

Pain, fatigue, fuzzy thinking: How long COVID disrupts the brain

Michelle Wilson got COVID three years ago. She's still waiting for her brain and nervous system to recover.

Wilson's memory is spotty, she's frequently in pain, and even a short walk leaves her exhausted.

"I actually bought a cane that turns into a seat so I can go to the botanical garden," she says.

It's a big change for Wilson, 66, who had worked as a nurse at Barnes-Jewish Hospital in St. Louis. But after years of waiting to get better, she says she's realized something:

"This might be as good as it gets."

It's a story shared by a growing number of COVID "long-haulers" — those patients who suffer from persistent symptoms long after the initial infection has passed. Many of those symptoms, experts say, appear to be tied to COVID's effects on the brain and nervous system.

Government surveys suggest that [millions of people](#) in the U.S. are living with neurological symptoms linked to long COVID. Many, like Wilson, were infected before vaccines became available.

"It's a public health crisis," says [Dr. Robyn Klein](#), who directs the Center for Neuroimmunology and Infectious Diseases at Washington University School of Medicine in St. Louis.

"There are a lot of people suffering and those people need treatment yesterday," says [Dr. Ziyad Al-Aly](#), who holds positions at both Washington University and the Veterans Affairs St. Louis Health Care System.

But treatment remains a distant promise.

"There's still a ton we don't know," says [Dr. Troy Torgerson](#) of the Allen Institute for Immunology in Seattle. Scientists are "nibbling away" at the problem, he says.

The virus appears to do most of its damage to the brain indirectly, scientists say.

An infection in the body triggers an immune response that leads to inflammation in the brain. And the inflammation can persist long after the virus has apparently been cleared, scientists say.

The brain may be especially vulnerable to COVID because the disease appears to weaken the blood-brain barrier, which usually protects the organ from both germs and the immune cells that follow them.

Another possibility is that COVID-related inflammation [affects the vagus nerve](#), which carries signals between the body and brain that are important to memory and attention.

From lungs to brain

Early in the pandemic, doctors tended to focus on what COVID did to a person's lungs.

In those days, Wilson was working in the post-anesthesia care unit at Barnes-Jewish Hospital.

"I got people ready for surgery, and woke them up after their surgeries," she says. "I loved that job."

But the job put her in close proximity to lots of potentially infected patients. And in November of 2020, Wilson got the disease.

When the symptoms grew worse, she went to the emergency department at her own hospital.

"I had bilateral pneumonia and I was in sepsis by that time," she says. "My blood pressure was really low and I had an irregular heartbeat."

The infection was primarily her lungs, but it was also disrupting her brain, including the circuits that control blood pressure and heart rhythm.

"Unfortunately, long COVID, as we know it now, can affect nearly every organ system, including the brain," Al-Aly says.

People with neurological symptoms do get better, he says, but full recovery is rare.

Three years after getting COVID, Wilson continues to struggle with a range of symptoms, including an unreliable memory.

"I have trouble with word retrieval, concept retrieval — and sometimes, like, remembering where I was going," she says.

Wilson also has problems sleeping at night, a condition Al-Aly says affects about 40 percent of people with long COVID.

"As a result, they wake up fatigued," he says, which contributes to their exhaustion from even moderate activity.

Poor sleep can also contribute to the pain that many long COVID patients report.

"It's not only 'my wrist is hurting' or 'my knee is hurting,'" Al-Aly says. "It's really almost like the whole body aches."

When Wilson first came home from the hospital, she was in agony.

"The pain across my chest and in my arms was so bad that I slept with pillows under both arms because I couldn't stand my arms to touch my chest," she says.

Now Wilson is able to do things like make breakfast or take a shower — so long as she takes her pain meds.

Immune system gone wrong?

There's growing evidence that even a mild case of COVID can cause long-term changes to the immune system that affect the brain and nervous system.

Torgerson of the Allen Institute was part of a team that studied blood samples from 55 people who had symptoms at least 60 days after a COVID infection.

"We saw persistent ongoing immune activation in about half," he says, even though only a handful had been sick enough to be hospitalized.

Once the immune system gets fired up, Torgerson says, it can affect the brain even if the virus itself doesn't infect brain cells.

For example, circulating immune cells and antibodies may cross from the bloodstream into the brain and damage neurons. Or the presence of an infection may activate a special set of immune cells found only in the brain.

Long COVID also has some striking similarities to autoimmune diseases, which occur when the immune system mistakenly attacks healthy cells, Torgerson says.

Lupus, for example, can cause inflammation that results in joint pain and fatigue. When Lupus reaches the brain, it can also cause the sort of brain fog often seen in long COVID.

A mouse model of COVID

To learn more about how long COVID affects a human brain, scientists have been studying mice that develop a mild version of the disease.

"Those animals have cognitive deficits a month after they were infected," Klein says. "They no longer have virus, they're no longer ill. But they can't remember and recognize things."

One reason may be that the infection weakens the blood-brain barrier in these animals, Klein says, allowing the body's immune response to affect brain cells.

The result is inflammation that causes subtle but significant changes in the brain.

"It's not like there's a multitude of dying neurons," Klein says. "What there is, is elimination of the connections between neurons."

Klein suspects that something similar is happening to the synaptic connections in the brains of people who get long COVID. And she says it appears this can happen even in people who don't get very sick.

"You and I may handle viruses differently," she says. "I may end up getting more inflammation in my brain than you because we have a different genetic makeup."

One way to protect the brain after an infection may be with drugs that reduce inflammation — and [studies](#) to test that idea are already underway. In the meantime, [vaccination](#) offers a way for people to reduce their risk of developing long COVID.

Michelle Wilson, though, got infected before vaccination was an option. And she'd like a treatment that can undo what COVID has done to her brain.

"We don't know everything about COVID yet," she says, "So I have hope."