



National Institute on Aging/U.S. National Institutes of Health

Progressive Supranuclear Palsy is thought to occur when the tau protein clusters around cells in the brain, as seen in the bottom of this diagram.

Rare brain disorder puzzles doctors searching for effective treatments

by Michelle Minkoff

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Robert P. Hanrahan and his wife Barb make time every day to enjoy life, often going picnicking in warmer weather, using baskets such as those they collected around the world when the former U.S. representative and his wife would go to Europe and Asia for both business and pleasure.



Courtesy of Lisa Richards.

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[Society for Progressive Supranuclear Palsy](#)

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Raising money for PSP research

Lisa Richards, 27, works as a district merchant for shoes and handbags at the Macy's on State Street during the week. But about every other weekend the Wicker Park resident makes the 90-mile trip up to her hometown – Oak Creek, Wisconsin, just outside Milwaukee.

Once she arrives, she goes grocery shopping, washes clothes, and does whatever she can to help her dad and siblings take care of her mom Judy, 58, who has Progressive Supranuclear Palsy, a rare neurodegenerative brain disease.

Richards realized there hadn't been a major event to create PSP awareness in the Chicago area, and decided she wanted to do something about it.

"Everyone in the world deals with things with differently, and my coping mechanism is to funnel my energy into something that makes sense and that matters," she says. "And with each and every person I talk to about what I'm doing, I'm just touching one more person that can learn more about this disease and think about it."

Richards is organizing Judy's 5K Run/Walk – which will take place on October 4 and raise money to support research and services sponsored by Cure PSP, the Society for Progressive Supranuclear Palsy.

To sign up or learn more about the event, email

judys5Krunwalk@hotmail.com

or scroll to the bottom of the

[Cure PSP events](#)

page.

Former U.S. Rep. Robert P. Hanrahan could tell you the names of everyone he worked with on Capitol Hill in the 1970s and the details of the bills he worked on involving healthcare, education and transportation. But if you were to ask him – he'd let his wife Barb do the talking.

If the 75-year-old Republican politician told you himself, it would sound like mumbling, because the muscles in his mouth, which would enable him to communicate clearly, have tightened up. So have many other muscles in his body. The thought processes telling these muscles what to do is now impaired, as a result of a rare neurodegenerative disorder.

So while Robert once organized the concerns of constituents in Chicago's third district, now Barb organizes the lives of the retired couple, who live in suburban Vernon Hills. She figures out the

best way to transfer Robert from a wheelchair to the bed, and helps him get dressed each morning.

The Hanrahans aren't alone – the former Congressman is one of the 4,500 people in the United States who have the rare disease known as Progressive Supranuclear Palsy, or PSP.

The condition's name refers to its symptoms, which worsen or progress as time passes, and the word "supranuclear" refers to the limitations in eye movements which are often the first visible sign of the disorder.

Dr. Tanya Simuni, director of the Parkinson's Disease and Movement Disorders Center at Northwestern Memorial Hospital, says about 10 to 15 patients, of the 1,500 patients her department treats, have PSP.

PSP shares many symptoms with Parkinson's and Alzheimer's diseases, but because of biological differences, the treatments are not interchangeable. Hanrahan was misdiagnosed, typical for the disease, and patients frequently spend years taking medications for an illness they don't have.

But doctors who are experienced with the disorder say there are distinct ways to distinguish PSP from other neurodegenerative conditions.

Dr. Timothy Hain, a neurology professor at Northwestern University's Feinberg School of Medicine, says, "While they can look superficially similar, it's easy to tell the difference if you know what you are looking for. You can tell so easily from the eyes, as they move up or down, they have a slowness. And then you know it's PSP, or some rare alternative."

Dr. Chris Goetz, director of the Movement Disorders Center at Rush University Medical Center, agrees and says the list of symptomatic clues that distinguish PSP also includes falls early on in the progression of the disease as well as difficulty swallowing.

Goetz says simply, "It's a question of the nuances."

Patients with PSP, as well as Parkinson's disease, the most common misdiagnosis, share the signs of parkinsonism, which isn't a disease, but a collection of the four symptoms of slowness, stiffness, tremors and balance difficulties. Simuni says at least two of these symptoms need to exist for a patient to be diagnosed with parkinsonism.

"Parkinsonism and Parkinson's disease are not the same. A diagnosis of Parkinsonism is like saying a patient has a cold, but not identifying the virus that is responsible for that cold," she says.

Dr. Lawrence Golbe, a professor of neurology at the Robert Wood Johnson School of Medicine in New Brunswick, N.J., added that another symptom that differentiates PSP patients is impulsiveness. He says this means patients may take steps too quickly while walking, which can result in falls.

If PSP were diagnosed earlier and not confused with other disorders, patients could use the knowledge to understand what will happen to them, and adapt their living environments to be more conducive to their future needs, such as adding ramps and installing assistance bars for support in the bathroom, doctors say. Medicines used for Parkinson's disease often provide some relief from muscle tightness and cognitive problems. Other medications can be used to treat depression.

