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2021

Neuropathology of Parkinson Disease

Jefin Jose
Virginia Commonwealth University

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Neuropathology of Parkinson Disease

Dennis W. Dickson, M.D.

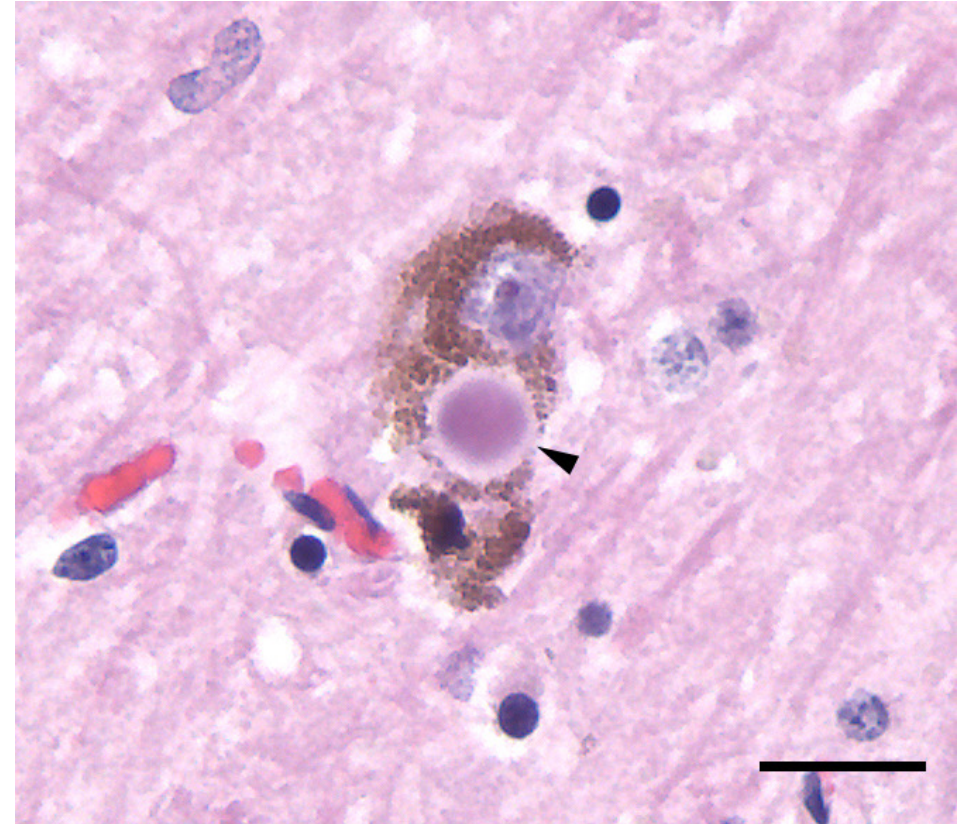
Jefin Jose

MJC Presentation

7/29/21

Lewy body disease

- In the case of Lewy body disease, α -synuclein builds up within neurons, leading to cell death
- This protein especially aggregates within the basal ganglia, which leads to movement impairment
- These movement impairments are the reason Lewy body disease is closely linked with Parkinson's disease

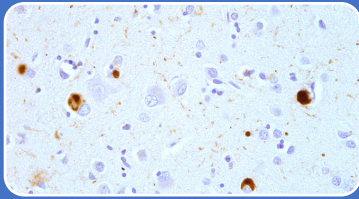


Parkinson's Disease

- The definition of Parkinson's disease is generally loose
- Parkinson's Disease (PD) is diagnosed based on a series of symptoms rather than a single cause
- Symptoms include
 - Bradykinesia
 - Rigidity
 - Postural instability
 - Tremors
- Usually, the result of lifestyle rather than genetic factors

