Fall 2009

Neurosciences News

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

New University research boosts hopes for people with impulse control disorders

Kleptomania, compulsive hair pulling, gambling addiction, and other impulse control disorders are notoriously difficult to diagnose and treat. Recent research through the University of Minnesota's Impulse Control Disorders Clinic offers hope to people suffering from these debilitating and often embarrassing behaviors.

Jon Grant, M.D., M.P.H., J.D., led a study targeting trichotillomania, or compulsive hair pulling, that was published in the July issue of the *Archives of General Psychiatry*. It tested the effectiveness of a widely available amino acid used in health food supplements, N-acetylcysteine, in reducing the hair-pulling urges of 50 people enrolled in a double-blind study.

"N-acetylcysteine has been around for years," says Grant, an associate professor of psychiatry at the University. "In liquid form, it's often used to help the liver bounce back from Tylenol overdose. It was recently investigated as a means of reducing the desires of rats addicted to cocaine, so we thought it might be useful for a range of compulsive problems."

Grant and his research team decided to explore N-acetylcysteine as an approach to curbing hair-pulling compulsion because trichotillomania—which Grant believes affects 2 to 4 percent of the population at some level—lacks any effective treatment and is poorly understood, even among physicians.

"It's been known since Hippocrates, but patients often come into the clinic saying, 'My doctor told me simply to stop doing it.' There's a lack of awareness that it's a psychiatric disorder," Grant says.

The study found that 56 percent of participants had significantly reduced their hair pulling after 12 weeks on a daily dose of N-acetylcysteine. By comparison, 16 percent taking a placebo reported less pulling.

Grant finds this outcome valuable in itself, but he is

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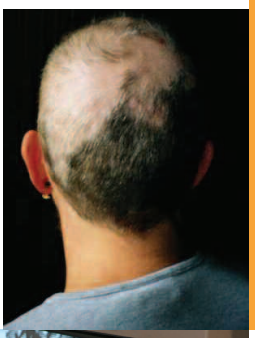
Photo by Emily Jensen

Studies led by Jon Grant, M.D., M.P.H., J.D., have offered a message of hope to people around the world who have impulse control disorders.

University of Minnesota
Driven to Discover℠

Impulse control disorders continued from cover

There's more help ahead for sufferers of impulse control disorders such as trichotillomania, kleptomania, and gambling addiction.



even more enthusiastic about the chemical lessons of the research. His team hypothesized that N-acetylcysteine would work by reducing the brain levels of glutamate, a chemical that triggers excitement. Most medications for trichotillomania instead alter levels of serotonin, a chemical thought to influence compulsive behavior.

"The study suggests that targeting glutamate can be an improvement over serotonin-based treatments," Grant says.

This research conveyed an enormous message of hope to people with trichotillomania around the world, Grant says. Since his study was published, he has received hundreds of e-mails from people who were desperate for any encouraging news about their disorder.

Even though health food stores commonly stock N-acetylcysteine supplements, Grant cautions against taking the antioxidant without medical supervision.

"Patients should contact their primary-care doctors about contraindications, and they should remember that even if a little bit of a supplement is helpful, a bucket-load of it won't help more," he says.

During the past decade, the Impulse Control Disorders Clinic—the first of a handful of academic centers nationwide focusing on compulsive conditions—has treated more than 200 patients annually for gambling addiction, shoplifting, obsessive-compulsive disorder, and body dysmorphic disorder, as well as other compulsive behaviors, including shopping, fire-setting, sexual addiction, alcohol dependency, and skin-picking.

Research conducted by the center's investigators complements this clinical work. A possible new treatment for compulsive stealing, or kleptomania, shows promise in another of Grant's studies.

Kleptomania, like other impulse control disorders, has no FDA-approved drug treatment.

Twenty-five people with a history of weekly stealing took part in Grant's double-blind study, published in the April 1 issue of the *Journal of Biological Psychiatry*, which measured the effectiveness of a drug often used to treat alcohol and opiate addiction.

"When you talk to people who have kleptomania, they often describe it like a drug addiction," Grant says. "They feel a high from the stealing behavior, and when they try to stop, they go through withdrawal-like symptoms that include irritability and restlessness. Often a good place to start is a medication useful for treating similar disorders. So we decided to try naltrexone, an alcohol-addiction drug that's been in use for 28 years."

The results of this small study were encouraging. Over eight weeks, those who took naltrexone stole significantly less than those who took a placebo.

