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Research Shows Parkinson's Disease Origins in the Gut

Analysis by Dr. Joseph Mercola | December 01, 2023

STORY AT-A-GLANCE

- Parkinson's disease may originate in the gastrointestinal tract
- Researchers injected misfolded alpha-synuclein, a protein linked to Parkinson's disease, into the guts of healthy mice, then tracked it
- One month later, it had turned up in the brainstem, while after three months it had traveled to the brain's amygdala and midbrain; within seven and 10 months, it had turned up in even more regions of the brain
- The researchers also injected the misfolded proteins into the guts of mice that had a severed vagus nerve; after seven months, no signs of cell death were present in the mice brains, and it appeared that the proteins were not able to advance to the brain
- Problems with memory and anxiety also appeared in the intact vagus nerve mice that received the misfolded proteins in their guts, which were not seen in the other groups of mice

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Your gut is a key player in your overall health, playing a role in your risk of chronic conditions like heart disease,[1] obesity,[2] sleep problems[3] and depression.[4] Parkinson's disease, a central nervous system disorder that causes symptoms such as tremors and balance problems, however, has long been a disease of idiopathic origins, meaning there's no known cause.

Research published in the journal Neuron[5] may challenge this notion, as it further supports the notion that Parkinson's disease may originate in cells in the gut and travel to the brain via the vagus nerve the 10th cranial nerve[6] that runs from your brain stem down to your abdomen.

If this is the case, it opens up new avenues for prevention and treatment, beginning with bolstering your gut health. However, there are other contributing factors to Parkinson's disease that should also be considered.

Proteins Linked to Parkinson's Can Travel From Gut to Brain

Alpha-synuclein is a type of protein naturally found in the human body. When the proteins are misfolded, they may clump together and cause damage to nerve cells that lead to areas of dead brain matter called Lewy bodies.[7] These areas of dead brain cells lead to Parkinson's disease symptoms such as problems with movement and speech.[8]

In 2003, research by German neuroanatomist Dr. Heiko Braak first suggested that Parkinson's disease may originate in the gastrointestinal tract.[9]

The featured study, which was conducted in mice, builds upon this, providing "the first experimental evidence that Parkinson's disease can start in the gut and go up the vagus nerve," study author Dr. Ted Dawson, professor of neurology at the Johns Hopkins University school of medicine, told The Guardian.[10]

Researchers injected misfolded alpha-synuclein into the guts of healthy mice, then tracked it to see where it ended up. One month later, it had turned up in the brainstem, while after three months it had traveled to the brain's amygdala and midbrain. Within seven and 10 months, it had turned up in even more regions of the brain.

Next, the researchers injected the misfolded proteins into the guts of mice that had a severed vagus nerve. After seven months, no signs of cell death were present in the mice brains, and it appeared that the proteins were not able to advance to the brain. The study also evaluated behavioral changes in the groups of mice, such as their ability to build nests.

After seven months, mice with intact vagus nerves that received the misfolded proteins in their gut built smaller, messier nests, a sign of problems with motor control. Mice that did not receive the injection, and mice that received the injection but had a severed vagus nerve, scored consistently higher on nest-building activities.[11]

Problems with memory and anxiety also appeared in the intact vagus nerve mice that received the misfolded proteins in their guts, which were not seen in the other groups of mice.[12] "This study supports the Braak hypothesis in the etiology of idiopathic Parkinson's disease (PD)," the researchers concluded.[13]

Speaking to Medical News Today, Dawson added, "Since this model starts in the gut, one can use it [to] study the full spectrum and time course of the pathogenesis of Parkinson's disease," and possibly discover ways to stop the symptoms from progressing.[14]

Low Carb Diet Also Increases Risk for Parkinson's Disease

An October 2023 study[15] demonstrated that the presence of damaged mitochondrial DNA in the bloodstream is sufficient to cause all symptoms of Parkinson's Disease. The DNA from the mitochondria exerted its changes to the nerve tissue through activation of the endotoxin/LPS receptor TLR4. This means that endotoxin alone, which is the main TLR4 activator, is also sufficient to cause Parkinson's.

