

Parkinson's Disease: Genetic Factors, Emerging Therapies, and Their Implication for the Future

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ABSTRACT: Parkinson's disease is a progressive neurodegenerative disease where the dopaminergic neurons in the substantia nigra become damaged and die over time. Every six minutes, an American is diagnosed with Parkinson's disease, making it the fastest-growing neurological condition globally.¹ Despite its scale, there has been no solution to cure this disease, truly making it a public health crisis. In this review, we will discuss gene therapy (GBA-1, SNCA, LRRK2), deep brain stimulation (adaptive, connective), and cell therapy (embryonic stem cells, induced pluripotent stem cells). Gene therapy is the process of introducing genetic material into the brain to target specific molecular pathways that have been damaged by PD. Deep brain stimulation is the implantation of electrodes in specific regions of the brain to deliver electrical pulses, helping to regulate abnormal brain signals often found in PD that cause motor symptoms. Cell therapy is the replacement of damaged neurons and restoration of dopaminergic function, decreasing the severity of motor symptoms. While these therapies are not completely developed, they have the potential to improve PD patients' quality of life by personalization, effectively slowing symptom progression and decreasing side effects. Moving forward, researchers and clinicians should respectively focus on addressing therapy concerns, such as the irreversibility of gene therapy, and closely follow these emerging therapies in order to offer their patients the best possible treatments.

KEYWORDS: Translational Medical Sciences, Disease Treatment and Therapies, Neurodegenerative Disease, Parkinson's Disease, Gene Therapy, Deep Brain Stimulation, Cell Therapy.

■ Introduction

Every six minutes, an American is diagnosed with Parkinson's disease, making it the fastest-growing neurological condition globally. Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the degeneration of dopaminergic neurons in the substantia nigra, a group of nuclei part of the basal ganglia that regulates voluntary motor control.² In a healthy individual, dopamine removes inhibitory signals in the basal ganglia, allowing for voluntary movement. However, in PD patients, the gradual loss of dopaminergic neurons over time results in insufficient levels of dopamine, ultimately leading to bradykinesia and a struggle to initiate voluntary movements. While the cause of Parkinson's disease is still unknown, one cause that is currently the subject of intensive research is Lewy bodies, intraneuronal proteinaceous inclusions which are primarily made up of alpha-synuclein, in the neurons of the substantia nigra, disrupting nerve transmission and ultimately damaging nerves and even leading to cell death.^{2,3}

The most common characteristics individuals with Parkinson's disease suffer from are motor symptoms, collectively called Parkinsonism. Parkinsonism can be caused by a variety of factors, such as drugs, toxins, and other diseases, which must be excluded before diagnosing a patient with PD. Parkinsonism motor symptoms include hand tremors, slow movements, limb rigidity, and problems with gait and balance. Additional motor symptoms often found in PD patients but not associated with Parkinsonism are slurred speech and reduced facial expressions. While the most significant symptoms of PD are

motor-related, other non-motor-related symptoms include behavior and mood changes, cognitive impairment, and sleep disturbances.² While novel therapies are not completely developed, they have the potential to improve PD patients' quality of life by personalization, effectively slowing symptom progression and decreasing side effects. Moving forward, researchers and clinicians should respectively focus on addressing therapy concerns, such as the irreversibility of gene therapy, and closely follow these emerging therapies in order to offer their patients the best possible treatments.

■ Genes associated with Parkinson's Disease

1.1. SNCA:

As previously stated, the cause of PD is unknown. However, through ongoing research, some potential causes have emerged. The most significant potential cause that this research paper will explore is genetics. The SNCA gene, the first gene discovered to be related to PD, controls the production of alpha-synuclein.^{4,5} Alpha-synuclein is most abundant in the brain, specifically at the presynaptic terminals of neurons.⁴ In 1997, researcher Roger Duvoisin from the Parkinson's Foundation first discovered this gene to be related to PD.⁵ More than 30 SNCA variants have been identified. These variants are inherited in an autosomal-dominant pattern, meaning only one SNCA gene variant is needed to significantly increase the risk of developing PD. SNCA variants also tend to cause young-onset Parkinson's disease (YOPD), which is PD occurring before