"A pill won't stop anyone from stealing," Grant says, "because people with kleptomania can always override the pill and take something when they desire to. But ideally, a medication that reduces cravings can be used in combination with therapy, much as we do with other addictions."

Ultimately these studies may lead to treatments for trichotillomania and kleptomania, and Grant sees more help ahead for sufferers of impulse control disorders as primary-care doctors increasingly learn to screen their patients.

"[Physicians] already screen for smoking and drinking, and it doesn't take much more time to ask about other behaviors that seem out of control," he says.

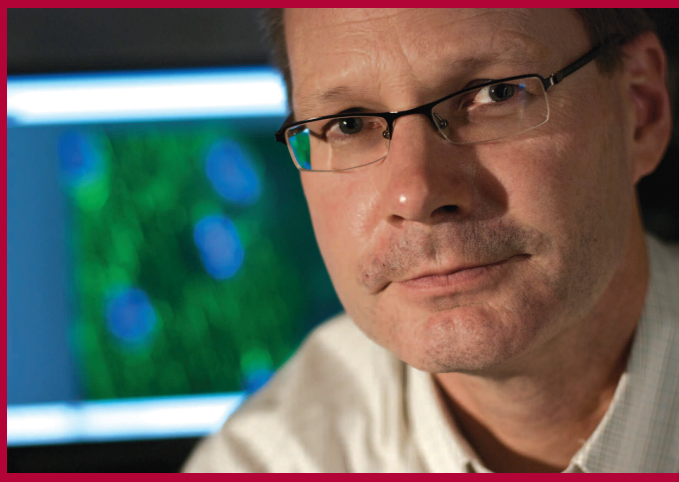
Grant on YouTube

Jon Grant explains his research on compulsive stealing at **www.youtube.com/watch?v=8PnYb_ZvMzU.**

Listen to Grant explain his studies on compulsive hair pulling at **www.youtube.com/watch?v=yIrh4yd4Nus.**

U research team's findings shed light on Duchenne muscular dystrophy

Photo by Richard Anderson



James Ervasti, Ph.D.

A research team led by University of Minnesota biochemist James Ervasti, Ph.D., is yielding promising results in the search for a treatment for Duchenne muscular dystrophy, the most common form of muscular dystrophy in children.

Duchenne, which affects only boys (though girls can be carriers), is caused by a genetic mutation preventing the body's production of dystrophin, a protein crucial to maintaining muscle structure. Without it, muscles stop working and deteriorate. The disease is often fatal by age 20.

Ervasti's team injected a mouse model with a substitute for the missing dystrophin, repairing the weakening muscle tissue. The substitute is a modified protein called utrophin—a dystrophin relative—with a cell-penetrating tag known as TAT. The team found that, once injected, TAT-utrophin spreads throughout the body efficiently.

This approach overcomes major hurdles in treating this systemic disease because it delivers the therapy to every muscle cell in the body. Also, because every cell makes utrophin naturally, the immune system does not reject the TAT-utrophin therapy.

While not a cure, Ervasti says this treatment could one day be an effective therapy for boys with Duchenne. If the treatment works in studies involving larger animals and humans, researchers hope to develop a drug for boys with Duchenne and start clinical trials within three years.

Ervasti's team also recently discovered a new function of the missing dystrophin protein that could help scientists develop new therapies.

Previous research had shown that dystrophin protected muscle cells by connecting two of the three filament types responsible for cell shape and durability. Ervasti's new research shows that dystrophin is also responsible for linking to the third filament type, called microtubules. If a person is missing dystrophin, the microtubules become disorganized, which might contribute to the symptoms of Duchenne.

Reap the benefits of leaving a legacy gift from retirement accounts

Retirement accounts are typically set up to allow people to save money on a tax-deferred basis during their working years. Over time, the value of a retirement account may increase beyond what the owner needs in retirement.

But leaving an IRA or other retirement account in estate plans for a loved one can have serious tax consequences, causing double taxation of the assets.

That's why many donors have found that using retirement plan assets to make a gift to charity can be an ideal way to leave a legacy.

When a person names the Minnesota Medical Foundation as beneficiary of a retirement plan using a beneficiary designation form, the individual's estate receives a charitable estate tax deduction for the full value of the account. Because the foundation is a tax-exempt charity, no income taxes are due on the donated assets.

