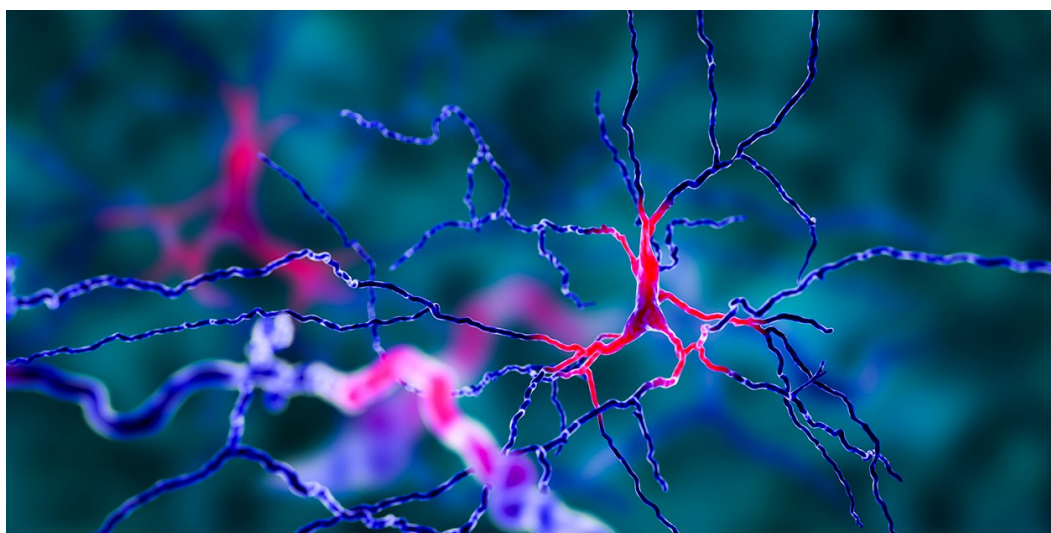


Inflammatory Bowel Disease Treatment May Reduce the Risk of Parkinson's

Genetics and big data intersect to uncover an unconventional strategy to decrease neuroinflammation.



Dopaminergic neuron: Degeneration of these brain cells are responsible for development of Parkinson's disease.

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While people with Parkinson's disease have a multitude of drug options available to combat symptoms of the neurodegenerative disorder, medications that prevent the disease are not among the choices. But a new study published in [JAMA Neurology](#) offers hope that a biologic therapy for inflammatory diseases could reduce the risk of developing Parkinson's.

Researchers from the Icahn School of Medicine at Mount Sinai in New York first considered the idea of repurposing an inflammatory bowel disease (IBD) drug for Parkinson's after they discovered a genetic mutation shared between the diseases. While searching for biomarkers for Crohn's disease, a common form of IBD, the team identified specific mutations in the LRRK2 gene — the same mutations associated with Parkinson's. If these

mutations were responsible for triggering both diseases, then people with Crohn's disease would be more likely to develop Parkinson's later in life.

To test their hypothesis, the investigators analyzed 175 million health insurance claims between 2010 and 2016 and found that people with IBD had a 28 percent higher risk of developing Parkinson's disease than people without IBD. They suspected that chronic, systemic inflammation was the culprit for both diseases, which meant the anti-TNF α therapy prescribed to reduce gut inflammation in IBD might also decrease inflammation in the brain. This therapy works by slowing the activity of TNF proteins that are overactive in people with inflammatory diseases.

The researchers revisited the insurance data and compared the rate of Parkinson's among those who had taken anti-TNF α therapy for IBD with those who had not. "We found that Parkinson's disease was 78 percent less common in people using this therapy to treat IBD," says lead author [Inga Peter](#), a genetic epidemiologist at Mount Sinai. "This was surprising because these people had an even lower risk of developing Parkinson's than the general population."

Previous research had shown that TNF inhibitors had disappointing results with brain diseases, like multiple sclerosis and amyotrophic lateral sclerosis (ALS), perhaps because the large molecules in the compound failed to cross the blood-brain barrier, or participants received the treatment too late, Peter says. But the new study suggests that people with IBD may have a "leaky" barrier that allows these molecules to enter the brain, or the drug does not need to pass through this barrier to be effective in the brain.

"Our goal is to eventually have some type of preventive medication to offer people who are at risk of Parkinson's disease," Peter says. "The age of onset of IBD is usually about 20 to 30 years before Parkinson's, so we have a window of opportunity to screen people with IBD who are at risk and do something about it."

Although the study's results were promising, TNF inhibitors are immune suppressants, so patients who take the medication to prevent Parkinson's would increase their risk of infections. Future studies are needed to understand when the benefits of prevention outweigh the risks from side effects, the right dosage, and who should take the medication, Peter says.

The researchers also did not have access to clinical information — smoking habits, caffeine use, or other prescriptions — that can influence a patient's risk of developing Park-

inson's. For example, people with Crohn's disease often avoid caffeine to decrease symptoms, but caffeine has been shown to decrease the risk of Parkinson's, says [Clemens Scherzer](#), a neurologist and genomicist at Harvard Medical School who was not part of the study.

Despite these limitations, the concept of using big data to predict the impact of repurposing a drug has powerful implications, Scherzer says.

"The traditional drug development model hasn't worked well for Parkinson's disease," he says. "Researchers have spent many years finding drugs that work well in mouse models only to see them fail in humans during clinical trials. This new approach turns the current drug development paradigm on its head by using large amounts of data upfront to see how a drug might work in a human before starting clinical trials."

Next, Peter will be studying the genetic landscape in patients with both IBD and Parkinson's disease to better understand the exact mutations that predispose people to both diseases. She also plans to investigate the blood-brain barrier in animal models with and without colitis to explore how anti-TNF α therapy interacts with the brain. Once these questions are answered, she hopes to see the therapy tested in clinical trials for slowing the progression and ultimately preventing Parkinson's disease.

"There is tremendous potential to leverage genetics to find connections between different diseases," Peter says. "Now gastroenterologists treat IBD and neurologists treat Parkinson's with different medications, but in the future doctors could coordinate care to prescribe one drug for both. We can treat the patient rather than targeting the disease, and that's precision medicine."