In addition to endotoxin/LPS, the other catalyst for mitochondrial damage causing Parkinson's would be stress. The presence of mitochondrial debris in the blood is mainly driven by cortisol through its catabolic effects on virtually all tissues incorporating amino acids, such as your muscles and bones. Cortisol increases are primarily driven by a low-carb diet as cortisol is released to liberate proteins from your tissue so your liver can convert them to amino acids.

Making sure you are eating enough healthy carbs like ripe fruit is one of the best ways to reduce cortisol. The average person needs about 200 to 250 grams of ripe fruit per day. If you are on a low-carb diet you will need to increase this slowly. Bioidentical

progesterone dissolved in vitamin E, (not in a skin cream) and applied to your gums is also another useful strategy as it is a potent cortisol blocker.

Microbiome Affects Success of Parkinson's Drug

Levodopa is a drug that acts as a precursor to dopamine. In people with Parkinson's, nerve cell damage in the brain causes dopamine levels to drop, which is why Levodopa is often given as a treatment to boost dopamine levels and alleviate symptoms. However, it doesn't work for everybody.

Levodopa's effectiveness may depend on the composition of the patient's microbiota. In some people, gut microorganisms may metabolize the medication before it has a chance to cross the blood-brain barrier, rendering it ineffective.

Research by scientists at the University of California, San Francisco and Harvard have now identified specific enzymes produced by gut bacteria that work together to metabolize Levodopa in the gut.[16] By blocking one or both of the enzymes, it's possible the drug's effectiveness could be improved for some people. According to the study:[17]

> *"We have characterized an interspecies pathway for gut bacterial l-dopa [Levodopa] metabolism and demonstrated its relevance in human gut microbiotas. Variations in these microbial activities could possibly contribute to the heterogeneous responses to l-dopa observed among patients, including decreased efficacy and harmful side effects."*

The bacterial species identified that metabolize Levodopa were Enterococcus faecalis and Eggerthella lenta. The scientists also identified a molecule capable of blocking an enzyme produced by Enterococcus faecalis, which preserved higher levels of Levodopa in gut microbes of Parkinson's patients, as well as in mice carrying the bacteria in their gut.[18]

Study author Peter Turnbaugh, Ph.D., associate professor of microbiology and immunology at UCSF, said in a university news release, "This study, together with other

recent publications, emphasizes the utility of detailed biological and chemical knowledge about how our associated microbes shape the treatment of disease."[19]

Severed Vagus Nerve Linked to 40% Lower Risk of Parkinson's

Adding further support that Parkinson's disease may start in the gut and travel to the brain via the vagus nerve is a study that involved people who previously had a resection of their vagus nerve, often performed in people who suffer from ulcers to reduce the amount of acid secretion and reduce the potential for peptic ulcers.[20]

Using the national registry in Sweden, researchers compared 9,430 people who had a vagotomy against the records of over 377,200 who had not undergone the surgery. Although the researchers did not find a difference in the gross number of people who developed Parkinson's between the groups, after delving further they discovered something interesting.[21]

People who had a truncal vagotomy, in which the trunk of the nerve is fully resected, as opposed to a selective vagotomy, had a 40% lower risk of developing Parkinson's disease.[22]

Gut Bacteria May Worsen Accumulation of Misfolded Proteins

Additional research published in 2016 also found a functional link between specific gut bacteria and the onset of Parkinson's disease. Using mice engineered to overexpress alpha-synuclein, the researchers found "gut microbiota are required for motor deficits, microglia activation, and αSyn [protein α-synuclein] pathology."[23]

What's more, researchers noted, "Antibiotic treatment ameliorates, while microbial re-colonization promotes, pathophysiology in adult animals, suggesting that postnatal signaling between the gut and the brain modulates disease." Other links were also seen in the study, including:[24]

- Oral administration of microbial metabolites to germ-free mice promoted neuroinflammation and motor symptoms
- Colonizing mice engineered to overexpress alpha-synuclein with microbiota from Parkinson's disease patients enhanced physical impairments in the mice compared to microbiota transplants from healthy human donors

The researchers concluded, "These findings reveal that gut bacteria regulate movement disorders in mice and suggest that alterations in the human microbiome represent a risk factor for PD [Parkinson's disease]."[25] The connection makes sense, as gastrointestinal symptoms, such as constipation, may begin decades before the onset of symptoms in Parkinson's disease.

