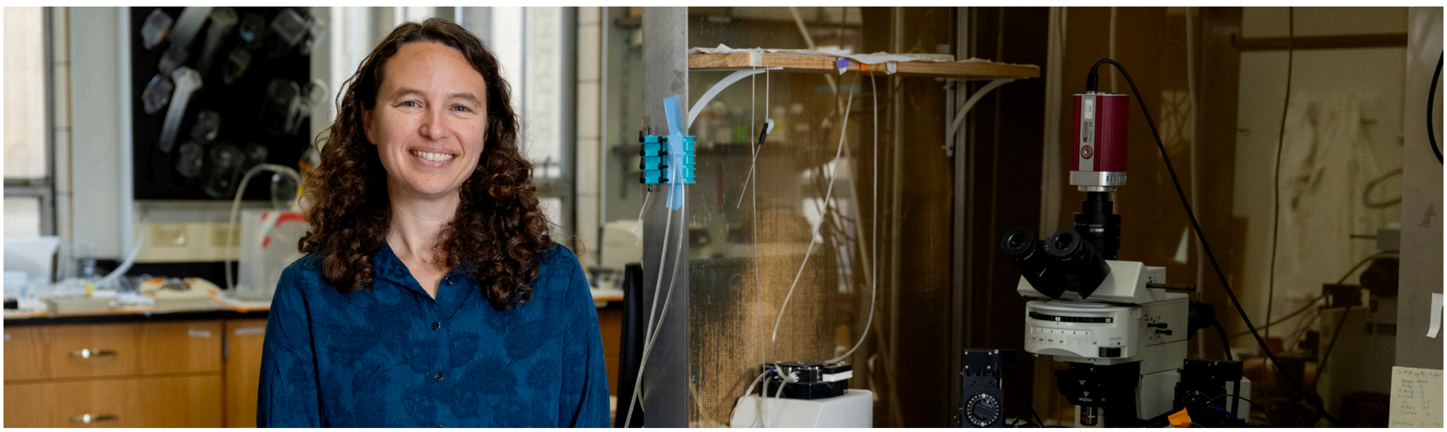
The Long Game

Years of CMU discoveries drive new Parkinson's treatment

OCTOBER 1, 2025



Aryn Gittis' research at Carnegie Mellon is shaping a new treatment for Parkinson's disease that could give patients longer-lasting relief.

For more than a decade, Carnegie Mellon University neuroscientist Aryn Gittis has been unraveling the mystery of how the brain controls movement. Her research is now pointing toward new treatments for Parkinson's disease.

Her lab studies the basal ganglia, a part of the brain that guides movement, habits and decision-making and is tied to the tremors, stiffness and motor control issues that mark Parkinson's disease. From her earliest experiments as a new faculty member, through rejected grants, surprising lab results and breakthrough discoveries, Aryn has been chasing the answer. Now, after years of research, she is on the cusp of something rare in foundational science: Doctors may use what she's discovered to help patients.

Later this year, a team at the University of Texas Southwestern Medical Center led by neurosurgeon Dr. Nader Pouratian will begin testing a deep brain stimulation (DBS) protocol built on insights from Aryn's lab. If successful, it could lead to longer-lasting relief for Parkinson's patients whose symptoms no longer respond well to medication.

"We're living in an exciting time for neuroscience research," says Aryn, the Dr. Frederick A. Schwertz Distinguished Professor of Life Sciences in CMU's Mellon College of Science. "Tools that let us watch circuits in real time have completely changed the kinds of questions we can ask. When I started my Ph.D., I never imagined we'd be able to do what we're doing now."

A turning point in deep brain stimulation

DBS has been used for years to ease the movement symptoms of Parkinson's disease, especially in patients who no longer respond to medication. The disease develops when brain cells that produce dopamine, a chemical essential for coordinating movement, stop working or die. In DBS, surgeons implant thin electrodes into specific areas of the brain, where an external device delivers targeted electrical pulses to help regulate movement.

The electric signals are effective at stopping the body from making movement problems, like tremors or balancing issues, but only while the stimulator is on. Once the stimulation stops, symptoms return almost immediately."

A turning point for Aryn's lab came when they identified specific types of neurons to target for longer-lasting relief.

She discovered that in order for patients to get long-lasting relief, two key populations of neurons needed to be nudged in opposite directions — one activated, the other suppressed. Standard electrical DBS, which delivers a broad "blast" of current, can't provide that kind of precision. But by carefully shaping stimulation patterns, what Aryn calls "burst stimulation," her group realized they could mimic separating the cells.

