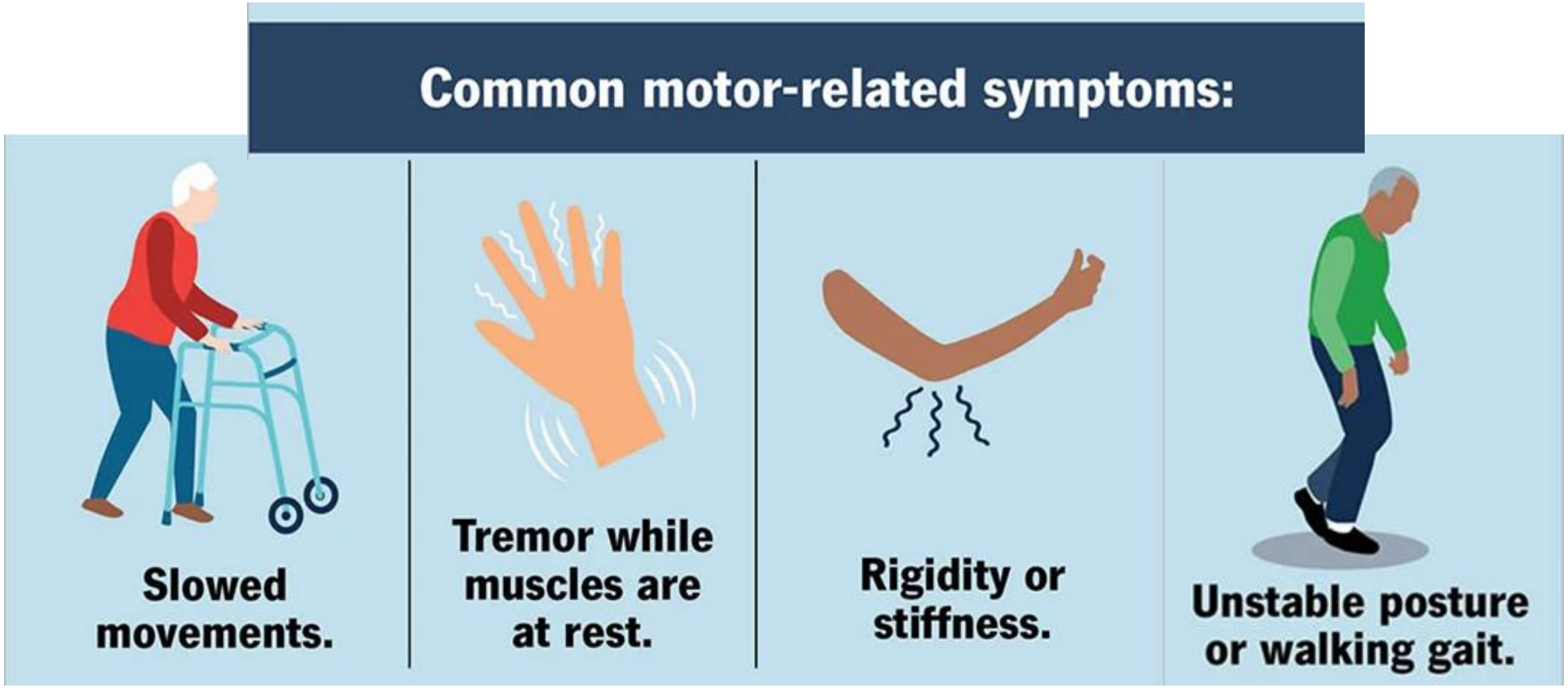
Parkinson's Disease

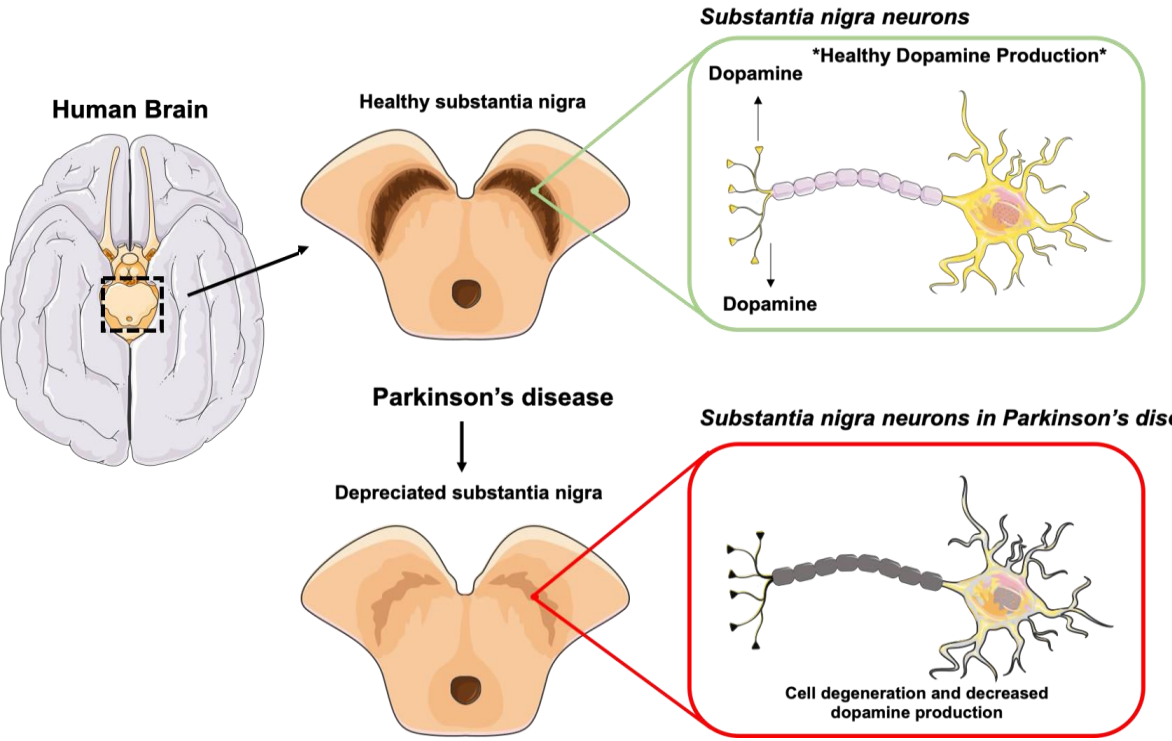
"What's new in Studies and Treatment"