age 50. Disease progression may also be faster in genetically related cases. While research is still ongoing, researchers have discovered that SNCA variants can lead to the accumulation of Lewy bodies through two mechanisms.⁵ First, the alpha-synuclein proteins do not fold or clump together properly.⁴ This is due to the amino acid alanine being replaced with the amino acid threonine or proline, ultimately leading to an incorrect 3-dimensional shape.⁴ Second, the variants cause an overproduction of alpha-synuclein proteins through excess copies in gene replication that cannot be destroyed fast enough, leading to clumping.^{4,5}

1.2. GBA:

The GBA or GBA-1 gene is the most common PD-related gene.⁵ The GBA gene codes for the lysosomal enzyme glucocerebrosidase (GCase), which maintains glycosphingolipid homeostasis.³ Variants of this gene are found in 5-15% of people with PD.³ Compared to other primary gene mutations of PD, variants of the GBA are considered only to increase the chances of an individual getting PD, not necessarily being a definitive cause. The majority of carriers of the GBA variant, even those with a family history of PD with the GBA variant, will not develop PD. Other risk factors in addition to the GBA variant, such as age or environment, are needed to significantly increase the risk of developing PD. Carrying a single heterozygous GBA increases the risk of developing PD, but having both genes, a homozygous variant, further increases the risk. Researchers are currently exploring the specifics of how GBA variants increase PD risk in brain cells.³ They hypothesize that GBA variants cause a loss of GCase activity and lysosomal dysfunction, impairing alpha-synuclein metabolism and leading to aberrant lipid metabolism and an accumulation of waste.³ Currently, pharmaceutical companies are testing drugs through clinical trials to target GBA to slow or even stop PD progression.⁵

1.3. LRRK2:

The LRRK2 gene is the second most common PD-related gene.⁵ It is a large protein, about 2527 amino acids.⁶ Its variants are found in 1% of people with PD and 5% of people with a genetic history.⁵ Although LRRK2 genes are generally considered causative of PD, some people who carry these variants will not develop PD. Similar to some other variants, the risk of developing PD increases with age and has a dominant inheritance pattern. Unlike other gene variants, certain ethnic groups have a higher prevalence of LRRK2 variants, such as Ashkenazi Jews (about 15%) and North African Berbers (about 40%). People with the LRRK2 variant-caused PD may experience less frequent motor difficulties and slower disease progression compared to other variants. Ongoing research explores how LRRK2 specifically leads to PD.⁵ Scientists believe mutations in the LRRK2 gene may cause an accumulation of α -synuclein, which is one of the main stimulants of microglial activation.⁶ This activation is also believed to contribute to neuroinflammation and neuronal death in PD.⁶

■ Gene Therapy

2.1. Dopamine-Related Gene Therapy:

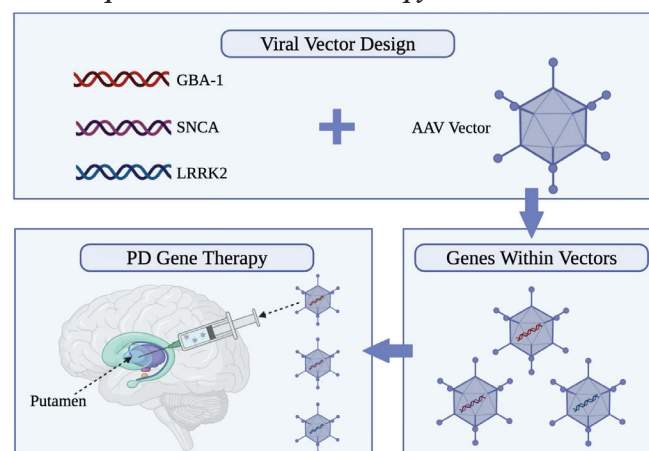


Figure 1: Adeno-associated viral (AAV) vectors carry PD-associated genes: GBA-1, SNCA, and LRRK2, for targeted delivery. The loaded AAV vectors are injected into the putamen, a motor-functioning area of the brain, to improve motor control for patients with Parkinson's disease. (Created with BioRender).