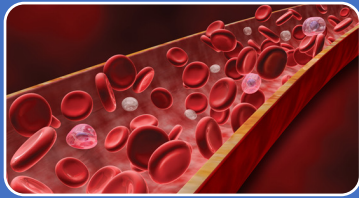


Parkinson's Disorders



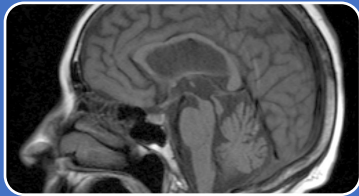
Lewy Body Disease

- Build of α -synuclein protein in neurons
- Somatic deficits



Multiple System Atrophy

- Build up of α -synuclein in glial cells
- Autonomic deficits



Progressive Supranuclear Palsy

- Build up of tau protein
- Characteristic eye movements

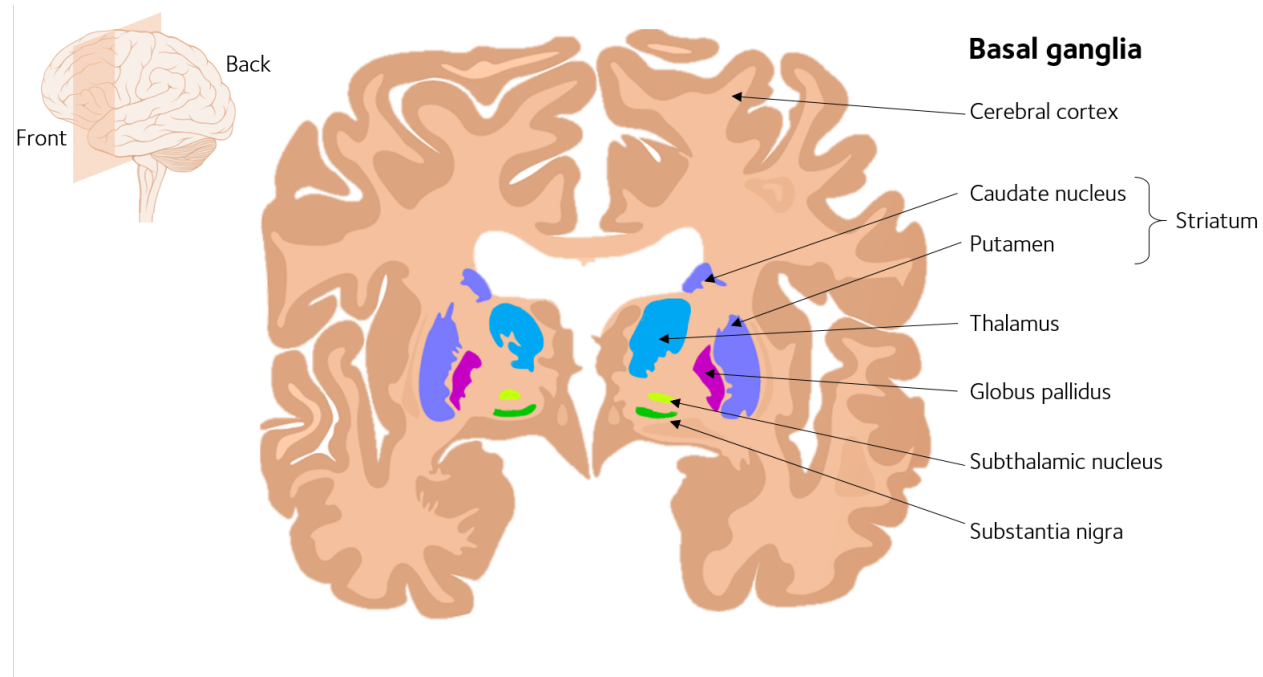


Corticobasal Degeneration

- Build up of tau protein
- Limb problems

Basal Ganglia

- Facilitates motor movement
- Composed of five parts: (1) caudate, (2) putamen, (3) globus pallidus, (4) substantia nigra, and the (5) subthalamic nucleus

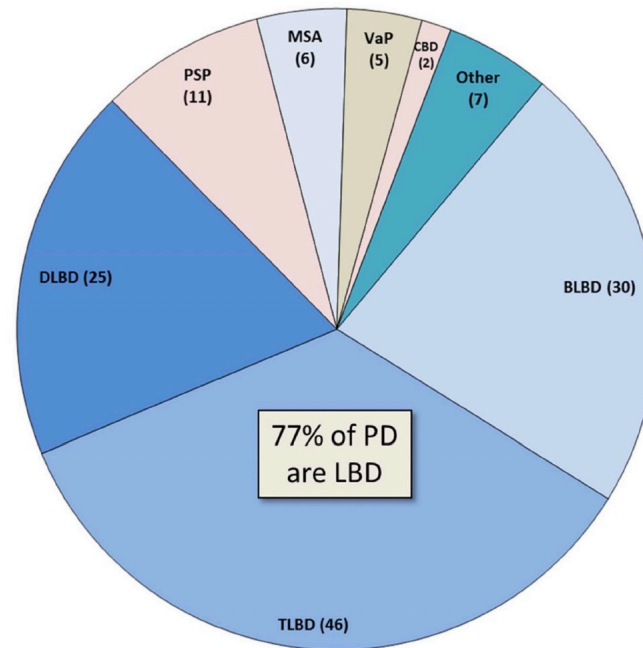


Denervation in substantia nigra & striatum

- Dopaminergic cells of the substantia nigra die because of an excess of calcium ions in the basal ganglia
- This calcium-induced cell death is accompanied by buildup of α -synuclein proteins which kills cells as well
- Thus, the substantia nigra is severely disfigured in Lewy body disease patients
- The input device (striatum) is also dying, leading to poorer reception and communication → reduced motor movement