Kasandra Diaz Ph.D.

- Parkinson’s disease (PD) is the second most common age-related neurodegenerative disorder worldwide, with an average onset of 60 years old.

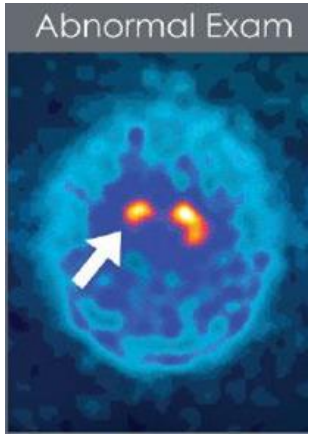
- The clinical features historically associated with PD are tremor, rigidity, bradykinesia, gait, and postural impairment.

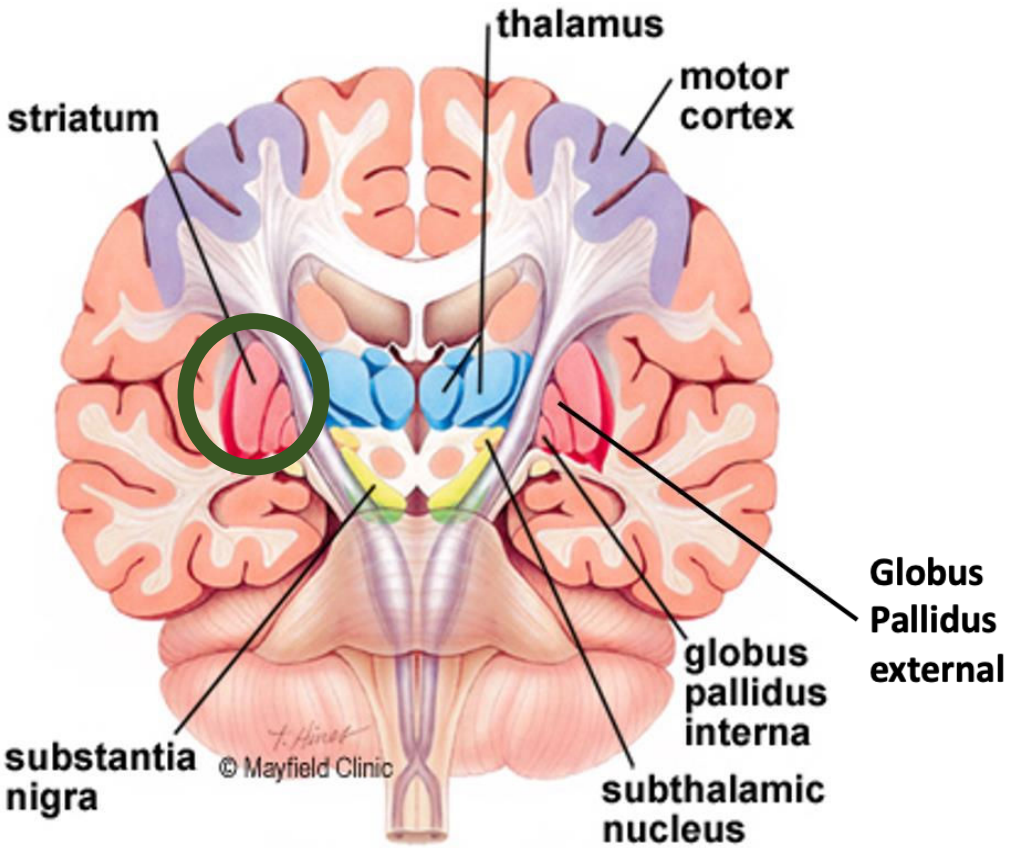



Human Brain
Healthy substantia nigra
Substantia nigra neurons
Healthy Dopamine Production
Dopamine
Dopamine
Parkinson's disease
Depreciated substantia nigra
Substantia nigra neurons in Parkinson's disease
Cell degeneration and decreased dopamine production