But there is no medication that can reverse the accumulation of the tau protein in the brain cells,

the protein that scientists believe is responsible for the development of PSP. The protein continues to be a mystery to doctors and scientists, since its discovery in 1975 by Marc Kirschner while at Princeton University.

Lester Binder, a professor of cell and molecular biology at Northwestern University, has been studying the tau protein for decades. He explains it travels along microtubules that are attached to brain cells, as a train car travels along railroad tracks. But in many neurodegenerative diseases called tauopathies, including Alzheimer's and Parkinson's disease and PSP, an unknown process occurs and as cells die, the protein comes off the track, accumulates in the cell and forms polymers, a type of large molecule.

It appears cells are not able to get rid of or digest this protein, and the accumulation blocks the normal cell mechanism. "In Parkinson's it's in a tiny area, and in PSP it's much, much more extensive," said Goetz.

In all tauopathies, there are two alleles, or varieties, of tau called H1 and H2. More than 90 percent of patients with tauopathies have the H1 allele. Scientists think this allele may change the balance of the protein and make it more likely for someone to develop a tauopathy.

The tau protein is found mostly in the central nervous system, and affects a patient in different ways depending on his or her neurodegenerative condition. In PSP, tau affects glial cells as well as nerve cells, or neurons, according to Binder. This is unlike other neurodegenerative disorders, in which neurons are the main cells affected. Glial cells comprise 80 percent of cells in the brain, and they protect neurons and provide support and nutrition for the brain.

Tau is more closely linked to glial cells in PSP, and more closely linked to neurons in Parkinson's disease.

"There is more neural death in PSP than in Alzheimer's, and one of the reasons may be that glial cells affect more neurons," says Binder.

"There are a lot of hypotheses as to what's going on, some people claim the brain becomes more inflamed over time, and that certain regions are more vulnerable than others," he says. "Some say certain regions do more for the brain and that means they lose their ability to respond quicker, so disease systems set in. But no one knows for sure."

Because the disease remains a mystery, doctors, patients and medical professionals each have their own way to describe the disease: "nasty," "ugly," "horrible." But they agree on the worst part: Many patients are very much aware of what is going on as their muscles stiffen, as physical deterioration often occurs sooner than cognitive dysfunction during the disease's progression. Patients lose function in their walking, speech, swallowing and perceiving spatial relationships, and there's no medication that can break up the debilitating protein.

Golbe says, "So far, all we do know is that PSP hasn't responded to any of the drugs we've thrown at it."

"We need to figure out what's happening to the neurons," says Binder. "If we could discover the mechanism, it would allow us to target drug discovery."

One such possible treatment is being explored in the first clinical trial testing the safety of using lithium to slow PSP's progression. The ten sites participating in the National Institutes of Health trial include Northwestern and Rush.

"Lithium is a drug that's been used for many years for managing psychiatric conditions, such as

bipolar disorder,” said Simuni, who is in charge of the trial at Northwestern.

But the reason the doctors are using lithium for PSP is different – animal studies have suggested that lithium may block the accumulation of the tau protein.

The trial is just the first step. “This is purely a safety study, it is not designed to answer the question of whether a drug is effective, or if it is able to slow progression, but the question: Is it safe to introduce the drug to PSP patients?”

“The difference between an effective and toxic range can be quite narrow,” says Dr. Kathleen Shannon, the neurologist who heads Rush’s portion of the trial. “We have to understand how the PSP patients metabolize it.”

Golbe agrees that lithium has potential as a long term solution, and could slow long-term progress.

But this Stage I trial is a long way from producing anything patients will see at the pharmacy anytime soon, so for now, medications are limited to treating symptoms.

Lacking medical treatments for the disease, many PSP patients and their families talk about the importance of finding a way to continue pursuing their passions. Hain tells the story of a patient he had who was a Baptist minister on the South Side. He continued giving sermons even as the disease progressed. As time went on, he gave the sermons sitting down, had caregivers dress him and bring him up and down from the pulpit, and finally he broadcast the sermons over the radio.

Some patients and caregivers find solace in a support group for PSP, held at The Abington of Glenview, a rehabilitation center. Support group leader Darren Loveless, an admissions director at the facility, says, “They need to know they are not alone, and meet people who have gone through the experience.”

The support group was started in the early 1990s with two families, but now there are 30 people on the mailing list.

The Hanrahans are among the families who now attend. So is Jack Ami, whose wife Sibya had PSP for 12 years. Ami remains active in the group even after his wife’s death in 2006, giving advice to those both newly diagnosed and those who have lived with the disease for years. Ami visits his wife’s grave twice a week, bringing a lawn chair and the latest issue of Time Magazine.

He says continuing to stay involved with the group is a way to help others manage all the details of living with the disease. “Other people just don’t understand what we had to go through. To this day, I’m still not quite sure how I did it. But you do what you have to do in order to take care of someone you love,” he says.