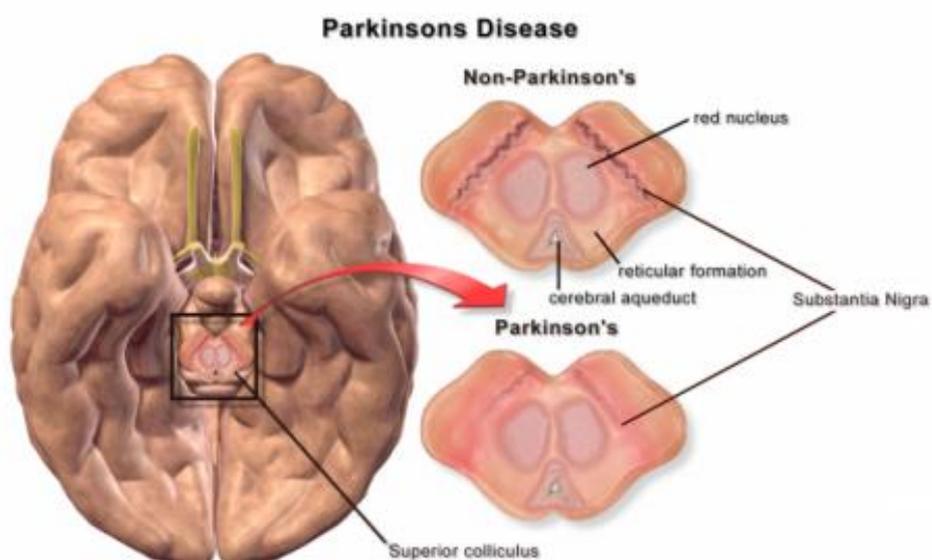


Perceiving Parkinson's

A Disease Of Neurons, Not Brain (Day 7)

In his 1817 paper, James Parkinson reasoned that the disease process in Parkinson's starts in the upper spinal cord and then spreads upwards to the brainstem. Well, he was nearly right.

It was not until 1919 that the Russian neuropathologist Constantin Tretiakoff discovered otherwise. In his autopsy series on the brains of 54 Parkinson's patients, Tretiakoff noted that each of the brains had sustained damage to a region of the upper brainstem called the **substantia nigra**, which is Latin for "black substance," rather than the upper spinal cord as Parkinson had postulated. Remarkably, each brain in Tretiakoff's autopsy series had lost most of the neurons of its substantia nigra - in other words, each brain had lost most of its black substance.



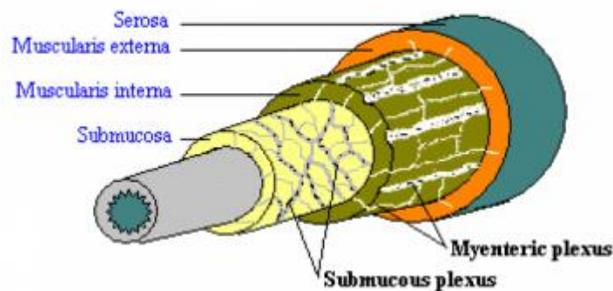
In Parkinson's, the neurons of the substantia nigra are lost (bottom right picture).

The substantia nigra contains neurons that produce the neurotransmitter **dopamine**, a chemical that plays an essential role in movement. In a person with Parkinson's, **50-90%** of these dopamine neurons are lost. It is neuron loss in the substantia nigra is largely responsible for the **motor symptoms** of Parkinson's - **tremor, bradykinesia, rigidity, and postural instability**.

In the decades after Tretiakoff's study, the case was more or less closed - most researchers thought of Parkinson's as a disease of brain characterized by neuron loss in the substantia nigra and several other nearby brainstem regions. However, it is now known that neuron loss in Parkinson's is **not restricted to the brain** - in fact, there are large populations of neurons elsewhere in the body, in the autonomic and enteric nervous systems, that also die.

The **autonomic nervous system** consists of specialized neurons within the spinal cord that branch out to innervate various internal organs; it controls internal body functions such as heart rate, blood pressure, and urination. In Parkinson's, many neurons in the autonomic nervous system are lost - for example, it has been shown that there is a **profound** death of neurons that innervate the heart.

The **enteric nervous system** or "second brain" consists of 500 million neurons that line the gut; it controls the functions of the entire gut, from esophagus to colon, and can operate independently of the brain and spinal cord. Somewhat surprisingly, the enteric nervous system contains about half of the dopamine in the entire body! In Parkinson's, **more than 90%** of the dopamine neurons in the enteric nervous system die off.



The myenteric and submucous plexuses (labelled in black) constitute the enteric nervous system.

Neuron loss in the autonomic and enteric nervous systems culminates in several of the **nonmotor symptoms** of Parkinson's. In the autonomic system, neuron loss produces symptoms such as **postural hypotension** (when a person's blood pressure falls upon standing) and **urinary incontinence** (lack of voluntary control over urination). In the enteric nervous system, neuron loss produces symptoms such as **postprandial bloating** (abdominal discomfort after eating) and **constipation** (bowel movements that are infrequent or hard to pass). Postural hypotension, urinary incontinence, postprandial bloating, and constipation are all **extremely common** in Parkinson's.

Clearly, Parkinson's is not just a disease of brain but **a disease of neurons throughout the body**. It afflicts the brain. It afflicts the autonomic nervous system. It afflicts the enteric nervous system. This is another clue to its etiology - Parkinson's is not restricted to neuron loss in the substantia nigra, it is a systemic condition that affects neurons all over the body.

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References

- (1) Parkinson. 1817. An Essay on the Shaking Palsy. Sherwood, Neely, and Jones. London.
- (2) Sulzer and Surmeier. 2013. Neuronal Vulnerability, Pathogenesis, and Parkinson's Disease. *Movement Disorders* 28(1), 41-50.
- (3) Ahlskog. 2015. *The New Parkinson's Disease Treatment Book*. Oxford University Press.
- (4) Mulak and Bonaz. 2015. Brain-gut-microbiota axis in Parkinson's disease. *World Journal of Gastroenterology* 21(37), 10609-10620.