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

Psychiatry 2.0

New leader brings inclusive approach—and an innovative treatment concept—to the University's Department of Psychiatry

A confident Sophia Vinogradov, M.D., stood at a podium in University of Minnesota Masonic Children's Hospital in September and addressed an auditorium filled with people eager to hear her take on the future of psychiatry at the U. She'd taken the helm of the Medical School's Department of Psychiatry just a few weeks earlier. This was her chance to sketch out her vision for the department going forward.

Afterward, an enthusiastic audience had clearly received the message: here was a new department head who was up for the task. "The biggest challenge facing the field of psychiatry today," Vinogradov says, "is the ever-widening translational gap between what we're learning through neuroscience research about the brain and how it functions, and how we use that knowledge effectively to help people."

This, she says, is her quest: to continue generating new knowledge that will alleviate suffering and, in the process, build the Midwest's premier psychiatry department.

Vinogradov comes to the U with a world-class résumé. She's an internationally recognized schizophrenia researcher, former vice chair of the Department of Psychiatry at the University of California, San Francisco School of Medicine, and former

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Photo by Brady Willette

Building a culture of trust is high on the priority list of new Department of Psychiatry head Sophia Vinogradov, M.D.

Psychiatry 2.0 *(continued from cover)*

associate chief of staff for mental health at the San Francisco VA Medical Center.

She comes to the University of Minnesota Medical School's Department of Psychiatry at a time of intense scrutiny. Last year, two reports called on the University to implement significant changes to better protect human research participants, especially those with diminished mental capacity.

"Dr. Vinogradov is the right leader to move reforms forward," says Brooks Jackson, M.D., M.B.A., dean of the Medical School, "and to build a new culture of trust and cooperation."

Jackson refers to the University's comprehensive work plan designed to strengthen its human research protections and commitment to ethics, a plan currently being implemented University-wide.

Vinogradov is already building on that work plan by establishing a Community Advisory Council for the Department of Psychiatry.

"I want to get the perspective of people not in the department—people who have the lived experience of mental illness, their family members, people from the nonprofit or legislative worlds," Vinogradov says. "Their points of view are so important to the work we do."

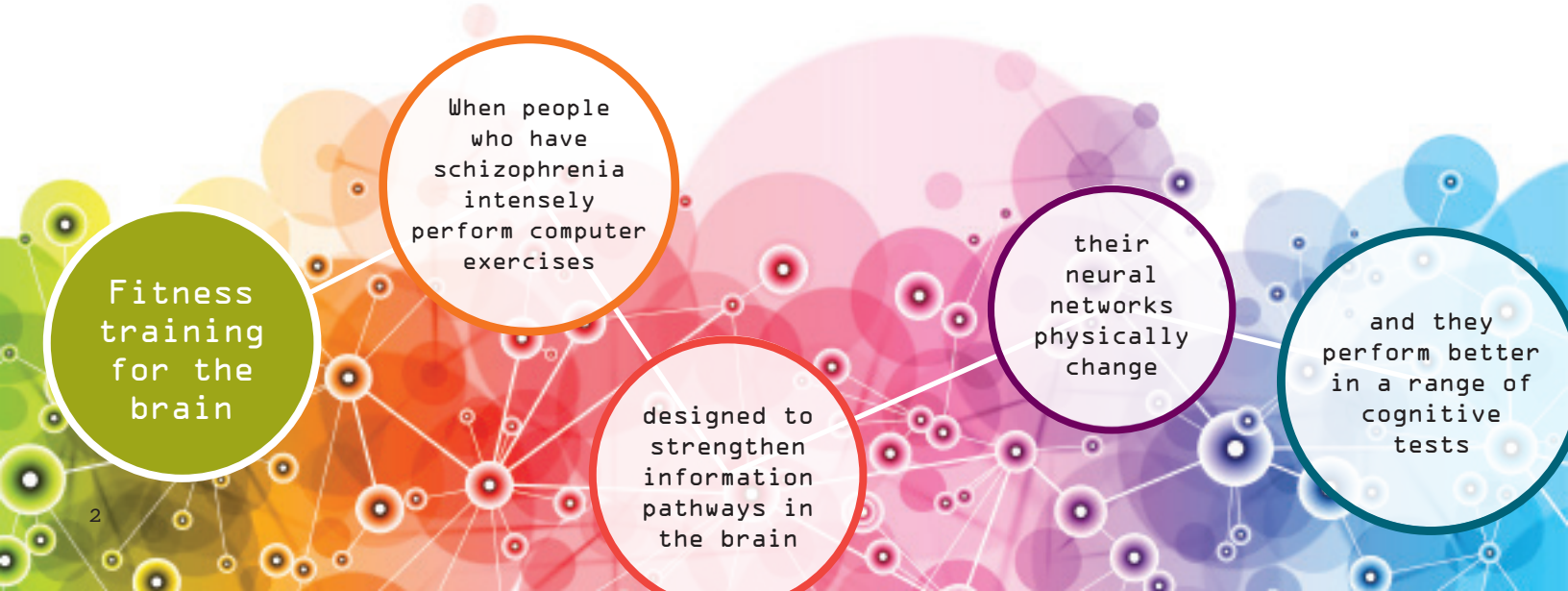
Beyond introducing specific reforms and councils, she also has committed to creating a culture of trust within her department so that people are driven to innovate.

