# Is Parkinson's an autoimmune disease?

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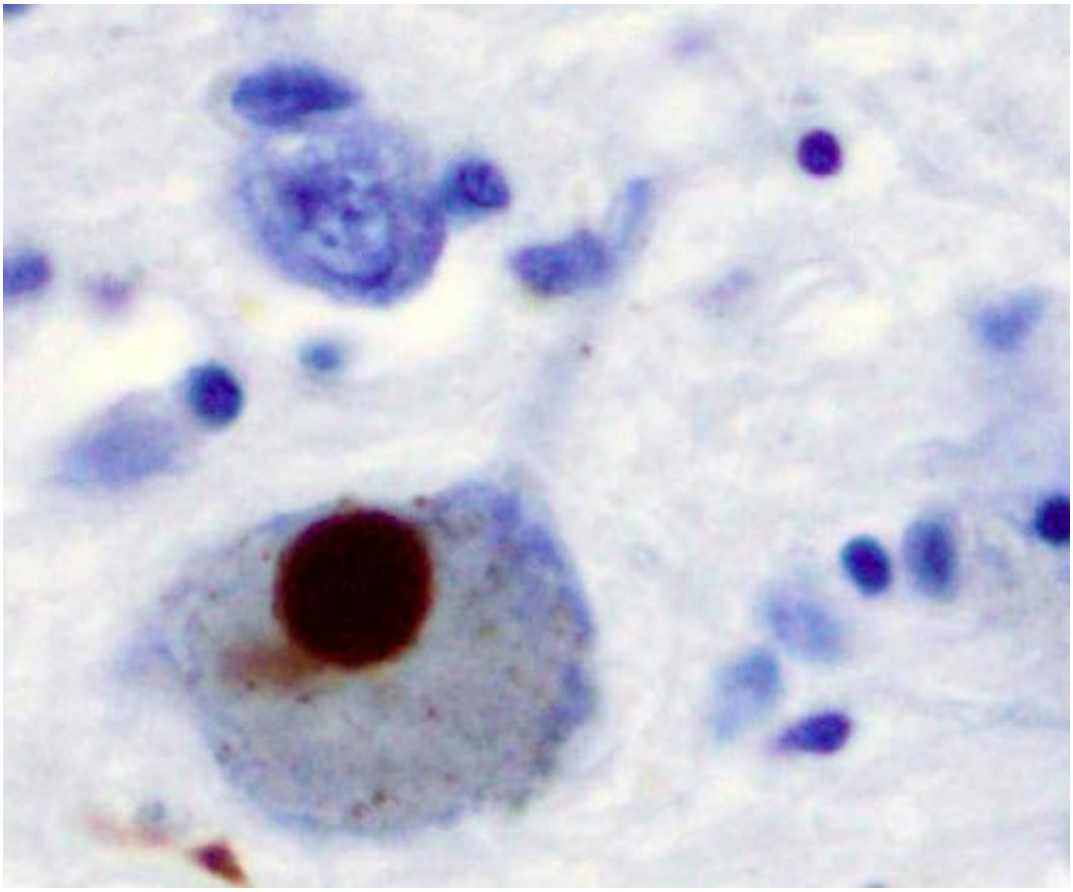

Immunohistochemistry for alpha-synuclein showing positive staining (brown) of an intraneural Lewy-body in the Substantia nigra in Parkinson's disease. Credit: Wikipedia

The cause of neuronal death in Parkinson's disease is still unknown, but a new study proposes that neurons may be mistaken for foreign invaders and killed by the person's own immune system, similar to the way

autoimmune diseases like type I diabetes, celiac disease, and multiple sclerosis attack the body's cells. The study was published April 16, 2014, in *Nature Communications*.

"This is a new, and likely controversial, idea in Parkinson's disease; but if true, it could lead to new ways to prevent neuronal death in Parkinson's that resemble treatments for autoimmune diseases," said the study's senior author, David Sulzer, PhD, professor of neurobiology in the departments of psychiatry, neurology, and pharmacology at Columbia University College of Physicians & Surgeons.

The new hypothesis about Parkinson's emerges from other findings in the study that overturn a deep-seated assumption about neurons and the immune system.

For decades, neurobiologists have thought that neurons are protected from attacks from the immune system, in part, because they do not display antigens on their cell surfaces. Most cells, if infected by virus or bacteria, will display bits of the microbe (antigens) on their outer surface. When the immune system recognizes the foreign antigens, T cells attack and kill the cells. Because scientists thought that neurons did not display antigens, they also thought that the neurons were exempt from T-cell attacks.

"That idea made sense because, except in rare circumstances, our brains cannot make new neurons to replenish ones killed by the immune system," Dr. Sulzer says. "But, unexpectedly, we found that some types of neurons can display antigens."

Cells display antigens with special proteins called MHCs. Using postmortem brain tissue donated to the Columbia Brain Bank by healthy donors, Dr. Sulzer and his postdoc Carolina Cebrián, PhD, first noticed—to their surprise—that MHC-1 proteins were present in two

types of neurons. These two types of neurons—one of which is dopamine neurons in a brain region called the substantia nigra—degenerate during Parkinson's disease.

To see if living neurons use MHC-1 to display antigens (and not for some other purpose), Drs. Sulzer and Cebrián conducted in vitro experiments with mouse neurons and human neurons created from embryonic stem cells. The studies showed that under certain circumstances—including conditions known to occur in Parkinson's—the neurons use MHC-1 to display antigens. Among the different types of neurons tested, the two types affected in Parkinson's were far more responsive than other neurons to signals that triggered antigen display.

The researchers then confirmed that T cells recognized and attacked neurons displaying specific antigens.

The results raise the possibility that Parkinson's is partly an autoimmune disease, Dr. Sulzer says, but more research is needed to confirm the idea.

"Right now, we've showed that certain neurons display antigens and that T cells can recognize these antigens and kill neurons," Dr. Sulzer says, "but we still need to determine whether this is actually happening in people. We need to show that there are certain T cells in Parkinson's patients that can attack their neurons."

If the immune system does kill neurons in Parkinson's disease, Dr. Sulzer cautions that it is not the only thing going awry in the disease. "This idea may explain the final step," he says. "We don't know if preventing the death of neurons at this point will leave people with sick cells and no change in their symptoms, or not."

**More information:** "MHC-1 expression renders catecholaminergic

neurons susceptible to T-cell-mediated degeneration." *Nature Communications*, 2014.

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