For more information, contact the Minnesota Medical Foundation at 612-625-1440, 800-922-1663, or giftplanning@mmf.umn.edu, or visit www.mmf.umn.edu/giftplanning.

Estate gift supports two tracks of leading Alzheimer's disease research

Photo courtesy of School Sisters of Notre Dame

It's an exciting time in Alzheimer's disease research at the University of Minnesota.

The world-renowned Nun Study, initiated here in 1986, returned to the University in March after nearly 20 years away and is still netting key insights into Alzheimer's disease and related disorders. And the leading-edge research conducted in the University's N. Bud Grossman Center for Memory Research and Care continues to gain momentum as it shifts its focus to prevention.

Advancing these initiatives is a gift of more than $1.4 million from the estate of the late Douglas Mohl, which is being split between the Nun Study and the Grossman Center.

A University alumnus and Gopher fan, Mohl died suddenly last year at age 68. Mohl's mother was treated at the University for Alzheimer's disease, and he was so grateful for the care she received that he decided to include Alzheimer's research at the University in his estate plans.

Today, Mohl's gift is already being put to good use.

"This generous gift will provide us with the resources needed as we prepare for a new and innovative study with this unique population," says Kelvin O. Lim, M.D., director of the Nun Study and professor and vice chair for research in the Department of Psychiatry. He also holds Drs. T. J. and Ella M. Arneson Land-Grant Chair in Human Behavior.

During the past two decades, about 700 nun volunteers from seven U.S. provinces of the School Sisters of Notre Dame have contributed to a better understanding of healthy brain aging via their journals, personal and medical histories, cognitive functioning tests, and dissection of their brains after death.

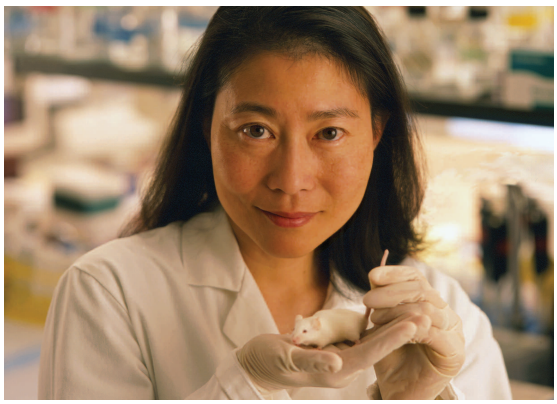
Researchers say the nuns are an ideal group to study because of their homogeneous and active lifestyle—many are involved in education and service well into their 90s.

At the Grossman Center, director Karen Hsiao Ashe, M.D., Ph.D., and her team have made remarkable progress in understanding the underlying mechanisms of Alzheimer's disease that lead to impaired memory.

From the same laboratory that created two types of mice—one that models the later stages of Alzheimer's and one that models the earlier symptoms of pre-dementia—to study the disease comes a new research focus: prevention.

"This gift will enable the Grossman Center to pursue clinical research collaborations with scientists at multiple institutions that will accelerate the timeline to prevention," says Ashe, who holds the Edmund Wallace Tulloch and Anna Marie Tulloch Chairs in Neurology and Neuroscience.

Photo by John Noltner



Karen Hsiao Ashe, M.D., Ph.D., and her lab team are making strides in understanding the mechanisms that lead to impaired memory.

Gifts in action

Philanthropy advances psychiatry department's research on early detection and treatment of schizophrenia

In the last decade, schizophrenia researchers have emphasized the importance of intervening early to treat this psychiatric disease, which typically first appears in a person's late teens through early 30s, according to the National Institute of Mental Health. Generally, the earlier that treatment begins, the better the outcome.

But unlike people who have other neurological or psychiatric disorders, those enduring the disruptions of schizophrenia often see a year or more go by between the appearance of their first symptoms and the beginning of treatment.

Today new programs in the University of Minnesota Medical School's Department of Psychiatry are closing that gap and improving early detection of the disease.

With support from the Minneapolis-based Wasie Foundation, the department last year started First Episode, a program designed to recognize and treat schizophrenia in young people as soon as possible. First Episode patients receive a thorough diagnostic evaluation to confirm the schizophrenia diagnosis and a treatment plan that might include medications and psychosocial therapy. The program also offers support for patients' families and accurate information about the psychosis.