Gene therapy in the context of Parkinson's disease is the process of introducing genetic material into the brain to target specific molecular pathways that have been damaged by PD.⁷ It is an emerging and promising approach to promoting dopaminergic growth and reducing neurodegeneration. It addresses both symptomatic relief and disease modification. Gene therapy will typically use viral vectors to deliver therapeutic genes directly to affected brain regions (**Figure 1**). One main approach in PD gene therapy is Dopamine Synthesis Enhancement, which converts L-DOPA to dopamine more efficiently, addressing a primary symptom of PD: loss of dopaminergic neurons. Aromatic L-amino acid decarboxylase (AADC), an enzyme part of the dopamine synthetic apparatus, is used in Dopamine Synthesis Enhancement by being delivered to the striatum or putamen (motor-functioning areas of the brain). Human trials showed reduced "off" time, lower need for L-DOPA doses, and improved motor function specifically in early-phase trials. L-DOPA is the primary clinical approach for PD treatment because of its ability to cross the brain barrier, thus enabling oral treatment and making it easier for PD patients to take. While L-DOPA can address the loss of dopaminergic neurons in PD patients, there are some drawbacks. First, L-DOPA is only a symptomatic treatment, meaning it cannot stop disease progression, thus limiting its scope of effectiveness. Additionally, severe side effects of L-DOPA include "OFF-states": periods of immobility and incapacity often followed by depression or hypomania due to inconsistent function of the drug. These "OFF-states" have been attributed to unpredictable gastric emptying, an overload of the blood-brain barrier carrier system which transports L-DOPA, and insufficient aromatic L-amino acid decarboxylase (AADC) levels. However, new formulations of L-DOPA have improved drug absorption. Many rodent studies found striatal vector-mediated AADC overexpression to be well tolerated and cause symptom improvement. Several non-human primate studies support this, showing that once a certain

level of transfection was reached, there was a decreased need for medication and improvement of motor control when off medication. Additionally, human trials (AAV2-AADC in the putamen of severe PD patients) showed safe results, an improvement in motor symptoms, and reduced UPDRS scores. Ongoing studies now aim to optimize the delivery and dosage of L-DOPA.

2.2. Neuroprotection and Growth Factor Approaches:

Furthermore, more research is being conducted on growth factors as a treatment target for neurodegenerative diseases such as PD. The primary focus has been on the glial cell-line derived neurotrophic factor family of ligands (GFL) that encompasses glial cell-line derived neurotrophic factor (GDNF), neurturin (NRTN), artemin (ARTN), and persephin (PSPN). The GFL signals via activation of the RET receptor complex and cofactor GFR α , initiating MAP kinase and PI3-kinase pathways, which support neuron survival and neuritogenesis. Several studies have shown that direct delivery of GDNF into the SN and the striatum reduces Parkinsonian behavior and improves neuritogenesis in toxin models of PD and phase 1 trials. However, phase 2 trials have failed due to poor drug distribution and an insufficient number of residual neurons for GDNF to affect. Due to phase 2 failure, other gene therapies are being explored, such as AAV-GDNF, which was successfully injected into the caudate nucleus. Similar to L-DOPA delivery, a new approach of AAV-GDNF vectors in the putamen is safe and effective at treating Parkinsonian behavior in murine PD models.⁷

2.3. Genetic Mutation-Targeted Therapies:

2.3.1. GBA:

Another primary approach to correcting genetic mutations, specifically GBA, is GCase enzyme replacement therapy.⁸ While its recombinant form was not initially able to be used for PD due to its inability to cross the BBB, viral vectors of GBA are now being directly injected into the midbrain. Several mouse studies have shown that this restores GCase activity, thus reducing waste, neuroinflammation, gliosis, and preventing cognitive and motor deficits. Different virus types, such as AAV9, AAV2/5, AAV1, and promoters, had the best results. Due to success in animal trials, the PROPEL study, a 2020 phase 1/2a clinical trial sponsored by Prevail Therapeutics, is testing AAV9-GBA1 (PR001/LY3884961) in individuals with moderate to severe PD who carry at least one GBA1 mutation. This study enrolled 20 patients who were separated into low and high dose groups (exact dose not disclosed) where PR001 was administered only once through intracisternal injection in cisterna magna.⁸ Close monitoring, blood and urine tests will start from Day 2 of administration to month 18, then a follow-up from month 18 to month 60.⁹ This study is currently ongoing and recruiting but results are said to be released in 2029.^{8,10}

