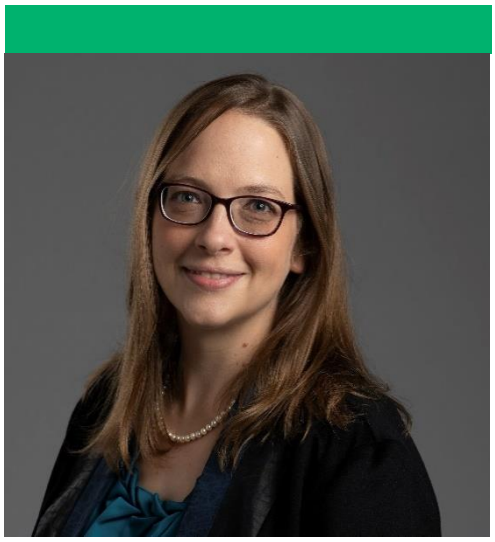
RUSH

Alana Kirby, MD, PhD



The Leslie Nan Burridge Faculty Scholar
in Parkinson's Disease Research

Advancement of Medicine

Thanks to support from the Burridge Faculty Scholar fund, 2025 was a productive research year for my lab. We investigate the brain mechanisms involved in Parkinson's disease.

Funds from the endowment have significantly supported my research activities in three main ways: support for my salary, support for the salaries of staff in my lab, and the purchase of equipment and supplies that enable a rapid turnaround in research activities. Support of my salary has also allowed me time to participate in educational and outreach activities.

Multiple outside grants based on activities supported by the endowment have been submitted. These are currently under review. So far, we have received two internal grants over the two years that I have been supported by the endowment.

Research

Since 2020, I have been investigating how deep brain stimulation, or DBS, changes brain activity using a rat model of Parkinson's disease. This year, we have been examining which brain areas are activated by DBS, focusing on areas involved in movement and motivation and deducing the circuit connections. We have identified three brain areas activated by DBS that are known to light up with movement. Studying these areas in detail, the strongest activation is also related to emotional regulation and motivation, so we are now studying additional brain areas. These results are expected to represent the last piece of a publication reporting our findings. They were presented at the Society for Neuroscience's 2025 meeting, the largest gathering of neuroscientists in the world. Preparation for publication is ongoing. On a local level, these results were chosen as one of the two best abstracts to be presented as a lecture at the Rush Research Mentoring Program symposium.

The project has received support from an R21 exploratory/developmental grant from the National Institutes of Health, or NIH, institutional grants (Cohn Fellowship) and the Burridge endowment.

We have broadened the scope of our investigations by focusing on the role of mitochondria (the powerhouses of the brain) in Parkinson's disease. I have been collaborating with **Raquel Romay-Tallon, PhD**, a research scientist in the lab, to investigate the effect of DBS on mitochondria. In the first half of 2025, we completed six months of intensive data collection using a rat model of Parkinson's disease with an optogenetic model of DBS, combined with a battery of tests, to demonstrate the effects of deep brain stimulation on behavior. We then collected brain tissues, enabling us to connect the effect of DBS treatment with specific changes in the brain. We are currently developing a novel technique to examine the specific mitochondria that we expect are supported by DBS. These mitochondria are in dopamine neurons, the cells most affected by Parkinson's disease. Dopamine neurons send signals from the substantia nigra to the striatum. We are specifically interested in the mitochondria that support dopamine release and signaling. We are using advanced immunostaining, confocal microscopy and computer image analysis to determine the effect of DBS on these mitochondria. Dr. Romay-Tallon and I have submitted an application to the NIH for an exploratory grant in 2025, which will be reviewed this spring. We have also submitted multiple foundation grants. We are working on an application for a large NIH grant based on these results and planning for submission in June 2026. With my research mentorship, Dr. Romay-Tallon received an institutional grant (Postma Family Pilot Award, 2024-2025) to help launch this project.

Another exciting aspect of my mitochondrial investigations is a collaboration with **T. Celeste Napier, PhD**, professor emerita at Rush, and **Amanda Persons, PhD**, associate professor at the University of Texas Medical Branch at Galveston, to investigate the effects of methamphetamine toxicity on mitochondrial function. This work was inspired by people who develop Parkinson's-like symptoms after using methamphetamine. In this study, we used a rat model of meth use and demonstrated mitochondrial toxicity, which is associated with the development of Parkinson's disease-like symptoms after the drug use ends. This is an exciting addition to the field and further supports the importance of mitochondrial function in protecting against Parkinson's disease. This work is being prepared for publication and will be submitted in early 2026.

We are particularly excited to pursue a separate project investigating microplastics and nanoplastics and their role in Parkinson's disease, dementia and other movement disorders. These tiny plastic fragments have been found in human brain tissue, but their role in initiating or promoting neurodegenerative diseases is unknown. This project has received additional support from an internal grant, the **Christopher G. Goetz, MD, Award**, to build rigorous techniques for the study of microplastics. We are ready to leverage the Rush Movement Disorders Brain Bank, an important resource available at the Rush Parkinson's Disease and Movement Disorders Program. This tissue bank contains brains from individuals with a variety of disorders (primarily Parkinson's disease and Lewy body dementia) over the past 12 years. We formed collaborations within Rush to enhance our success and submitted two foundation grants in early 2026 on this topic.