"Neuroscience has proven that fear is a mind-killer," she says, "and that compassion and happy moods facilitate problem solving. We need to promote safe, open dialogue that acknowledges that we all make mistakes."

Brain training

Vinogradov's own research has focused primarily on what she calls "computerized brain exercises" designed to strengthen information pathways in the brain, which are weakened in people who have schizophrenia. In fact, many psychiatrists have come to believe that the cognitive difficulties faced by people who have schizophrenia are even more debilitating than the hallucinations also associated with the disease, she says.

Vinogradov has found that when people who have schizophrenia do these computer exercises intensively, their neural networks will physically change. In one study, she used specially designed computer software to put 55 people through brain "fitness training." After the volunteers had completed the computer training, Vinogradov found that they performed better in a range of cognitive tests, including memory and verbal learning, than other volunteers in a control group who instead had played simple computer games. Vinogradov's work in this area was named one of the Major Discoveries of 2012 by the Brain and Behavior Research Foundation.



THE STORY BEHIND THE

Frederick B. Wells Jr. Fund

Frederick Brown Wells was a prominent Minneapolis businessman in the first part of the 20th century. He rose through the ranks at grain dealer F. H. Peavey & Company and was married to one of the owner's daughters, Mary Drew Peavey.

One of the couple's four children, Frederick B. Wells Jr., however, struggled with dementia praecox, which would later become known as schizophrenia. That prompted the senior Wells to establish the Frederick B. Wells Jr. Fund in 1944 in his son's honor. More recently, now that the children and grandchildren Wells named as beneficiaries have passed away, the money has become available for research into schizophrenia prevention, management, and treatment at the University of Minnesota.

Because the value of the Wells fund today is so large—to date totaling about $14 million—it will distribute about $900,000 annually to the Department of Psychiatry for this work. It remains one of the most generous gifts to the University (and the largest for mental health research) in the institution's history.

Photo by Lee Brothers, courtesy of Minnesota Historical Society

The generosity and foresight of the late Frederick Brown Wells, in this photo dated 1917, today provides the University's Department of Psychiatry with about $900,000 annually for schizophrenia research.

Not surprisingly, given her expertise in this subject, Vinogradov hopes to get a treatment center for this kind of brain training up and running quickly in Minnesota. Key to that effort, and others, is the Frederick B. Wells Jr. Fund, a philanthropic gift that allocates about $900,000 annually for schizophrenia research at the University (see above).

"That endowment was really part of the draw for me to come to Minnesota," says Vinogradov. "This generous, farsighted endowment will allow me to seed ideas that are so hard to get traditional funding for, to get new programs off the ground. The impact of the Wells trust just can't be overstated."

'The pieces are in place'

During her September presentation, Vinogradov shared an image of the Grand Canyon, an image she says symbolizes the gap between the impressive advances happening in neuroscience research and how doctors in the field diagnose and treat patients. She calls it the "translational gap."

"I strongly believe that we need to commit to generating new knowledge that will alleviate suffering," she says. "To take the incredible knowledge we're gaining through research and translate it into new ways to help people—that's why we're here, right?"

As part of this plan—one she calls "Psychiatry 2.0"—Vinogradov also intends to engage a new army of helpers, formerly known as research volunteers, whom she calls "citizen scientists." She envisions that these urgently needed citizen scientists will share information to help physicians generate personalized care plans that are grounded in neuroscience.

And she's confident that the team she's creating will come together to achieve greatness.

"The University of Minnesota already has world-class neuroimaging capabilities, incredible researchers working in the neurosciences, and one of the best public health schools in the nation," she says. "We also have a clear opportunity here to create the preeminent psychiatry department in the Midwest. All the pieces are in place. Now it's time to capitalize on those many, many strengths."

In it for the long haul

With donor support, U researchers are getting closer to a cure for Alzheimer's disease

How can we stop Alzheimer's disease? It's a question that has challenged University of Minnesota neuroscientist Karen Hsiao Ashe, M.D., Ph.D., for her entire career.

"Research is sort of like a baseball game," says Ashe, who is founding director of the University's N. Bud Grossman Center for Memory Research and Care. "Not much happens for a while, and then someone hits a homerun."

Ashe's research is centered on finding what causes Alzheimer's, with an end goal of stopping, reversing, or even preventing the disease process. She and her team narrowed in on the protein tau, believed to contribute to cell death and memory impairment, as the likely culprit about 12 years ago. Tau is normal and healthy for the body, but in people who have Alzheimer's disease, it changes and clumps together irregularly.

