University of Minnesota

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Neurosciences News

A publication for those who support brain, nerve, and muscle disease research, education, and care at the University of Minnesota

Research in motion

U scientists explore freezing of gait, a debilitating complication of Parkinson's disease, and actions that can get patients moving again

Up until about four years ago, Mike Fahning thought of his Parkinson's disease as an irritant. His medications seemed to be managing the involuntary movements that are a hallmark of the disease, with which he was diagnosed at age 38.

But one Sunday afternoon in 2010, Fahning was at home doing housework when suddenly he couldn't move. His medications, which he has to take every few hours, had worn off, and he was stuck.

"It was literally like having cement shoes," he recalls. "I was really frustrated. I had this laundry basket on the ground, and I started kicking it down the hall. As I kicked this laundry basket with my feet, it prompted me to walk. It was a really weird deal."

Fahning brushed off the incident, until he went to his job as chief financial officer of an auto dealership the next day and it happened again—in the middle of the busy dealership's showroom. So he did the only thing he could think of. He set down the soda bottle he was holding and kicked it toward his office.

"It prompted me to walk," he says. "It was just bizarre."

Though Fahning wasn't familiar with the term at the time, he was experiencing "freezing of gait," a complication of Parkinson's disease that is simply described as a temporary and involuntary inability

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Photo by Scott Streble

Mike Fahning's freezing of gait may literally stop him in his tracks up to eight times a day, but he never freezes while he is biking—a freeing activity for him and many others who have Parkinson's disease.

Research in motion *(continued from cover)*

to move. It can happen any time but most commonly occurs when a person is changing directions or walking through a cluttered room or narrow space like a doorway. Because the start and end of a freezing episode are unpredictable, falling becomes a risk, too.

"About 70 percent of people with advanced Parkinson's disease will have freezing," says Colum MacKinnon, Ph.D., a movement disorders researcher and an assistant professor of neurology in the University of Minnesota Medical School. "If you ask them what their number-one problem with quality of life is, they'll tell you it's issues with their mobility. It's a big deal for these patients."

Understanding cues

The freezing phenomenon is not well understood. Nor is it understood why certain actions, or "cues," can put an end to a freezing episode.

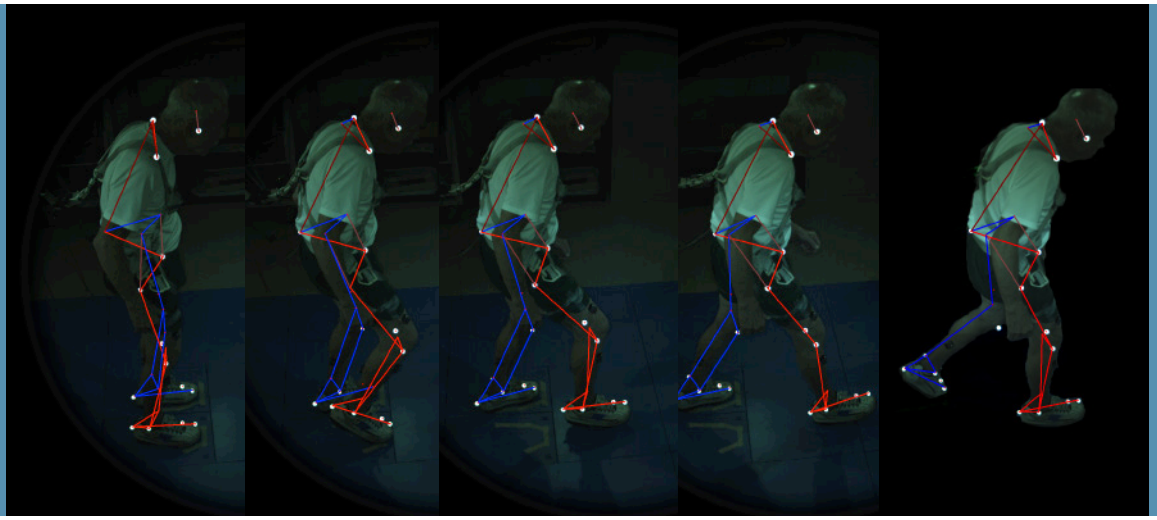
For Fahning, kicking an object can often get him moving again. (His three sons even rigged up a tennis ball on a rope that he often carries around in his pocket in case he gets stuck when no one is around to help him.) Stepping on to a new tile on a tile floor or aiming a laser pointer on the floor in front of him can also help. Other cues that can work to "unfreeze" people who have Parkinson's disease include a tap on the shoulder, a countdown (3-2-1-go), or watching a clock (planning to take a step when the second hand reaches 12, for instance), MacKinnon says.

But cues don't always work, and they seem to work best when the stimulus is coming from another person or a machine rather than from the person with Parkinson's. "No one really knows what's going on in the brain that makes that happen," MacKinnon says.

