Apt/ERGO-GCE	DPV	1 fM–1 nM	0.6 fM	Lakard et al. (2022)
ZnO-Gold nanoros modified AIDES	IV	1aM–10 pM	1aM	Adam et al. (2021)
On-Line Stacking Capillary Electrophoresis	$\mu$ CE	0.04–6 $\mu$ g/ml	10 ng/mL	Tan et al. (2022a)

classified as impedimetric, conductometric, potentiometric, and amperometric sensors. Biosensors provide a potentially game-changing tool for the rapid and precise detection of biological protein markers linked to a variety of infectious and noncommunicable diseases. Nanotechnology has the potential to increase accuracy and precision, paving the way for nanobiosensors. Nanomaterials can be used to increase biosensors performance. Nanomaterials can also increase analyte concentration on the electrode surface, speed up analyte transport, and enhance the anti-fouling properties of biosensors. To develop bio-affinity-based biosensors for a range of applications, biosensors integrate nanomaterials with biorecognition components of various sizes. A sensor is a device that directly measures the test substance (analyte) in a sample. A device of this type should preferably be capable of continuous and reproducible reactions while without damaging the sample (Huang et al. 2021b). A system known as a nanosensor uses at least one nanostructure to detect various substances, including gases, chemicals, biological agents, electric fields, light, and heat (Naresh and Lee 2021). The system's sensitivity is significantly increased by the inclusion of nanoparticles (Khan et al. 2019). The parameters of the system change considerably when the recognition event happens in the biosensor, enabling the transducer to read it and convert the perturbation into an electrical signal (Polat et al. 2022). In some cases, the system's signal labels are necessary to provide this readable signal. This type of sensor is known as a label-based biosensor (Koyappayil and Lee 2021). Labels are generally made of organic chemicals, nanoparticles (NPs), or proteins (proteins or enzymes) that generate a fluorescence or electrochemical signal (Mollarsouli et al. 2019). The primary disadvantage of label-free assays is the absence of significant changes in detecting the target event (Immunosensors 2019). Many sensors based on nanopores have been developed. For instance, Singer and his colleagues reported DNA detection and sequencing using a nanopore-based technology (Lin et al. 2021). The pore was created in a free-standing silicon nitride membrane with a silicon chip as the frame. Unfortunately, the real applicability of single-pore devices for research is constrained by fabrication methods. In addition, extremely complex and cutting-edge technology is required to process the signals produced by such small devices. Nanomaterials provide new possibilities for biosensing devices; they can enhance several aspects of the performance of the biosensor, including sensitivity, stability and shelf life, signal-to-noise ratio, duration of response, and other aspects (Kumar et al. 2023). As a result, they are promising prospects for cutting fabrication costs, allowing for the development of cost-effective sensing devices in contrast to existing detection alternatives, as well as the capacity to build small compact devices. Unfortunately, one barrier to the commercialization of nanobiosensors is the safety and toxicity of nanomaterials, as well

as their composition and properties (Kumar et al. 2023). There is still a vigorous debate concerning these materials and their effects, which need more research.

## Future perspectives

Nanotechnologies, for example, are being used to develop nanomedicine and nanobiosensors for the detection and treatment of Parkinson's disease. Some nanomaterials have properties that make them ideal for improving the early diagnosis and treatment of neurodegenerative diseases. Some nanoparticles are also used to improve pharmaceutical products like sunscreen. Nanotechnology is used to create nanobiosensor for various applications. A biosensor is a device that provides a surface for probe-target interactions and converts the interactions into quantifiable signals. Optical, cantilever deflection, electrical, and electrochemical signals are examples of signal output. The signal generated by a particular bioanalysis interaction is converted into another signal that can be detected and measured by a nanobiosensor. The application of nanobiosensor is rapidly expanding, notably in the detection of neurodegenerative diseases such as Parkinson's. A nanobiosensor is a device that combines a transducer and a receptor so that it can convert a biological response into an electrical signal. The design and development of biosensors have dominated the centre stage for researchers or scientists over the past ten years due to the wide range of nanobiosensor applications, including health care and disease diagnostics. Nanomaterial formulations, for example, have been shown to lower oxidative stress and inflammation in Parkinson's disease and to overcome earlier limitations in blood–brain barrier bridging. Because of the better outcomes, nanobiosensors have a massive effect on how healthcare has progressed. The components of a biosensor are critical to its operation. The area of research into Parkinson's disease is developing quickly since many of the important mechanisms behind Parkinson's disease neurodegeneration are now understood, allowing for the testing of novel therapeutic modalities in both the laboratory and the clinic. Parkinson's disease is a neurodegenerative disease that may be clinically identified based on its motor characteristics, with nonmotor symptoms frequently being noticed. Although the exact cause is still unknown, it is thought to be a mix of genetic and environmental risk factors, most often sex and age. Severity of parkinsonism, rate of deterioration of parkinsonism, poor response to levodopa, early gait impairment, and symmetry of parkinsonism are all potential risk factors for higher mortality. The likelihood of misdiagnosing Parkinson-plus syndrome as idiopathic Parkinson's disease may be caused by some of these characteristics, thus it is critical to be aware of this difficulty in the differential diagnosis. There are several medicinal and surgical therapies