2.3.2. SNCA:

Another upcoming experiment relies on the development of CRISPR-based technologies, specifically dCas9, to decrease

SNCA gene expression, leading to lower alpha-synuclein protein levels.¹¹ By lowering alpha-synuclein protein levels, this form of gene therapy may be able to slow or halt PD progression. Scientists will use CRISPR to alter precise locations of the genome and penetrate the neuronal cells derived from induced pluripotent stem cells, which this research paper will dive into further in cell therapy. In the future, the outcomes of these pre-clinical models will be observed for their long-term effects. If the outcome of these preclinical models is favorable, then the Michael J Fox Foundation will plan on performing clinical trials and ultimately seeking regulatory approval.¹¹

2.3.3. LRRK2:

The last main new approach to gene therapy targets the LRRK2 gene. A company called Denali Therapeutics, based in South San Francisco, partnered with Biogen to create drugs in pill form called DNL201 and DNL151, also known as BII122. These are kinase inhibitors, in hopes of delaying progression of PD in early-stage patients with the LRRK2 gene mutation by reducing the activity of LRRK2 proteins, thus improving the function of lysosomes.¹² In a press release from January 2020, Denali Therapeutics announced that both compounds have shown little to no side effects.¹³ Later that year, in August, it was announced that while both compounds can advance to clinical trials, DNL151 is preferred as it has more flexible dosing regimens. Currently, one of the ongoing and seemingly successful Phase 2 clinical studies is LUMA, which started in April 2022 with study completion estimated in December 2025. This study is large, global, and placebo-controlled in the hopes of decreasing PD symptom progression. It enrolled 650 patients with early-stage PD aged 30 - 80 who were diagnosed with PD within 2 years of starting the study, and people with LRRK2 gene mutation and those with idiopathic PD.¹³

2.4. Gene Therapy, Conclusion:

Overall, gene therapy offers a promising symptomatic solution for PD. While mainly being a symptomatic treatment, it has the potential to improve the quality of life of PD patients with a variety of genetic mutations, with decreased progression of symptoms and increased dopamine production, meaning more motor control. If gene therapy can stop PD disease progression and not just treat symptoms, that is a huge potential benefit for patients. On the other hand, researchers should be extremely cautious when using CRISPR technology as the changes are irreversible.

■ Deep Brain Stimulation

3.1. Traditional Deep Brain Stimulation:

Deep-brain stimulation is the most commonly performed surgical treatment for PD.¹⁴ It is the implantation of wires called electrodes in specific regions of the brain to deliver electrical pulses, helping to regulate abnormal brain signals often found in PD that cause motor symptoms. Since its approval from the U.S. Food and Drug Administration (FDA) in 2002 for Parkinson's, DBS has helped reduce medication needs and motor symptoms.¹⁵ DBS is only available for those who have had PD for 4 years or more and who benefit from medication

but still struggle with motor control, such as significant “off times” and dyskinesia.¹⁴ DBS usually only works on lessening motor symptoms and involuntary movements such as stiffness, slowness, and tremors, but cannot significantly help imbalance, gait, or any non-motor symptoms. DBS has also been shown to worsen memory, so DBS is not recommended for those with dementia.¹⁴