Postmortem characterization of PD patients

- The researcher investigated 132 patients diagnosed with Parkinson's disorder and found that Lewy Body disease (build up of α -synuclein) was the cause in most of these patients

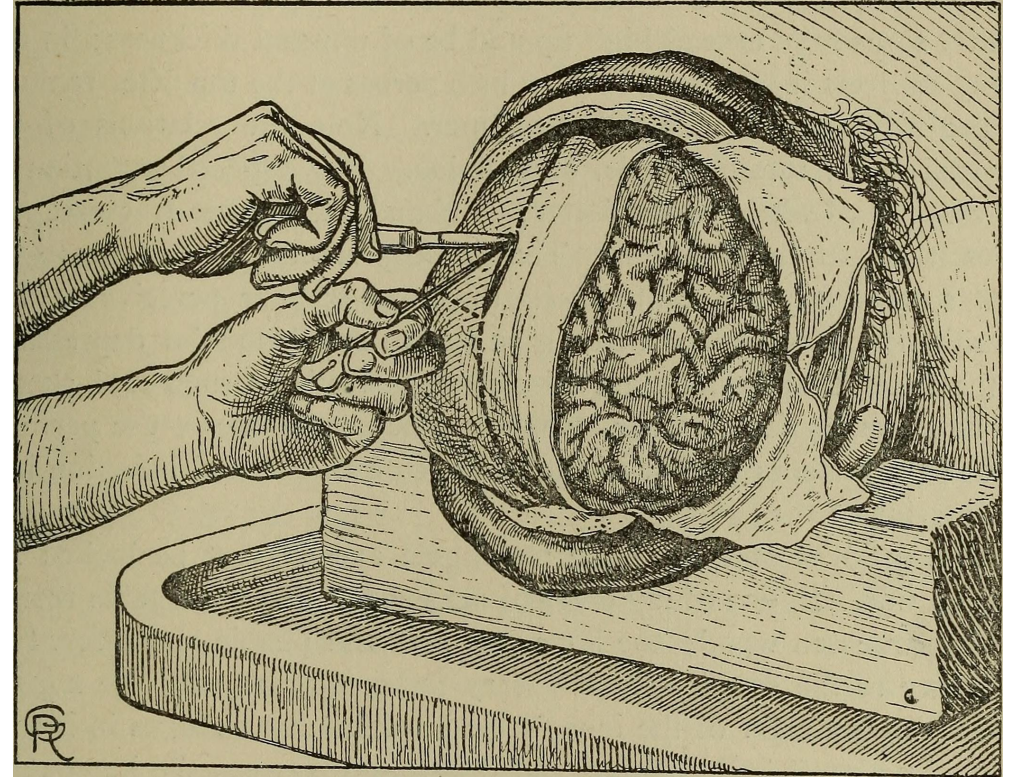


Misdiagnosis in neurodegenerative diseases

- “The diagnostic accuracy of pathologically confirmed MSA in the Mayo Clinic brain bank is less than that for PSP (about 70%).”
- “Cases with autopsy confirmed MSA are most often misdiagnosed clinically as either PSP (47%) or atypical PD (34%).”
- There seems to be a theme of misdiagnosis in neurodegenerative disorders.
 - What are some potential issues that arise when misdiagnosing these disorders?
 - What could we do to prevent misdiagnosis?