that may be utilised at various points along the course of the disease to address symptoms of both motor and nonmotor characteristics, even though there are currently no neuroprotective treatments. We could soon have better alternatives thanks to the range of ongoing trials on novel nanobiosensor and nanomedicine. The application of nanotechnology in the medical area facilitates in the detection and treatment of various diseases by improving the sensitivity of equipment and different parameters of medications, consequently boosting their efficacy (Ngowi et al. 2021). Due to their ability to penetrate the BBB, NPs provide a viable alternative for detecting and treating brain diseases, which have proven to be difficult for many years (Thangudu et al. 2020). Herapeutic usefulness and low toxicity should be prioritised to attain a high outcome and prevent more brain damage. Moreover, improving their sensitivity to target specific biomarkers by formulation with specific antibodies is crucial. With more studies, the potential of nanotechnology in the treatment of brain disorders and conditions will be limitless. To develop in the field of label-free sensing, new technologies that allow the target binding to be significantly modified, such as nanochannel blocking, are necessary. Another option is to enhance existing transducers so that they can read even tiny changes linked to target recognition, for as by modifying the electrodes with nanomaterials or employing the same nanomaterials as electrodes. To address the aforementioned shortcomings, nanochannel arrays emerged as a viable alternative, ushering in a new line of nanochannel/nanopore-based biosensors. To begin, the overall result of the array may be thought of as the parallel and simultaneous behaviour of all single channels, thus a little signal from a single channel is multiplied by the sum of all channels in the array, resulting in a larger signal that is simpler and more practicable to read. In addition, compared to the equipment and resources required for single pore/channel creation, device fabrication of a wider area with an array of channels is a simpler and more realistic solution that can be carried out using standard chemistry procedures.

## Conclusions

Parkinson's disease is a nervous system disorder that primarily affects the brain subregions that produce dopamine. Parkinson's disease symptoms include both motor and non-motor symptoms that are clinically diagnosed. Parkinson's disease also affects the central nervous system, which includes the brain, spinal cord, and the nerves that connect them. There is no known therapy for Parkinson's disease. These medications, however, merely address the symptoms of the condition. Other treatments for Parkinson's disease exist, such as deep brain stimulation, which involves implanting electrodes in particular areas of the brain. These

electrodes produce electrical impulses that regulate brain function. These surgeries, however, are expensive and are only used when the disease has advanced. Nanotechnology, by providing lower devices, provides a feasible alternative to the existing diagnosis and treatment of Parkinson's disease. Protein aggregations have therefore been discovered as biomarkers for the early detection of Parkinson's disease. Efforts have been made to discover novel biomarkers and treatment approaches. Nanotechnology has the potential to deliver innovative techniques for the diagnosis and treatment of Parkinson's disease through the use of nanobiosensors and nanomedicine. Some nanosensors have the potential to disrupt cell metabolism and homeostasis, changing cellular molecular profiles and making it difficult to distinguish sensor-induced artefacts from fundamental biological phenomena. Despite nanotechnology's potential to diagnose and treat Parkinson's disease, there are still unaddressed concerns, such as how to separate sensor-induced artefacts from fundamental biological processes and how to precisely eliminate the nanotoxicity of nanotherapeutic drugs. Therefore more research is needed to address these concerns.

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**Availability of data** Available upon request.

## Declarations

**Conflict of interest** The authors declare that they have no competing interests.

**Ethics approval and consent to participate** Not applicable as this study has not involved any animal or human.

**Consent for publication** All authors agree for Publication.

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