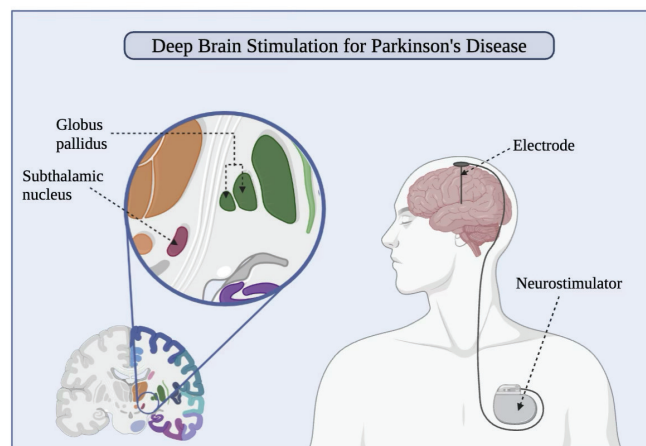


Figure 2: An electrode placed within the basal ganglia is connected to a neurostimulator implanted under the collarbone. Electrical impulses are delivered to the globus pallidus internus and subthalamic nucleus to regulate abnormal neural activity and restore motor control in patients with Parkinson's disease. (Created with BioRender)

In DBS surgery, a surgeon inserts thin electrodes into areas of the brain that control movement, commonly the subthalamic nucleus or globus pallidus interna.¹⁴ While some clinics allow the use of brain imaging to position the electrodes correctly while a patient is asleep, most patients are forced to stay awake and answer questions and perform common tasks. Once the electrodes are in place, it is connected to a neurostimulator implanted under the collarbone, which delivers continuous electrical pulses. The settings of the neurostimulator will later be adjusted post-surgery to optimize symptom control and adjust to new medications. After DBS, most people have been able to decrease the use of medication for PD. However, the downside to traditional DBS is that the right combination of drugs and personalized DBS settings to offer the most benefits and least side effects can take several months to a year to be determined, making it less ideal for PD.¹⁴ Another downside to traditional DBS is that it provides constant electrical stimulation, meaning for those whose symptom severity fluctuates throughout the day, DBS can sometimes be too much or too little, limiting its overall effectiveness.¹⁵

3.2. Adaptive Deep Brain Stimulation:

One ongoing small study from Nature Medicine tested adaptive DBS, which has the potential to personalize PD symptom treatment.¹⁵ By using custom computer algorithms and artificial intelligence, adaptive DBS can detect symptom fluctuations by monitoring the brain activity of each patient. When it detects a change in symptom severity, it will counteract by delivering a precisely calibrated electrical pulse. Not only can adaptive DBS adjust to symptom severity, but specific motor issues, such as more stimulation for bradykinesia

and less for dyskinesia. Moreover, it adjusts to the effectiveness of medication, providing more stimulation when medication wears off and less when it's active. This study enrolled PD patients undergoing deep-brain stimulation in the subthalamic nucleus (STN) and ten PD patients with a globus pallidus (GPi) target, and performed traditional DBS surgery on them.¹⁶ Collecting each patient's brain activity, they used the data to personalize algorithms for adaptive DBS and surgically switched to adaptive DBS.¹⁵ To compare the traditional form of DBS with adaptive DBS, patients switched between those two forms every two to seven days over two months, a total of 1 month spent on each. To keep the study constant, the patients and most of the researchers didn't know which type of stimulation was being delivered, called the double-blinded study, thus eliminating the placebo effect. Every day, patients report their symptoms. This study was able to provide an advanced version of DBS to improve motor symptoms in PD patients and is expected to be completed by 2028. With more clinical testing and widespread technology availability, adaptive DBS could become the new standard for PD motor symptom treatment.¹⁵ Because the selection of traditional DBS parameters is often based on trial-and-error experimentation, which could take months, adaptive DBS has given hope to the PD community.

3.3. Connectomic Deep Brain Stimulation:

The next solution is connectomic DBS, a type of DBS to improve tremor control while avoiding side effects by using connectomic imaging models to optimize stimulation of the cerebellothalamic and pallidothalamic tracts.¹⁷ This form uses connectomic imaging models to make more precise parameters for certain disease phenotypes, increasing personalization for each PD patient. In a recent 2025 study sponsored by Duke University, people 18 years or older diagnosed with PD who have had bilateral subthalamic nucleus DBS for at least 3 months and suffer from tremors or motor control are currently being recruited. Similar to the adaptive DBS study, this connectomic DBS study is randomized, double-blinded, and crossover. By comparing pathway-targeted stimulation strategies, this trial has the potential to increase DBS precision, target symptoms without causing side effects, and advance personalized care in Parkinson's disease.¹⁷

3.4. Deep Brain Stimulation, Conclusion:

Looking ahead, scientists are focusing on expanding clinical trials and refining algorithms. In the future, they hope to make these advanced forms of DBS more widely available. If successful, they could become the standard of care, offering people with Parkinson's more precise, effective, and individualized treatment.