DaTscan™

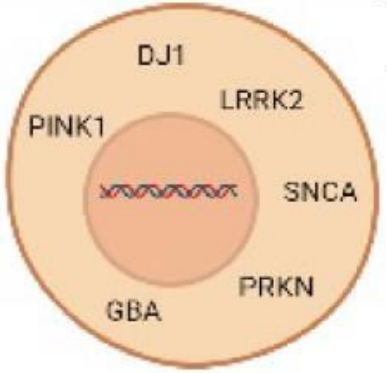

Normal Exam


Abnormal Exam


thalamus
motor cortex
striatum
Globus Pallidus external
globus pallidus interna
substantia nigra
© Mayfield Clinic
subthalamic nucleus

Age

- Approximately 1% of persons over the age of 60 have PD.



Genetics

- Approximately 10% of persons with a PD diagnosis have a genetic mutation (LRRK2, GBA1, PINK1, SNCA).

Environment

- A strong link has been shown between Parkinson's and exposure to pesticides and herbicides. Of these, paraquat, a commercial herbicide widely used in the US, has been linked to the disease.

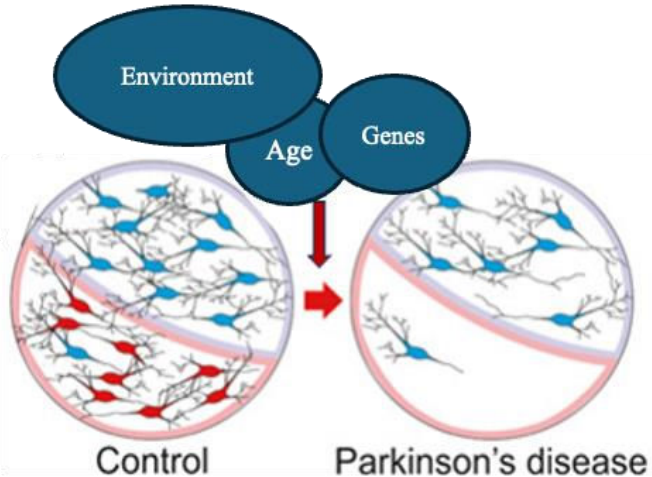
Gender

- Parkinson's is more common in men than women.

Lifestyle

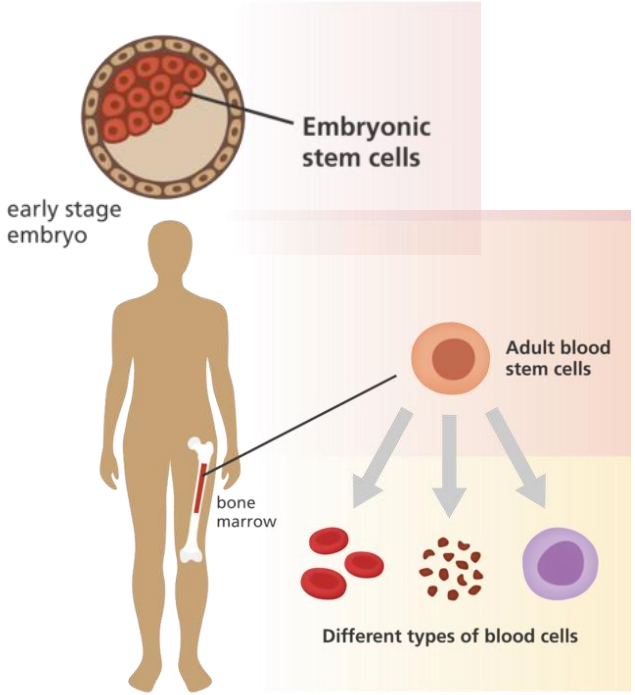
- Physical inactivity, dehydration, poor diet, and stress can aggravate symptoms and, perhaps, worsen disease progression.

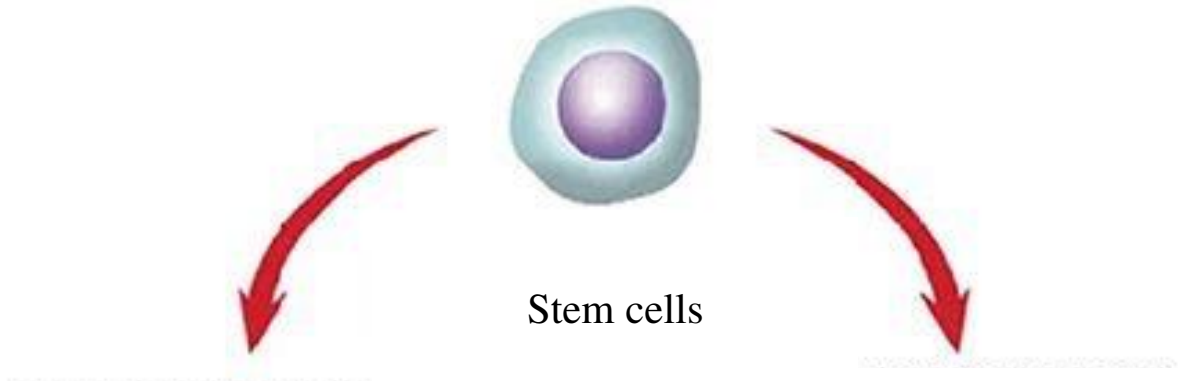
While the etiology of PD is not well understood, several factors, including gene dysfunctions, mutations, and environment, appear to play a role.