Research also shows that people with Parkinson's have increased expression of the bacterial endotoxin-specific ligand toll-like receptor 4 (TLR4), intestinal barrier disruption, enhanced makers of bacterial translocation and higher proinflammatory gene profiles in the colon compared to people without the disease.[26]

Inflammation driven by TLR4 may be another route involved in Parkinson's disease development and related neuroinflammation and neurodegeneration.

Pesticides Also Linked to Parkinson's

The gut is one intriguing avenue that needs to be further explored in Parkinson's, but other factors are also likely involved, including exposure to external toxins like pesticides. Pesticide exposure is strongly linked to Parkinson's disease and may increase the risk by 80% in some cases.[27]

It's believed pesticides may contribute to dopaminergic neuron death,[28] and even low-level exposure may mimic the effects of mutations that cause Parkinson's disease.[29,30] In one study, when researchers exposed dopamine-producing neurons to two pesticides (paraquat and maneb), it prevented mitochondria from moving properly, leading to energy depletion within the neurons.[31]

"People exposed to these chemicals are at about a 250% higher risk of developing Parkinson's disease than the rest of the population," study author Scott Ryan of University of Guelph said in a news release.

"Until now, the link between pesticides and Parkinson's disease was based primarily on animal studies as well as epidemiological research that demonstrated an increased risk among farmers and others exposed to agricultural chemicals. We are one of the first to investigate what is happening inside human cells."[32]

What's more, people with a genetic predisposition for Parkinson's disease may be more affected by exposure to pesticides, and put at risk by lower levels. "People with a predisposition for Parkinson's disease are more affected by these low-level exposures to agrochemicals and therefore more likely to develop the disease," said Ryan. "This is one of the reasons why some people living near agricultural areas are at a higher risk."[33]

Tips for Lowering Your Parkinson's Risk

Avoiding exposure to pesticides by not using them in your home or garden and eating organic or biodynamically grown food as much as possible is an important tool for lowering your Parkinson's risk. Minding your gut health is another important avenue, which can be accomplished by the following:

Do	Avoid
Eat plenty of fermented foods — Healthy choices include lassi, fermented grass fed kefir, natto (fermented soy) and fermented vegetables.	**Antibiotics**, unless absolutely necessary, and when you do, make sure to reseed your gut with fermented foods and/or a high-quality probiotic supplement.
Take a probiotic supplement — Although I'm not a major proponent of taking many supplements (as I believe the majority of your nutrients need to come from food),	**Conventionally-raised meats** and other animal products, as CAFO animals are routinely fed low-dose antibiotics.

Do	Avoid
probiotics are an exception if you don't eat fermented foods on a regular basis.	
Boost your soluble and insoluble fiber intake, focusing on vegetables, nuts and seeds, including sprouted seeds.	**Chlorinated and/or fluoridated water —** Especially in your bathing such as showers, which are worse than drinking it.
Get your hands dirty in the garden — Exposure to bacteria and viruses can help to strengthen your immune system and provide long-lasting immunity against disease. Get your hands dirty in the garden, which can help reacquaint your immune system with beneficial microorganisms on the plants and in the soil.	**Processed foods —** Excessive sugars, along with otherwise "dead" nutrients, feed pathogenic bacteria. Food emulsifiers such as polysorbate 80, lecithin, carrageenan, polyglycerols, and xanthan gum also appear to have an adverse effect on your gut flora. Unless 100% organic, they may also contain GMOs that tend to be heavily contaminated with pesticides such as glyphosate. Artificial sweeteners have also been found to alter gut bacteria in adverse ways.[34]
Open your windows — Research shows that opening a window and increasing natural airflow can improve the diversity and health of the microbes in your home, which in turn benefit you.[35]	**Agricultural chemicals**, glyphosate (Roundup) in particular is a known antibiotic and could potentially kill many of your beneficial gut microbes if you eat foods contaminated with it.

Do	Avoid
Wash your dishes by hand instead of in the dishwasher — Research has shown that washing your dishes by hand leaves more bacteria on the dishes than dishwashers do, and eating off these less-than-sterile dishes may decrease your risk of allergies by stimulating your immune system.[36]	**Antibacterial soap**, as it kills off both good and bad bacteria and contributes to the development of antibiotic resistance.

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