After meeting patients' immediate needs, First Episode helps them meet a long-term goal of returning to clear and logical thinking. In its first year, the program treated 99 patients and helped two-thirds of them go back to work or school, says S. Charles Schulz, M.D., chair of the University's Department of Psychiatry.

"Families struggle to help their loved ones affected by schizophrenia," observes Jan Preble, The Wasie Foundation's director of philanthropic programs. "If there's a way to intervene early, that's wonderful."

The foundation supports another schizophrenia initiative in the Department of Psychiatry—the Youth Psychiatrist Fellowship, now in its second year. Fellows work with University psychiatrists in the First Episode clinic and assist with imaging research, which helps the fellows gain expertise in early phases of the psychosis.

Help for patients can be possible even before a schizophrenia diagnosis is made, Schulz says. His department also is studying the disease's "prodromes," the nonspecific symptoms that can precede the onset of schizophrenia.

"Patients often hear muffled sounds, feel suspicious of others but are not delusional, or have trouble with grades," Schulz explains. "These people may benefit from therapy or low doses of medications. By acting so early, we hope to forestall or diminish the severity of the psychosis."

The Wells Family Fund of the Minneapolis Foundation has funded the hiring of a coordinator to launch a new prodrome program. The family's interest in early intervention goes back decades.

"Sixty years ago, after his son had schizophrenia, my great-grandfather gave money to the University for schizophrenia research," says Wendy Wells. "We're amazed at the kind of research they're doing, and [the possibility of] early intervention to delay or perhaps prevent the onset of schizophrenia is such an exciting prospect."

To learn how you can support schizophrenia research at the University of Minnesota, contact Cassidy Titcomb of the Minnesota Medical Foundation at 612-625-9613 or c.titcomb@mmf.umn.edu. Make a gift today at ***www.mmf.umn.edu/neuro.***

S. Charles Schulz, M.D.

ALS/PLS benefit raises research funding and spirits

Gwen and Curt O'Hagan say their event feels like "the most wonderful Christmas you've ever had."

Curt O'Hagan is fond of remarking that seven years after his diagnosis of primary lateral sclerosis (PLS), a degenerative motor neuron disease similar to the faster-progressing amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease), he is *still* a pest to his friends and family.

And they're thrilled about it. To honor O'Hagan, they generously support Curt's Classic, a golf event sponsored by Crystal Lake Golf Club in Lakeville to benefit PLS/ALS research at the University of Minnesota.

O'Hagan's PLS diagnosis, which followed his career as a longtime salesman for The Dow Chemical Company, did not come easily. After a series of inconclusive EMG scans, MRIs, and blood tests, he sought treatment from Gareth Parry, M.D., a neurologist who practices at the University's ALS/PLS clinic, one of the largest in the country.

"He diagnosed my PLS when nobody else could," O'Hagan says. The disease has greatly affected his speech, balance, and movement, and he now gets around with a walker or on an electric scooter for longer distances. But O'Hagan's wit and sense of humor remain untouched, and he puts them on display at Curt's Classic during a dinnertime speech that he writes and his sister delivers.

The origins of the golf benefit go back to a dog walk in 2007 when Gwen O'Hagan, Curt's wife, found herself asking God where he was in the midst of Curt's challenges. The next day, the manager of Crystal Lake Golf Club, where Curt and Gwen had both worked for years, said he wanted to organize a fundraiser in Curt's honor.

Within 45 days, the Crystal Lake staff and the O'Hagans put together an event that raised $12,200 and attracted 119 golfers and 200 attendees at the dinner and silent auction later that evening. In 2008 the event grew even larger and raised $15,600. The third annual event took place October 6 and raised an estimated $15,800.

The owners of the course donate golf time and facilities and staff plans the event, leaving all the proceeds for ALS and PLS research and treatment at the University.

"We're hoping to establish an endowment for pilot research studies that will lead to larger funding for pivotal research," Parry says. "We want to better understand the pathophysiology of the diseases and discover new treatments."

Curt O'Hagan's weekly routine now includes exercise, muscle stretching, appointments with a personal fitness trainer and chiropractor, and massage sessions. But the golf event creates a special energy.

"The feeling at the golf course is exciting, like the most wonderful Christmas you've ever had," Gwen O'Hagan says. "People return every year to reconnect, and the atmosphere is very upbeat and fun."

So in addition to needed funding, Curt's Classic has also raised the spirits of the person it honors. "We feel lucky for our friends, our family, and the activities that surround us," Gwen says.