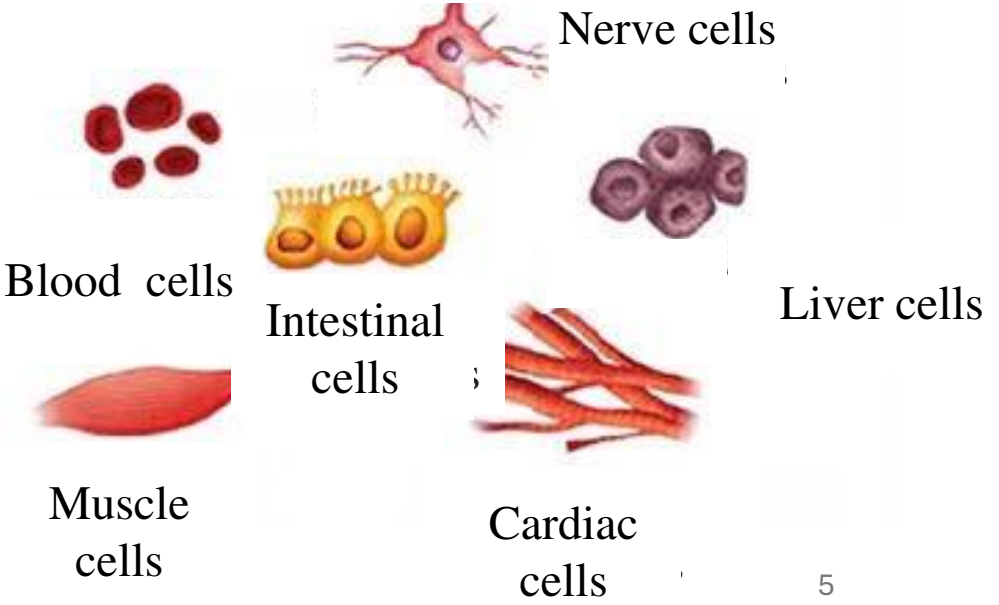


- Stem cells are cells with the potential to develop into many different types of cells in the body, including the heart, brain, spinal cord, and more.

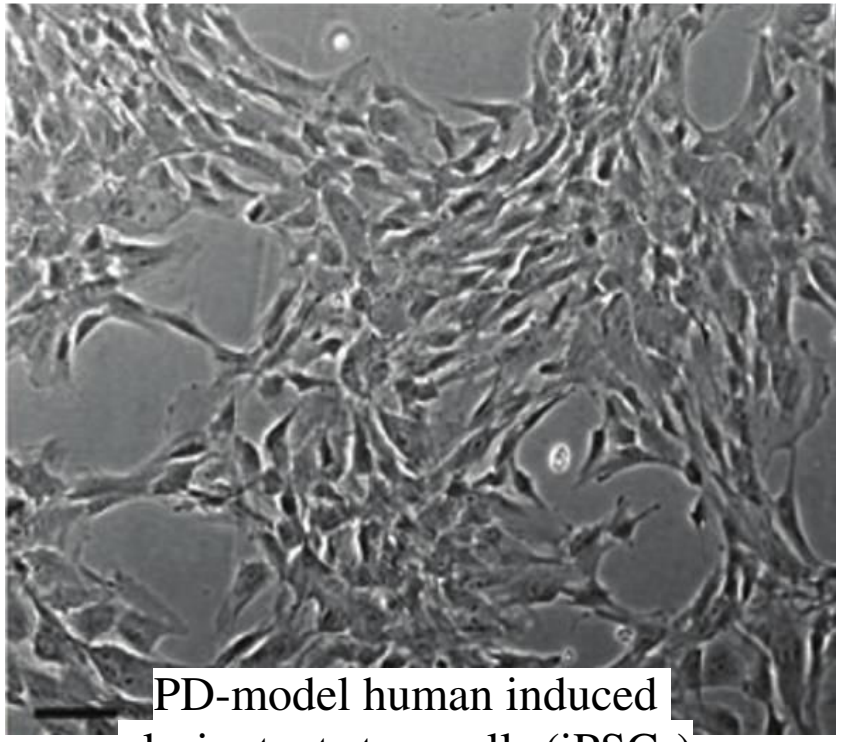
- Stem cells serve as the body's repair system. There are two main types of stem cells: embryonic stem cells and adult stem cells.





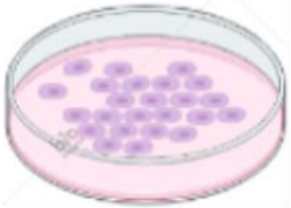


- In the lab, by studying patients' stem cells, we can see how those cells become damaged at the molecular and cellular level and cause diseases like Parkinson's.

