Parkinson's Disease:

A Complex Neurodegenerative Disease

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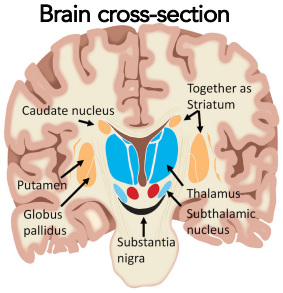
What is it? Neurodegenerative diseases (ND) are characterized by progressive nervous system dysfunction leading to neuronal cell death. ND ultimately lead to movement (motor) difficulties, decline in cognitive functioning (dementia), or a combination of both. The two most common ND are Alzheimer's disease (AD) and Parkinson's disease (PD). The substantia nigra is an essential structure in the central nervous system, recognized for its roles in motor (movement), cognitive (thinking), and limbic (emotions) functions. PD begins from the death of dopaminergic neurons located in the midbrain, substantia nigra pars compacta region.

What are the risk factors for PD?

- Advanced aging
- Gender (Male > Female)
- Heredity (previously found in family)
- Exposure to environmental toxins
- Repeated head trauma (contact sports)
- Type 2 diabetes (30% increased risk)

Brain cross-section



What causes PD (listed alphabetically)?

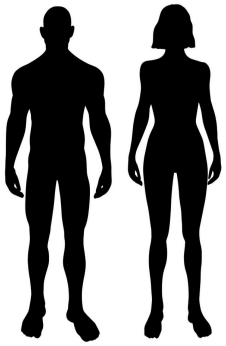
- Advanced aging
- Environmental toxins
- Genetics
- Immune system dysfunction
- Intracellular protein aggregation
- Neuroinflammation and oxidative stress
- Reduction in mitochondria activity

What are the symptoms of PD?

Motor-related Symptoms:

Death of dopaminergic neurons in the basal ganglia (substantia nigra) results in the Cardinal motor signs of PD:

- bradykinesia (slowness of movement),
- tremor (trembling in hands, arms, legs, jaw, and face),
- muscle rigidity (stiffness of the limbs and trunk) and
- postural instability (impaired balance and coordination).



Non-motor-related Symptoms:

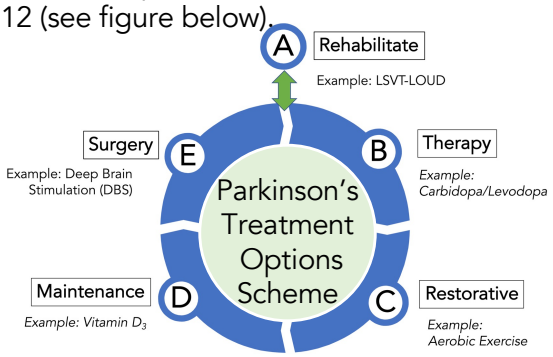
There are numerous non-motor symptoms in PD, including (to list a few) depression, psychosis, REM sleep disruption and hallucinations, fatigue, pain, executive function disruption, low blood pressure, difficulty swallowing and speaking, urinary problems including incontinence, and gastrointestinal disruption including constipation.

How common is PD?

- PD occurs most often in people aged 60 and older with an idiopathic cause, as given above.
- Cases of PD in younger people (<40 years old) are usually linked to a specific genotype.
- ~1.5 million people in the USA live with PD (globally, it is >10 million), with ~90,000 new cases yearly.
- The symptoms occur gradually over several years, and the progression varies from person to person regarding the timeline and extent to which they manifest.

What are the treatment options for PD?

- At present, PD remains an incurable disease; as such, treatment goals in PD management are focused on slowing or halting disease progression. The complexity of the factors contributing to PD development demands a multi-pronged therapeutic intervention plan. I proposed such a scheme in Church, Frank C. "Treatment options for motor and non-motor symptoms of Parkinson's disease." *Biomolecules* 11, no. 4 (2021): 612 (see figure below).
- PD limits movement ability and results in functional instability. The traditional first line of therapy is usually carbidopa/levodopa or a dopamine agonist; they both work well for motor symptoms. The complex non-motor symptoms will not be discussed in this review. Many use a Complementary & Alternative Medicine (CAM) approach to treat their PD.



- As reviewed by Mitchell, Alexandra K., Rebecca R. Bliss, and Frank C. Church. "Exercise, Neuroprotective Exerkines, and Parkinson's Disease: A Narrative Review." *Biomolecules* 14, no. 10 (2024), aerobic exercise and resistance training improve many of PD's motor and non-motor symptoms, while neuromotor therapy and stretching/flexibility exercises positively contribute to Quality of Life in people with PD. Exercise may alleviate PD's physical and neurological symptoms; therefore, exercise should be considered a primary treatment strategy for PD.