That's why he and his colleagues are investigating the most effective ways to use

The University's Colum MacKinnon, Ph.D. (center), with research partners Jackie Vaschon, M.S., and Chiahao Lu, Ph.D., record muscle and brain activity in their lab. They hope to learn what's going on in the brains of people who have Parkinson's as they prepare to move and then actually move.

Photo by Scott Streble



The U team is studying the timing and intensity of visual, auditory, and vibrotactile cues to help figure out which cues can be the most effective in ending a freezing episode.

Image courtesy of Colum MacKinnon, Ph.D.

cues and how clinicians and caregivers should present cues to most reliably overcome freezing episodes. A subsequent series of experiments will examine the brain physiology behind freezing and why cueing works. These studies are funded by the National Institutes of Health.

The group's current research involves measuring movement with high-speed cameras and recording muscle and brain activity of people with Parkinson's disease and healthy people as a comparison as they prepare to move and then when they actually move. They're studying the timing and intensity of auditory cues, visual cues, and vibrotactile cues (such as the buzz of a vibrating phone) to help figure out how clinicians should teach patients to use them.

These experiments will help to answer two important questions: Which paradigms let people who have freezing episodes best prepare to move? And why do they work?

'Something significant'

It's only through understanding the problem that solutions may be found.

"Dr. MacKinnon is focusing on an aspect of Parkinson's disease that brings great disability but has not received much attention," says University of Minnesota neurologist Paul Tuite, M.D. "His research strives to provide technical insight into understanding freezing and, therefore, may yield treatments. As clinicians, we have little to offer [today] in ameliorating this problem."

Department of Neurology chair Jerrold Vitek, M.D., Ph.D., believes MacKinnon's work stands to make a real difference in how people who have Parkinson's address their gait freezing. "I am convinced his work will greatly benefit patient care in the future," Vitek says.

And that's music to Fahning's ears. He deals with freezing episodes up to eight times a day as his medications wear off. And sometimes they happen at inopportune times, like this past winter when he crossed his dark street in the evening to get his mail and got stuck outside for 20 minutes.

Fahning, 50, was one of the first in line to participate in MacKinnon's research studies. Now he's encouraging others to join him to help advance knowledge about Parkinson's disease.

"A great mentor of mine said, 'Mike, it doesn't matter what you do in life, but try to do something significant,'" Fahning says. "I'm not sure what that's going to be, but if being a part of a clinical study can help me feel like I'm a part of something, whether it's today or whether it's down the road, that's what I want to do."

See what freezing of gait looks like at **give.umn.edu/freezing.**

To learn more or make a gift to this research, contact Tracy Ketchem of the University of Minnesota Foundation at 612-625-1906 or tketchem@umn.edu.

Filling a need

U launches new clinic for people who have bipolar disorder

Photo by Scott Streble

David Bond, M.D., Ph.D., will lead the University's soon-to-open Bipolar Disorder Clinic.

David Bond, M.D., Ph.D., has spent his professional life delving into problems that lie deep within the human brain. Having recently completed his Ph.D. in neuroscience, and with in-depth experience in both clinical treatment for people who have bipolar disorder and research into brain malfunctions, Bond proved to be an unbeatable candidate to lead the University's new Bipolar Disorder Clinic, which is scheduled to open this summer.

"What we're hoping to do here," he says, "is provide the best possible treatment for people with bipolar disorder by setting up a first-episode mania program. We know that intervening early can make a huge difference in the course of brain illness—that's really been shown at the U's First Episode Psychosis Program, which opened in 2008."

Individuals who have bipolar disorder experience huge emotional swings, ranging from severe depression to abnormally high levels of energy that can lead to erratic or even dangerous behavior.

Affecting more than 35,000 people in the Twin Cities area alone, Bond says, this serious brain illness can also be life-threatening: as many as 20 percent of people with bipolar disorder will attempt suicide in their lifetime, and, on average, people with the disease live 10 to 11 years fewer than the general population.

One of the most significant reasons for that shorter life span is obesity, which affects about one-third of people who have bipolar disorder—and as scientists now know, along with obesity comes a host of other medical problems, including heart disease, diabetes, and high blood pressure. That link between obesity and bipolar disorder has been the focus of much of Bond's research.

"All other things being equal, we now know that obesity leads to more severe illness in bipolar patients," Bond says, referring to his earlier investigations on how obesity affects brain structure and function.

"Compared to normal-weight patients, those who gain significant weight spend more time depressed, don't respond as well to standard mood stabilizing medications, and are less likely to fully recover from mood episodes. Because that link has been established, it potentially gives us a new way to intervene."