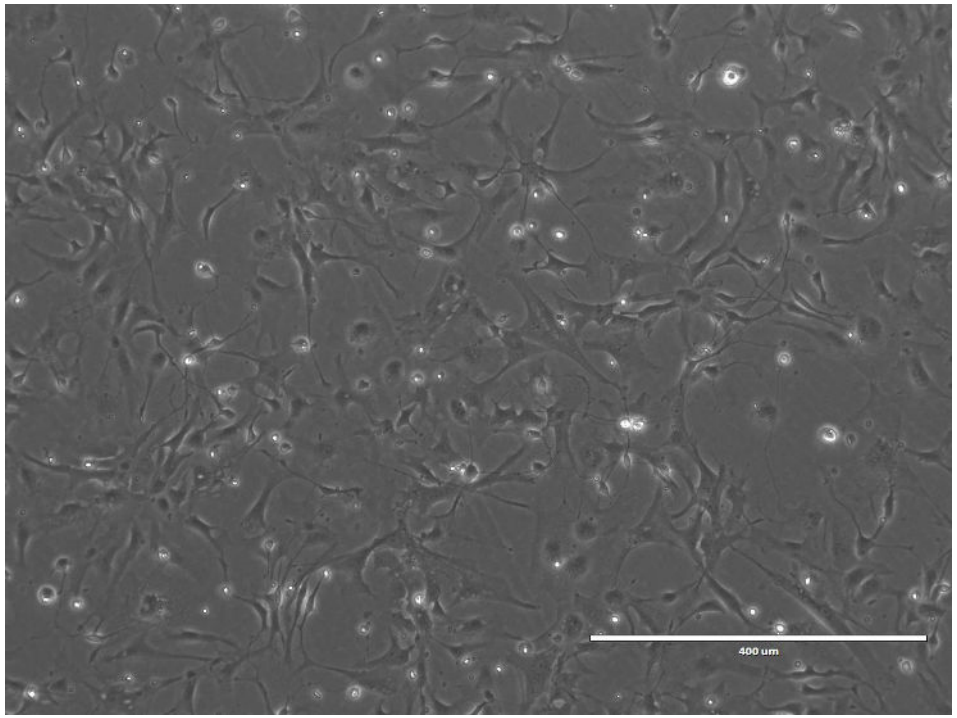


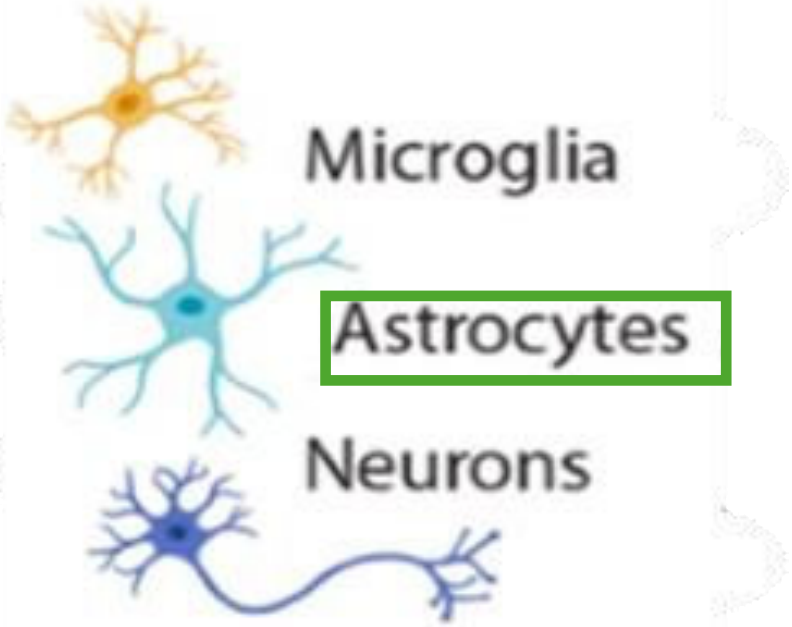
PD-model human induced pluripotent stem cells (iPSCs)

Patient's Skin Cells



iPSCs





- In the brain, glia accounts for over 50% of the cells and can be divided into various subtypes, of which astrocytes are the most populous.