I have been building collaborations within and outside Rush in 2025. Ongoing projects include a study of the gut-related consequences of GBA mutations in Parkinson's disease (with **Helen Dainton-Howard, MD**, now at Medical University of South Carolina, **Dr. Goetz**, and **Ali Keshavarzian, MD**, and his team in the Section of Gastroenterology), and a publication is underway. I am currently preparing to or have submitted grants with **Liudmila Romanova, PhD**, assistant professor of neurology at Rush, and **Robin Pourzal, PhD**, assistant professor of orthopedics at Rush, on the topic of microplastics in the lining of the brain, and with **Isabel Martinez-Pena y Valenzuela, PhD**, assistant professor of physiology at Midwestern University, on the topic of muscle damage in LRRK2 PD. I have also worked in her capacity as the director of the Movement Disorders Video Repository to support research endeavors within the division, including with **Aimee Karstens, PhD**, a neuropsychologist at Rush.

Speaking Engagements

I have given several notable educational presentations this year.

I was once again invited to speak at the American Academy of Neurology Annual Meeting, a large meeting of neurologists with an international audience. I gave a lecture titled "Update in Movement Disorders" as part of the well-attended annual "Updates in Neurology," a daylong course highlighting recent advances in neurology.

I was very pleased to be invited by the International Parkinson and Movement Disorder Society to speak at a course for neurology residents about functional neurological disorders. I have spoken at

this course before, and it is very engaging. It is hosted by the Pan American Section, which sponsors residents from across North and South America to attend a weekend-long course to foster their knowledge of movement disorders and interest in pursuing this subspecialty.

In December 2025, I spoke at a Rush course about synuclein tests in the diagnosis of Parkinson's disease, a topic of great clinical interest to me. Finally, I was invited to speak at a conference for undergraduate women and gender minorities in physics, which was particularly meaningful to me given my past experiences studying physics as an undergraduate and graduate student.

I also continued in my role as co-director of the Parkinson's Disease Patient and Caregiver Symposium. The 2025 symposium was delayed to April 2026 to synchronize with the Parkinson's Foundation for a co-hosted event. This will focus on the gut-brain connection in Parkinson's disease.

Publications, Presentations, and National Leadership (Abbreviated)

Published papers include:

- Di Luca D.G., Prasad S., Kirby A., Merello M., Bhatia K.P., Goetz C. "Peer Reviewing a Case-Based Manuscript in Movement Disorders Neurology." *Mov. Dis. Clin. Pract.* Epub Jun 2025.
- González D.A., Tosin M.H.S., Warner-Rosen T., Afshari M., Barton B., Fleisher J.E., Hall D.A., Kirby A.E., Kompoliti K., Mahajan A., Patel N., Swan C., Goetz C.G. "Loneliness in Parkinson's disease: Subjective experience overshadows objective motor impairment." *Park. Relat. Disord.* 136:107867. May 2025

Invited presentations include:

- Kirby A. "Update in Movement Disorders" Updates in Neurology, American Academy of Neurology Annual Meeting, April 2025. Denver, CO.
- "Neuronal Activation Patterns and Behavior Elicited by Deep Brain Stimulation of the Subthalamic Nucleus" Rush University Movement Disorders Research Day, May 2025. Chicago, IL.
- Kirby A. "Where are we with Synuclein Testing?" Movement Disorder Grand Rounds, July 2025. Chicago, IL.
- Kirby A. "Functional Movement Disorders" 10th Annual Movement Disorders School for Neurology Residents, Sept 2025. Denver, CO.

- Kirby A. “Decisions around Diagnostic Testing in Parkinson’s Disease” Rush Neurology Therapeutics and Management Updates Conference, Dec 2025. Chicago, IL

Posters include:

- Romay-Tallon, R., Gonzalez, CM., Brown, AD., Napier, TC., Kirby, AE. Deep brain stimulation of the subthalamic nucleus engages limbically oriented subfields of the substantia nigra pars reticulata in a rat model of early Parkinson's disease. Program No. 326.25. 2025 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience, 2025. Online.
- Romay-Tallon R, Gonzalez C, Brown A, Napier TC, Kirby AE. Mitochondrial homeostasis in a model of early Parkinson’s disease. Program No. 326.24. 2025 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience, 2025. Online.

The Year Ahead: 2026 and Beyond

We have three papers which are currently in preparation: the brain activation of DBS; the beneficial mitochondrial effects of DBS; and the toxic mitochondrial effects of methamphetamine use. We also have three main research areas of focus: improving microscopic techniques to investigate mitochondria; investigating microplastics in Parkinson’s disease brain tissues and brain linings; and combining studies in humans and rodents to investigate the causes of Parkinson’s disease progression. I am very interested in moving these techniques in a new direction to investigate the cognitive impacts of Parkinson’s disease and how these come about based on changes in the brain. I am hopeful that we will have time to add this project in 2026.

Given the current funding and scientific environment, I am also hoping to build collaborations and diversify our research funding portfolio. I would also like to support the scholarly growth of staff in my lab through collaborative projects. Dr. Romay-Tallon was recently awarded the title of instructor and has been accepted to the Rush Research Mentoring Program. I am dedicated to mentoring and supporting her professional development.

RUSH

With Gratitude

Dear Burridge Family,

Thank you very much for your generous support. I have endeavored to use this support to grow the Parkinson's disease-focused research in my lab. These funds have allowed me to make the most of opportunities that require immediate funds (e.g., to establish a new research technique or hire or retain staff with special skills that move research forward). This flexibility provides an outsized impact on research outcomes and collaborations. Furthermore, I am reminded every time I use these funds that my work is in honor of and in service to patients with Parkinson's disease, and there is an urgency to make a real difference. I am honored to receive this support.

Sincerely,

Alana Kirby, MD, PhD