It turned out the brain gave them a helping hand: Its wiring already supported that kind of separation, though no one had ever looked for it before. That unexpected feature was a big part of what made the discovery possible.

"I thought this was going to be a super difficult study that might take 15 or 20 years — maybe even require pharmacology," Aryn says. "But we got a little lucky."

That discovery, refined with the help of collaborators like CMU computational biologist Andreas Pfenning and Pitt mathematician Jonathan Rubin, produced the burst stimulation protocol moving into patient trials. In early operating room tests, Pouratian saw encouraging signs: reduced stimulation time, fewer side effects and evidence of brain activity shifting back toward healthy patterns.

"It suggests we're not just putting a Band-Aid on symptoms," Aryn says. "We might actually be restoring the brain to a healthier state."

Science takes time

The pace of progress — from the first paper in 2017 to a clinical trial in 2024 — was unusually fast. For Aryn, those seven years passed quickly, though the path was steep and filled with obstacles.

Grant reviewers were initially dubious that the groups of brain cells her lab was targeting even mattered. Like many bold ideas, her work faced early skepticism and rejections, before gaining recognition in journals such as Nature Neuroscience and Science. Support from the National Science Foundation, including an NSF-NIH Collaborative Research in Computational Neuroscience grant, helped carry the work forward and ultimately laid the foundation for the upcoming clinical trial.

"I think people often don't share the failures," she says. "You get ideas rejected all the time. Sometimes, the more exciting the idea, the more resistance you face. As a junior scientist, that can be hard. But you just keep going."

That persistence was bolstered by colleagues and mentors, including CMU neuroscientist Alison Barth, who helped her navigate the lean early years of funding.

"From the very beginning, it was obvious that Aryn had this rare mix of discipline and vision. She could put her head down, do the experiments, write them up and keep moving forward without hesitation — which is where a lot of scientists stumble," Barth says. "Aryn was often ahead of the field. She saw the potential of new circuit-mapping tools before most people did and immediately made discoveries that changed how we thought about Parkinson's. That kind of perseverance and confidence in her ideas, even when reviewers or colleagues doubted her, is really what pushed this work forward."

A lab that grows people

Just as critical to Aryn's progress are the students who have grown with the lab.

Shruti Nanivadekar, an M.D./Ph.D. candidate with an engineering background, helped set up the lab's first electrical stimulation system in mice. Her experiments contributed to a 2021 paper in Science that showed that stimulating the right cell groups can work better than stimulating the whole area.

"Shruti hadn't really done a lot of work with mice before, her background was in engineering, but she figured out how to get our system up and running and got these experiments done that we needed. And then the results were amazing. So I said, 'let's write this for Science.' And we did," Aryn says.

Arini Bhargava, an undergraduate student majoring in neuroscience, worked closely with Nanivadekar, and credits the Aryn lab culture for that success.

"Dr. Gittis has created an environment that's both supportive and rigorous. She encourages everyone — from new students like me to postdocs — to think deeply about their projects and hold themselves to a high standard," she says.

Aryn's research goes beyond Parkinson's symptoms to explore the broader role of the basal ganglia. For example, graduate student Maxime Vounatsos is uncovering unexpected links between the basal ganglia's motor circuits and the brain's emotional centers — connections that could help explain how Parkinson's relates to anxiety, fear and PTSD.

And then there are alumni like Kevin Mastro, Aryn's first graduate student, now a postdoctoral fellow at Harvard Medical School. During his time in the Aryn lab, he was involved in the work that showed that targeting specific brain cells could restore movement in a mouse model of Parkinson's disease, a discovery that laid the groundwork for the clinical trial now underway.

"I always admired how efficient of a thinker Aryn is — she has this ability to find the through line, to get to the heart of the story," Mastro says. "That completely changed how I approach problems. Instead of collecting data for months and figuring it out later, she pushed us to pause every week, ask what we'd learned and let that guide the next step. That way of thinking still influences how I do science now."

Next steps in movement disorder research

Even as the clinical trial begins, questions remain. Why do the long-lasting benefits of burst stimulation appear only in advanced stages of Parkinson's disease? Which brain regions outside the basal ganglia are essential for sustaining recovery? And how can neurosurgeons decide which patients — and which electrode sites — are best for this new approach?

Aryn's lab is already probing those mysteries, supported by major awards like the 2024 McKnight Neurobiology of Brain Disorders prize.

She is realistic about the uncertainties, but optimistic about the trajectory.

"I tell my students to stay focused on their day-to-day experiments," Aryn says. "It's a long process."