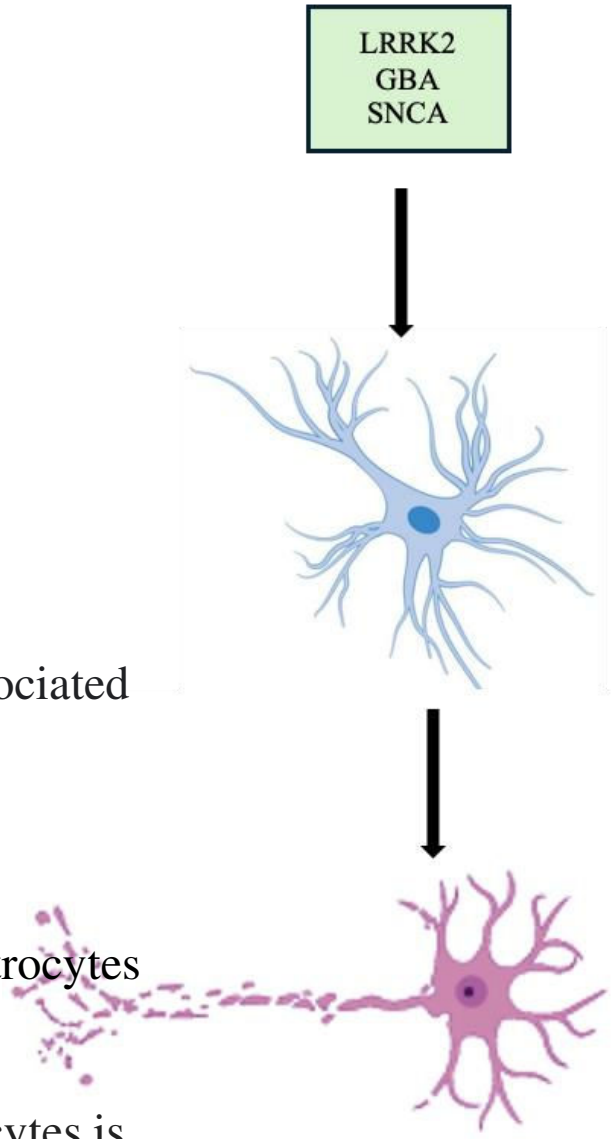
- While dopaminergic neurodegeneration in the basal ganglia is the main feature of PD, other neural cell types, including astrocytes, have been shown to play a role in PD development.

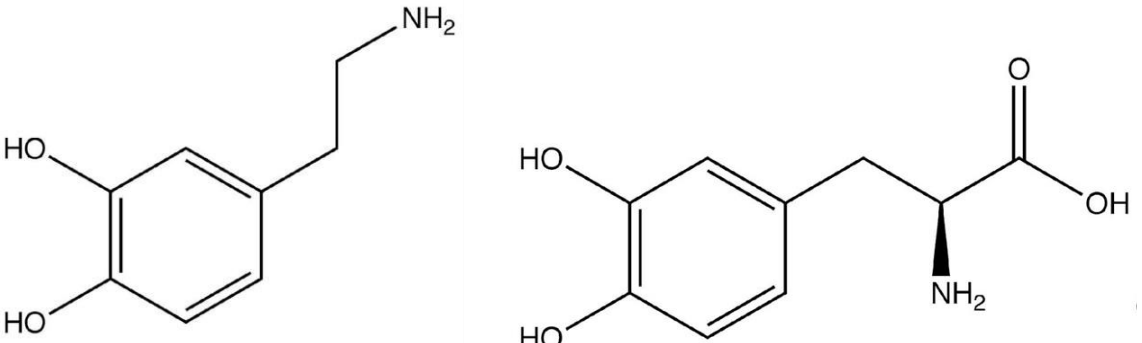
- Among their many functions, astrocytes mediate the brain's immune response.

- Several studies have determined that gene mutations (LRRK2, GBA, and SNCA) associated with the development of Parkinson's play important roles in astrocyte function.

- Our research has shown that changes in astrocytes are associated with neuron degeneration.

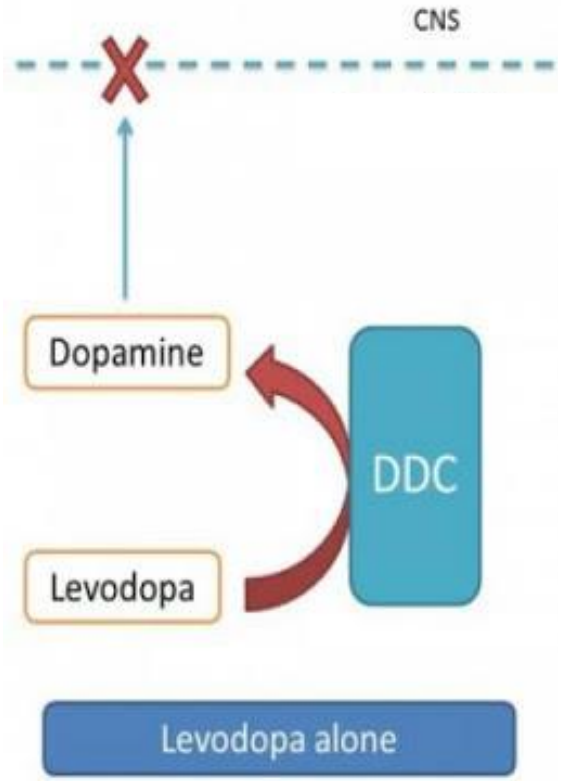
- Thus, studying the functional role of astrocytes is important for understanding the full spectrum of PD pathogenesis and developing novel therapeutic strategies to treat PD.