■ Cell Therapy

4.1. Types of Stem Cells Used:

The last therapy discussed in this research paper is cell therapies. Research into stem cell therapies has expanded, showing itself to be a promising solution for PD. Cell therapy is a stem cell-derived treatment aimed at replacing damaged neurons

and restoring dopaminergic function, thus decreasing the severity of motor symptoms.

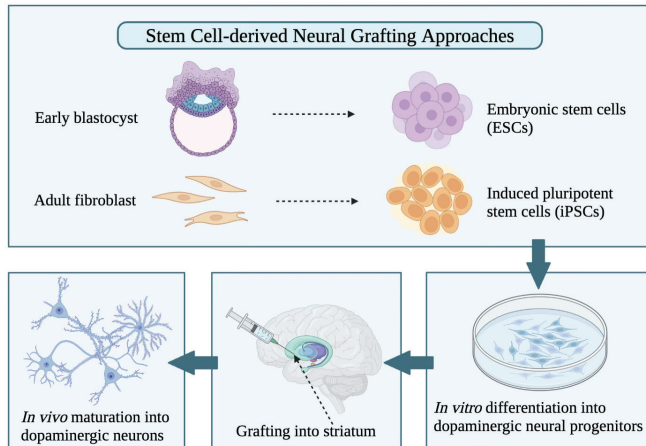


Figure 3: Two approaches for stem cell-derived neural grafting: embryonic stem cells (ESCs) derived from blastocysts and induced pluripotent stem cells (iPSCs) derived from adult fibroblasts. Each cell type is differentiated in vitro into dopaminergic neural progenitors and subsequently grafted into the patient's striatum, where the cells mature in vivo into functional dopaminergic neurons, restoring the patient's lost dopamine production. (Created with BioRender)

Stem cells are undifferentiated cells that are precursors to a specialized cell determined by growth factors.¹⁸ One type of stem cell used for PD is embryonic stem cells (ESCs). ESCs are isolated from the inner cell mass of an early blastocyst and generated from excess embryos from in vitro fertilization. Scientists are now able to turn embryonic stem cells into dopaminergic neuron progenitors that closely resemble the authentic nigral neurons lost in Parkinson's disease. However, even with improved models, results are inconsistent. A large study of over 500 grafts showed that success depended on having many tyrosine hydroxylase (TH) positive cells, a key enzyme in dopamine production, in the grafts that contained neural progenitors with caudal midbrain markers such as CNPY1 and EN1. Now, researchers can generate dopaminergic progenitors with much higher purity and reliability. Progress with ESC therapy has been iterative and has led to many new findings in neurodevelopmental biology. Now that scientists have successfully developed dopaminergic neuron progenitors in the lab, the next focus of ESC therapy will be testing clinical efficacy, with many new clinical trials beginning to test this.

Induced pluripotent stem cells are another type of cell often used for PD. iPSCs are created by "reprogramming" an adult somatic cell into a stem cell through the use of transcription factors that induce pluripotency when expressed. Similar to ESCs, the iPSCs can be differentiated into dopaminergic neurons once "reprogrammed." One potential advantage to iPSC-derived grafts is that autologous grafts can be made using a patient's own fibroblast, meaning the neural grafting product would not be suppressed by the immune system, unlike ESC-derived grafts.¹⁸

4.2. Stem Cells Clinical Trials:

In one 2018 phase I/II clinical trial conducted by Kyoto University Hospital in Japan, six patients aged 50–69 received bilateral transplantation of dopaminergic progenitors from induced PS cells in the putamen.¹⁹ In another recent phase I/II clinical trial published by *Nature* conducted in the U.S. and Canada, twelve participants received transplantation of a human embryonic stem cell (ESC).²⁰

Both studies divided the participants in half: one group with a higher dose of cells, the other with a lower dose.²¹ All participants were given immunosuppressive medication to prevent their immune systems from attacking the new dopamine-producing cells. Results showed no serious adverse events after transplantation in either study. MRI scans have also shown no signs of tumor formation.