Sign up for e-updates

Join our mailing list at **www.mmf.umn.edu/subscribe** to receive e-updates with the latest news about brain, nerve, and muscle diseases from the University of Minnesota.

the LINE UP

News from the Bob Allison Ataxia Research Center

BAARC grant allows expansion of vast DNA library

A $100,000 grant from the Bob Allison Ataxia Research Center is making possible a University of Minnesota resource that could help researchers solve the mysteries of a debilitating neuromuscular disease.

The funding will allow researchers to collect and store DNA samples from thousands of people with hereditary ataxia.

"Our primary purpose in creating the library is to try to understand the big picture of the genetic causes of ataxia," says Laura Ranum, Ph.D., who oversees the project.

The library will build upon an international DNA collection from ataxia patients and their families begun some 20 years ago, after the initial discovery of mutated genes that caused a few types of inherited ataxia. Analyzing the samples in the DNA library can help investigators discover the underlying mechanisms of other types of ataxia.

"The exciting thing is that whenever a disease-causing gene is discovered, we have something concrete to use in understanding how the disease works at the cellular level," Ranum says. "And we can look for similar mechanisms in other genes."

The library can illuminate the study of other genetic diseases as well. "These ataxia mutations affect very few families, so they haven't traditionally been the focus of large efforts to move genetics forward," she adds. "But we can use the ataxia collection to advance the study of genetics and biology in general."

Laura Ranum, Ph.D.

8th annual Karen's Hope golf event raises $62,600

The 8th Karen's Hope Ataxia Benefit—held June 15 at the Oak Marsh Golf Course in Oakdale—raised $62,600 this year for the Bob Allison Ataxia Research Center, an affiliate of the Minnesota Medical Foundation.

In its history, the golf event has raised more than $400,000 for ataxia research at the University of Minnesota.

Save the date for next year's event on Monday, June 14, 2010.

2010 DIAMOND AWARDS

Thursday, January 28, 2010
Hilton Minneapolis

Don't miss Minnesota's premier baseball charity event! This year's Diamond Awards, which is expected to draw more than 400 guests, will celebrate the Minnesota Twins 2009 baseball season and raise crucial funds for University of Minnesota medical research targeting brain, nerve, and muscle disorders.

Attendees of this 5th annual event will have the chance to mingle with current and former Minnesota Twins, be part of a televised awards dinner featuring baseball greats, and much more.

Since its inception, Diamond Awards has raised more than $2 million. Proceeds support the University's innovative research and patient care in ataxia, muscular dystrophy, multiple sclerosis, Parkinson's disease, and ALS (Lou Gehrig's disease).

Visit www.minnesotadiamondawards.org for more information and to find us on Facebook and Twitter.

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After a stroke, every minute counts

"Time is brain" is a familiar refrain in neurology circles. That's because the more quickly a stroke victim receives treatment, the greater the likelihood of recovery.

The most common kind of stroke, called ischemic stroke, is caused by a blockage of blood flow to a region of the brain. Ischemic strokes account for 85 percent of all strokes suffered in the United States each year.

The other 15 percent are called hemorrhagic strokes—those caused by bleeding that most often results when a weakened portion of a blood vessel, known as an aneurysm, bursts.

Thanks to quick work by physicians with the Zeenat Qureshi Stroke Research Center at the University of Minnesota, patients here are getting the critical treatment they need faster—when minutes can mean the difference between a quick recovery with few, if any, long-term effects and permanent disability or death.

At the Stroke Center, the elapsed time between a patient's arrival at one of its medical facilities and neurointervention is 43 minutes. Nationally, the average is 60 minutes.

What's more, at the Stroke Center, almost 20 percent of ischemic stroke patients receive acute neurological treatment to open the blocked vessel, in line with research showing that 20 percent of stroke patients need that type of care. Nationally, however, only 2 percent of patients receive acute treatment.

Formed in 2006, the Stroke Center is one of only a handful of its type in the country—with a cross-disciplinary team of doctors, nurses, and other specialists trained in interventional neurology, neurosurgery, or neuroradiology to improve outcomes for stroke patients.

"The science of stroke is expanding quickly," says Adnan Qureshi, M.D., executive director of the Stroke Center. "We are seeing advancements in both rapid diagnosis and treatment."

Neurosciences News Fall 2009

Published twice a year by the Minnesota Medical Foundation

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