Dopamine

L-DOPA



- Levodopa treatment does not ameliorate **all** motor symptoms associated with PD (Sethi, K.,2008)

General Overview

Personalized Stem Cell Therapy for Parkinson’s Disease

- While it isn't yet widely available or part of the standard of care, Stem cell treatment is a promising experimental therapy strategy for persons with PD.

- Stem cell therapy aims to replace damaged or dying neurons, thus stopping the progression of the disease. However, these benefits remain theoretical as the therapy is in the early stages of research and clinical trials.

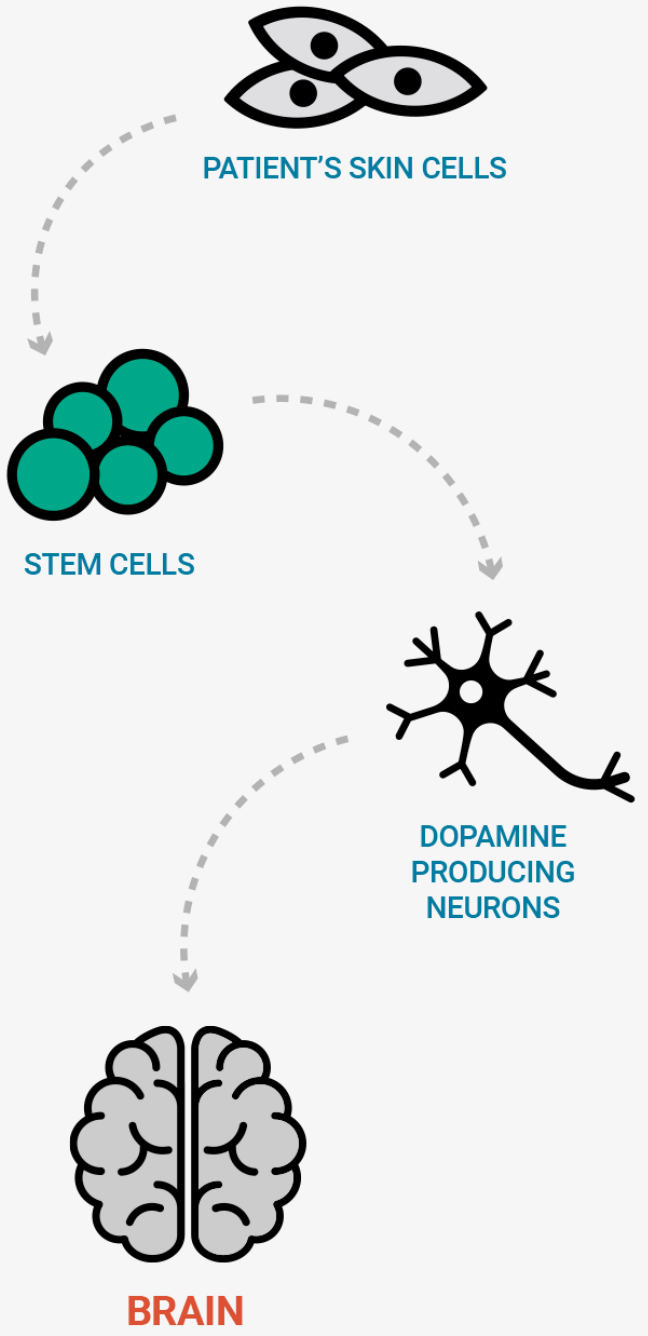


Table 1.