Among the six participants of the iPSC study, four showed improvement on a standard scale used to measure Parkinson's motor symptoms when they were off their traditional PD medication, and five showed improvement when on medication. Additionally, brain scans using a specialized tracer that detects dopamine production showed an average of 44.7% increase in dopamine activity in the putamen, with an even greater increase in those who were on a higher dose of transplanted cells.

The results of the ESC study were similar to the results of the study involving iPSC, as signs of improvement were evident. Brain scans taken 18 months after the transplant showed increased activity in the putamen, indicating that the transplanted cells had survived and were potentially functioning.²¹ Moreover, those who received a higher dose of cells showed an average of 23 points higher on the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) when they were off their medication.²⁰

4.3. Cell Therapy, Conclusion:

Although these studies show promising results, there are some disadvantages to stem cell therapies.¹⁸ Specifically for ESC therapy, there is an ethical concern regarding cell grafting techniques as they involve the destruction of an embryo, which continues to be a concern for many. Contrastingly, because iPSCs use an adult cell, this makes iPSC therapy also disadvantaged, as adult cells are less differentiated than embryonic cells. Because of multifaceted approaches, it cannot yet be determined which therapy is better without more advanced clinical trials. Another concern regarding stem cell therapies involves the safety of the treatment, specifically the potential for tumor formation, which can form due to graft overgrowth or mutations in the cell culture. However, some recent studies, such as the ones discussed above, have changed their differentiation methods, leading to more refined cell products of increased purity, thus not causing tumors.¹⁸ And while more research is needed to confirm the safety and effectiveness of this treatment, particularly in larger and longer studies, it suggests the possibility that stem cell therapy can provide a solution to PD motor symptoms without causing severe adverse side effects.²¹

■ Conclusion

Even though Parkinson's Disease is the fastest-growing neurological condition in the world, because there has been no solution to cure or prevent PD, it costs families and the U.S. government \$52+ billion annually. Meeting this challenge necessitates federal research funding for Parkinson's. A \$600 million annual federal investment in Parkinson's-specific research at the National Institutes of Health by 2028 could potentially turn mere discoveries into cures, helping to save or improve millions of lives.

Gene therapy offers a promising symptomatic solution for PD for those with a variety of genetic mutations by slowing the progression of symptoms and increasing dopamine production, meaning more motor control. Deep brain stimulation, while still early in clinical development, also holds the potential to be the standard of care for PD patients by offering more precise, effective, and individualized treatment. Lastly, if scientists address safety and ethical concerns, cell therapy can also help PD patients by providing a solution to PD motor symptoms without causing severe adverse side effects.

An estimated 1.1 million people in the U.S live with PD, demonstrating an urgent need for treatments that slow or stop the progression of PD with fewer side effects. DBS has the highest potential of being the most accurate PD treatment as it is already FDA-approved for PD and is personalized to each patient, ensuring that each patient receives the care they need. Gene therapy is also promising; however, understanding side effects is critical, as this process is irreversible. Cell therapy has the most barriers, as ESC therapy has ethical concerns over the destruction of an embryo, whereas adult cells in iPSC therapy are less differentiated than embryonic cells, making the therapy less effective. By being extremely cautious with gene therapy, personalizing deep brain stimulation, and finding solutions to the ethical concerns of cell therapy, the treatment of PD is promising. In this review, we discussed the treatments of PD: gene therapy, deep brain stimulation, and cell therapy, and the pros and cons of these treatments. Moving forward, researchers and clinicians should respectively focus on addressing therapy concerns, such as the irreversibility of gene therapy, and closely follow these emerging therapies in order to offer their patients the best possible treatments to improve their quality of life.

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