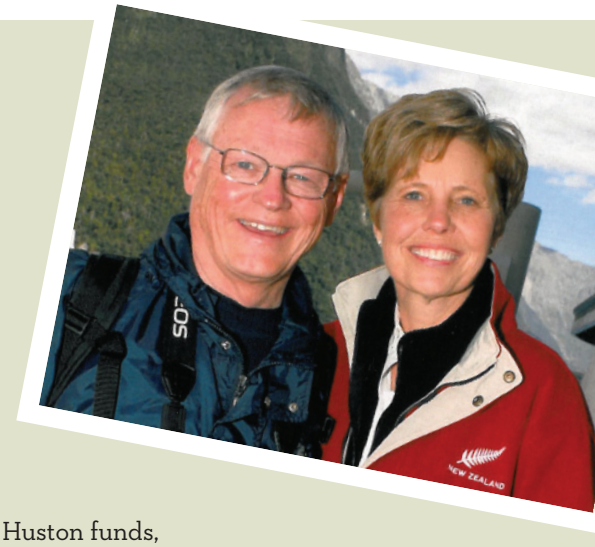
Department of Psychiatry chair S. Charles Schulz, M.D., for one, is impressed by Bond's achievements and drive to make life better for people affected by bipolar disorder.

"More and more research is noting better outcomes of young people who start treatment early," Schulz says. "Dr. Bond is adding a very constructive focus on reducing symptoms and improving health."

At the University's new Bipolar Disorder Clinic, Bond says, staff will help patients find ways to maintain healthier lifestyles through improved diet, exercise, and sleep habits.

"We know medications help with this disease," says Bond, "but if we can intervene early and also help patients maintain a healthy weight, is it possible to slow or even reverse the course of the disease? If that's the case, diet could be key to not only improving their mental health but their general health as well."

Bipolar disorder research and students get a lift from a 'gracious' person's estate gifts



Dick Huston, D.V.M., and his wife, Glenda, were so passionate about education that, years ago, they established scholarships at nine different colleges, including the University of Minnesota. After Glenda died suddenly during a trip to Cairo in 2010, her careful estate planning resulted in not just a substantial increase for the Glenda Taylor Huston Scholarship of Courage at the U but also funds to support bipolar disorder research at the institution.

Mental health was a cause near and dear to Glenda's heart, explains Dick Huston. "Glenda had a son with bipolar disease," he says, "so we experienced firsthand just how devastating that disease can be. Supporting this department … at the U was very important to her."

The Glenda Taylor Huston Fund for Bipolar Disorder Research will enable University doctors to launch a new clinic for people who have bipolar disorder, where they'll focus on treating those who have experienced a first episode of mania. The hope is that early intervention will make a notable difference in the lives of people suffering from the disease.

"Glenda suffered from significant medical problems during her life," says Huston, who continues to support both Glenda Taylor Huston funds, "but she was the most incredible person you could ever meet—so gracious, so brave. I was fortunate to have her in my life as long as I did."

Grateful for the opportunities he has had to meet student scholarship recipients and the University doctors involved in getting the new bipolar clinic up and running, Huston is confident that the funding his late wife had set aside will truly make a difference.

"The students I meet at the U never fail to amaze me—how hard they work, how creatively they think," he says. "It encourages me that we have kids like that coming up. And the new bipolar clinic … well, Glenda would have been so happy to see that come to life."

A gift with a double tax benefit

Giving a gift of appreciated stock, bonds, or mutual fund shares that have been held more than one year can provide an immediate benefit to brain, nerve, and muscle disease research at the University of Minnesota—and it may be more tax-efficient than giving cash.

By making your gift using appreciated securities, you may receive a double tax benefit. You avoid capital gains tax on the appreciation of the donated asset, and you may claim an immediate deduction for the current fair-market value of the property—up to 30 percent of your adjusted gross income.

You may carry forward any unclaimed portion of the deduction for up to five additional years, subject to the same annual limit. Because the donated property is appreciated, the benefit of your gift to the University may be considerably greater than its original cost to you.

For more information about making a gift of appreciated securities, or to learn about other ways to support brain, nerve, and muscle disease research at the University, please contact Catherine McGlinch of the University of Minnesota Foundation at 612-626-5456, 800-775-2187, or mcgra022@umn.edu.

A bold directive

U named one of 25 regional stroke centers charged with revolutionizing stroke care nationwide

Photo by Jim Bovin

Mustapha Ezzeddine, M.D., says the project has the potential to change the way stroke is treated—far beyond the emergency room's walls.

The University of Minnesota has been named one of 25 institutions that will lead a nationwide network of regional stroke centers as part of a new effort driven by the National Institutes of Health to reduce the impact of stroke in the United States.

About 795,000 new strokes are reported each year, making stroke the fourth leading cause of death in the country.