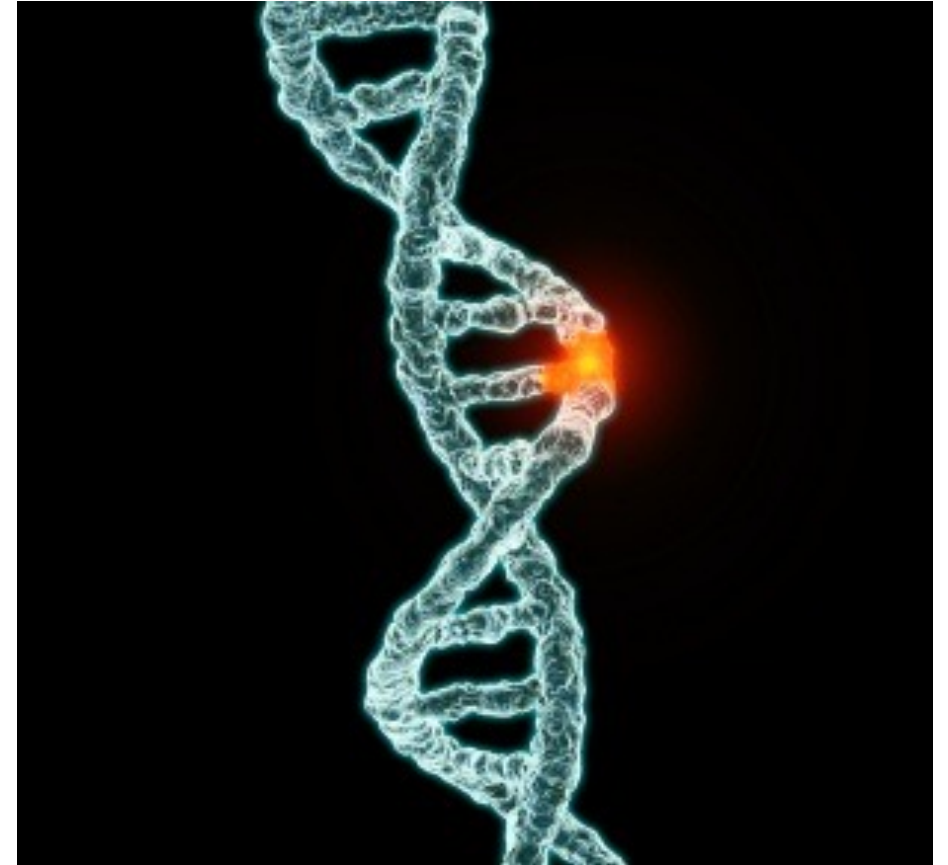
Postmortem studies

- The author believes that postmortem studies are the most accurate as scientists can confirm the development of protein aggregates in specific locations
- However, the same level of accuracy is not achieved in antemortem diagnosis and treatment
- Detection tools should be developed to better diagnose patients while they are living



Genes affecting PD development

- PD onset as the result of inheritance is uncommon (no clear genetic link)
- However, several proteins can play a role
 - Dysfunctional α -synuclein protein
 - LRRK2
 - DCTN1 → Perry Syndrome
 - POLG1
 - PINK1 (established)
 - PRKN (established)



Braak stages in PD development

- Stages 1-2: protein aggregates are largely within the medulla oblongata and the olfactory bulb (affecting autonomic functions and smell)
- Stages 3-4: Pathological changes in substantia nigra
 - By now, the symptoms are evident
- Stages 5-6: Inclusions in the cerebral cortex
 - Day to day life is severely affected



Conclusion

- This survey of autopsies demonstrates the importance of analyzing postmortem brains to study neurodegenerative disease development
- Misdiagnosis of neurodegenerative disorders can be traced to the lack of accurate detection tools
- Analyzing autopsies can reveal the physiological differences in patients with PD (synucleinopathy vs. tauopathy)

Discussion Questions

- Many of the problems involving the differences in neurodegenerative diseases lie in the general definitions. Should we try to diffuse the idea of Parkinson's disease and promote more specific pictures like Lewy body buildup or tau protein buildup (as in Alzheimer's disease)?
- What is causing the difficulty in diagnosing these diseases as the patients are alive? Should doctors use more invasive methods (e.g. biopsy) to diagnose disease?
- Many of the current treatments for neurodegenerative diseases are not disease-modifying. They attack the symptoms instead. How can we produce disease-modifying treatments?

Discussion Questions

- There is a wide variety of diseases causing PD. How would this hinder or help the awareness and treatment of this disease?

Classification	Examples
Degenerative parkinsonism	
α-Synuclein	Parkinson's disease, multiple system atrophy
Tau	Progressive supranuclear palsy; corticobasal degeneration; Guam Parkinson dementia complex; chronic traumatic encephalopathy
TDP-43	Perry syndrome; frontotemporal lobar degeneration (FTLD-TDP)
Nonspecific	Genetic PD (<i>PINK1</i> , <i>PRKN</i> , <i>POLG1</i> , some forms of <i>LRRK2</i>)
Non-degenerative parkinsonism	
Vascular	Vascular parkinsonism
Toxic	MPTP; manganese poisoning
Drug-induced	Antipsychotic medications
Infectious	Influenza virus (post-encephalitic parkinsonism)

- Should we switch to osteopathic forms of medicine rather than allopathic forms of medicine for patients that do not have genetically-linked disorders? That is, should doctors put a greater emphasis on lifestyle changes rather than the medicines they prescribe for patients?

Citation

- Dickson, D. W., MD. (2018). Neuropathology of Parkinson Disease. *Parkinson Relat Disord*, 46(1), 30-33.
doi:10.1016/j.parkreldis.2017.07.033