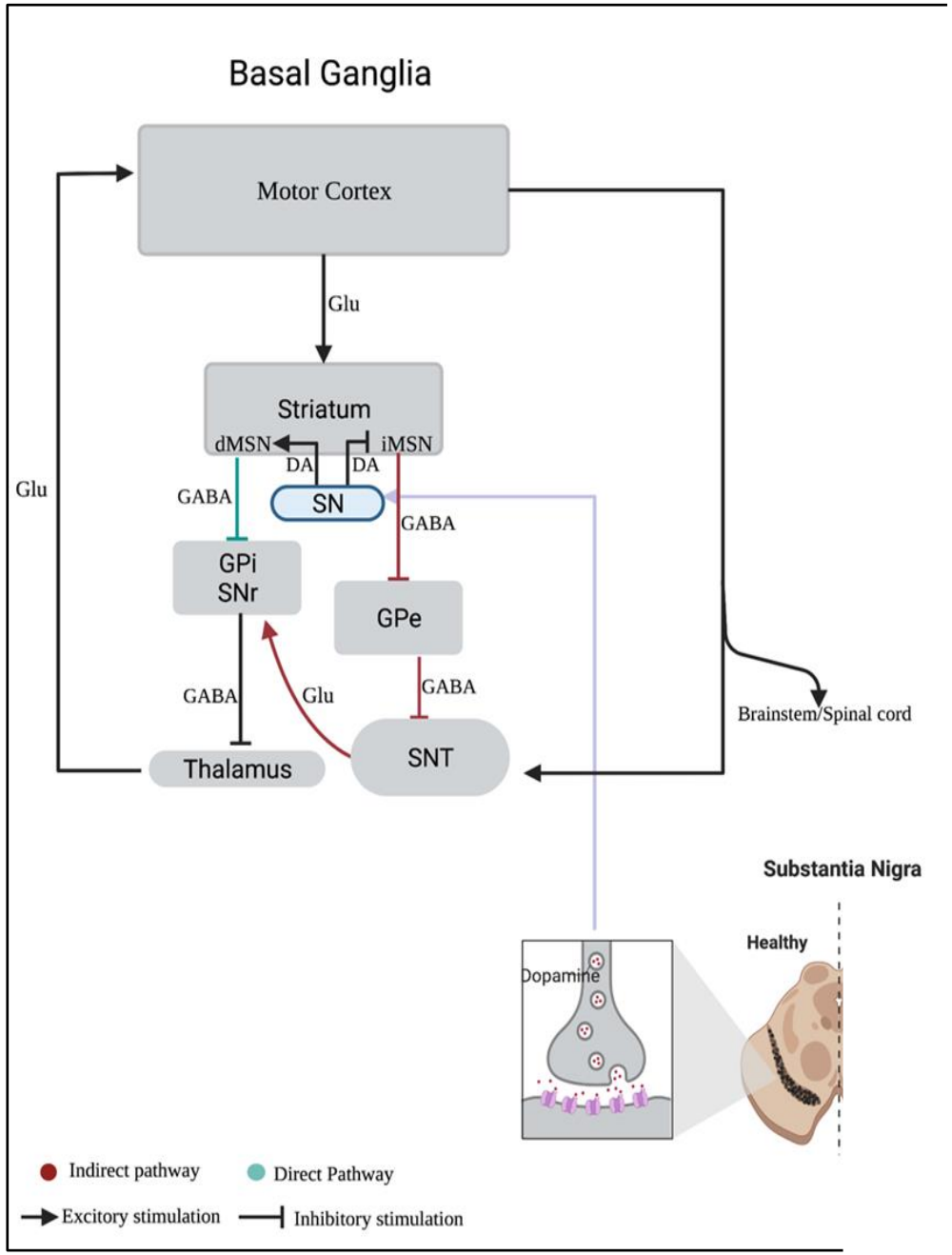
List of clinical trials using fetal tissue or pluripotent stem cell-derived mDA cells

Cell source	Title	Country	Sponsor	Cell numbers	Immune matching	Phase	Status (number of participants)	Trial start	Clinical trial ID	Reference
hiPSCs or autologous NSCs										
Autologous hiPSC-derived mDAPs	Transplantation of autologous midbrain dopaminergic neuron precursors derived from a Parkinson's disease patient's induced pluripotent stem cells	USA	Harvard University	4 M per side	Autologous	N/A	Completed (1)	2017	IND17145	Schweitzer et al. [85], 2020
Allogeneic hiPSC-derived mDAPs	Kyoto trial to evaluate the safety and efficacy of iPSC-derived dopaminergic progenitors in the treatment of Parkinson's disease	Japan	Kyoto University Hospital	2.4–5.4 M per side	Allogeneic, HLA-matched and non-matched	Phase I/II	No longer recruiting (7)	2018	UMIN000033564	Takahashi [94], 2020
Allogeneic hiPSC-derived mDAPs	Kyoto trial to evaluate the safety and efficacy of	Japan	Kyoto University Hospital	2.4–5.4 M cells per side	Allogeneic, HLA-matched and non-matched	Phase III	No longer recruiting (7)	2018	UMIN000033565	Takahashi [94], 2020
Allogeneic hiPSC-derived mDAPs	Kyoto trial to evaluate the safety and efficacy of Tacrolimus in the iPSC-based therapy for Parkinson's disease	Japan	Kyoto University Hospital	2.4–5.4 M cells per side	Allogeneic, HLA-matched and non-matched	Phase III	No longer recruiting (7)	2018	UMIN000033565	Takahashi [94], 2020

Cha Y, Park TY, Leblanc P, Kim KS. Current Status and Future Perspectives on Stem Cell-Based Therapies for Parkinson's Disease. J Mov Disord. 2023 Jan;16(1):22-41. doi: 10.14802/jmd.22141. Epub 2023 Jan 12. PMID: 36628428; PMCID: PMC9978267.

CONCLUSION

- Parkinson’s disease is the second most common age-related neurodegenerative disorder worldwide.
- Symptoms' onset can be primarily attributed to the death of DA-producing neurons in the substantia nigra compacta.
- Cells , like astrocytes, have been shown to play a role in PD etiology.
- Although it is the standard of care, Levodopa treatment does not alleviate **all** motor symptoms associated with PD.
- Stem cell treatment is a promising experimental therapy strategy for persons with PD.
- Like Levadopa/Carbadopa, stem cell treatment will not have any disease-modifying effect, but it aims to improve most if not all, PD-specific motor impairment.


Basal Ganglia
Motor Cortex
Glu
Striatum
dMSN
iMSN
DA
DA
GABA
SN
GABA
Glu
GPi
SNr
GPe
GABA
Glu
GABA
Brainstem/Spinal cord
Thalamus
SNT
Substantia Nigra
Healthy
Dopamine
Indirect pathway
Direct Pathway
Excitory stimulation
Inhibitory stimulation