"Stroke is a major cause of disability and death around the world and in Minnesota, and despite progress in medical therapies available today, we are still a long way from being able to achieve the desired cures and recovery," says Mustapha Ezzeddine, M.D., associate professor in the Department of Neurology and principal investigator (PI) of the University's part of the project. Department of Emergency Medicine professor Michelle Biros, M.D., M.S., is co-PI.

Through this new national stroke network, 25 primary sites will work with nearby satellite facilities, capitalize on teams of researchers representing every medical specialty needed for stroke care, and address the three prongs of stroke research: prevention, treatment, and recovery. The goal is to streamline research and share data so that advances in stroke care get to patients as fast as possible.

"This really includes the top tier of all stroke investigators in this country," Ezzeddine says.

The University of Minnesota was selected to participate because of its extensive experience with clinical trials and the comprehensive care it provides, says Ezzeddine. That care involves specialists from emergency medicine, neurosurgery, interventional neuroradiology, vascular neurology, neurointensive care, neuroimaging, stroke rehabilitation, and pediatric neurology.

Each of the 25 centers involved in the network will receive funding for five years, with $200,000 for research and $50,000 for training stroke clinical researchers per year for the first three years. Additional funding will be driven by the completion of milestones.

Ezzeddine says the new network has the potential to change the way stroke is treated—far beyond the emergency room.

"It's not just the acute treatment," he says. "What's different about this network is that it's also focusing on secondary prevention—so how do you prevent another stroke from happening?—and focusing on recovery and rehabilitation."

And, in the process of uncovering new treatments for stroke, Ezzeddine hopes that the network will lead to improved therapies for other conditions, such as traumatic brain injuries and spine injuries, as well.

The **Line Up**

News from the Bob Allison Ataxia Research Center

On to the next step

Because of philanthropic support, research focused on developing the first-ever treatment for spinocerebellar ataxia type 1 (SCA1) continues to move forward.

Working with Beverly Davidson, Ph.D., of the Children's Hospital of Philadelphia, Harry Orr, Ph.D., and his University of Minnesota team are working to develop a gene therapy for SCA1. One method to treat dominantly inherited genetic disorders such as SCA1 is to remove the toxic gene product through a method known as RNA interference (RNAi). It's thought that RNAi can cause the disease-encoding molecules to degrade and thereby stop expression of the toxic protein.

If proven effective, this therapy could potentially be used to treat other neurodegenerative diseases, such as Huntington's disease and genetic forms of Alzheimer's and Parkinson's diseases, as well.

Up to this point, this research has been largely supported by philanthropy, particularly a $50,000 matching gift challenge from benefactors Richard and Maureen Schulze. Nearly 100 additional donors stepped forward to take part in the challenge, together raising another $66,932 for the project.

Research results from the first stage of this work were more promising than the researchers expected, which meant that they were able to move on to the next step faster than expected—using less money than expected. The team has carried over the remaining dollars to support the next step of their investigation, but they'll need an additional $650,000 to fund it fully.

"If the research continues to move forward at the rate it is now, we are optimistic that we're potentially two to three years away from clinical trials for patients," Orr says.

Philanthropy will continue to advance this project. For more information about the research or to make a gift, contact Tracy Ketchem of the University of Minnesota Foundation at 612-625-1906 or tketchem@umn.edu.

Stand Up 2 Ataxia Golf Tournament

Thursday, June 26

Oak Glen Golf Course, Stillwater, Minnesota

Enter your family foursome, a team of competitive co-workers, or a group of friends in this first-time event. The tournament, a four-person scramble, and the silent auction and dinner that follow it will benefit the Bob Allison Ataxia Research Center at the University of Minnesota.

To register or for more information, visit **standup2ataxia.org.**

University of Minnesota

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Photo by Jack McTigue

U now home to world's largest imaging magnet

After a monthlong journey by boat from England, across the Atlantic, and through the Great Lakes, the world's largest human imaging magnet made its way from Duluth, Minnesota, to its new home at the University of Minnesota's Center for Magnetic Resonance Research, arriving on December 6.

The 110-ton Agilent Technologies magnet is the world's first 10.5 Tesla, whole-body human magnetic resonance imaging (MRI) magnet. (In comparison, most medical MRIs utilize 1.5–3 Tesla magnets.) Tesla is a unit of measurement that describes the strength of magnetic field. Eventually, the University's new magnet will be used for brain research and human body imaging. But because a magnet of this strength has never been used to map the human brain or body, for the first five to 10 years it's at the University, scientists will be developing and fine-tuning the technology that will allow the machine to create useful images.

The magnet was made possible by an $8 million grant from the National Institutes of Health.

(Left) Center for Magnetic Resonance Research director Kamil Ugurbil, Ph.D., is internationally known for pushing the limits of imaging technology.

View a time-lapse video of the new magnet's installation at ***give.umn.edu/mb/magnet.***

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