In a new study using mice modeling human Alzheimer's disease, they looked for a mechanism that could be affecting tau and found that caspase-2, a naturally occurring enzyme, may be to blame. The researchers also discovered that tau accumulates in neurons when caspase-2 "cuts" healthy tau at a particular point. The research was published in the prestigious journal *Nature Medicine* in October and was funded by the National Institutes of Health, the Thomas M. Grossman Family Charitable Trust, Beverly Grossman, and Karin Moe.

By reducing levels of the enzyme or preventing it from cutting tau entirely, Ashe believes, it could be possible to recover memory deficits or even restore cognition.

Finding a compound to accomplish this, of course, is the first step in a long and expensive process—one that will cost hundreds of millions of dollars, Ashe estimates. Universities alone can't afford this; drug companies are essentially the only ones who can.

That's why Ashe has partnered with a drug company on the next phases of the research. Her lab is currently screening 21,000 compounds from the company in hopes of identifying a few for further development and testing. Her lab also will screen existing medications in case there's a drug already on the market that could be used against Alzheimer's.

It's an enormous task, and it left Dwight and Patsy Broome wondering how the approximately $85,000 they raised from constituents of their National Rural Letter Carriers' Association Auxiliary could matter.

Ashe says the money is absolutely useful in supporting all of the background work needed to find the elusive Alzheimer's cure. To her, donors' financial support and confidence are equally significant.

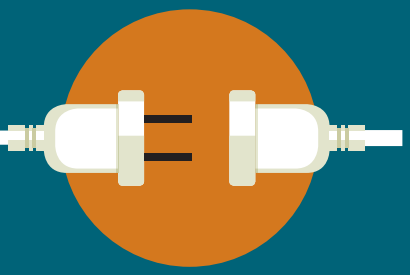
"The faith that people have in us is really, really important, and it translates into inspiration and working harder and being creative and not giving up," she says. "The human intangible gift is just as important as the check."

Support this research at ***give.umn.edu/giveto/ashelab.***

Patsy and Dwight Broome, with Karen Kaler (far left, who is University President Eric Kaler's wife) and neuroscientist Karen Hsiao Ashe, M.D., Ph.D. (second from left), traveled across the country to raise awareness of Alzheimer's disease and money for research at the University as part of the National Rural Letter Carriers' Association Auxiliary's annual "Program of Miracles" drive. At every speaking engagement, Dwight Broome would ask how many people knew someone affected by dementia. "Just about everybody raised their hands," he says.

Photo by Jim Bovin

Rewiring the unwired



A personal quest to better understand schizophrenia could show the way to more effective treatments

A rhyme coined by a Canadian neuropsychologist in the 1940s—"neurons that fire together, wire together"—may yield an important clue to unlocking the mystery of schizophrenia.

Or rather, its corollary might. That's the exciting theory of University of Minnesota neuroscientist Matt Chafee, Ph.D., who suspects that a timing glitch in neural "firing" could be the cause of the brain "unwiring" that manifests as schizophrenia. If so, it opens up a new world of treatment possibilities.

For Chafee, the quest to better understand and treat schizophrenia is personal. His beloved older brother has suffered from it since age 16.

"[He] is one of my favorite humans—an amazing individual, a really lovely person," Chafee says. "And he has been absolutely heroic with this disease. The amount of suffering this causes … it shouldn't have to happen to anybody."

Besides their clinical symptoms, people who have schizophrenia experience certain cognitive deficits, Chafee explains. "We have cognitive tasks that can measure those deficits." In animal studies, he has been able to replicate the same specific disruption of the synaptic process that may cause schizophrenia—and has seen exactly the same temporary cognitive failure patterns.

"We train them to perform the same tasks, and give a compound that temporarily blocks the synaptic receptor in the brain that's thought to be dysfunctional in the disease, the NMDA receptor," he says. "Then we measure deficits."

If his theory holds up, Chafee believes it could show the way to more effective treatments. And not just for schizophrenia, but potentially for other neuropsychiatric disorders as well, including autism spectrum disorder and bipolar disorder.

These aren't neurodegenerative diseases, Chafee explains: there's no cell death, but rather an "unwiring" process. If the brain can "unwire" itself, it's likely possible for it to "rewire" itself, he says.

That "unwiring" may well be reversible through electrical stimulation, Chafee speculates. "By forcing greater synchrony in circuits, that might allow them to rewire," he says. "It could be transcranial direct current stimulation. It could also be deep brain stimulation. There are other electrical stimulation methods that are noninvasive that could be restorative."

A $500,000 anonymous gift is helping to support Chafee's research, and he hopes that additional support will allow him to sustain and expand crossdisciplinary collaboration with colleagues in psychology, computational neuroscience, functional imaging, biomedical engineering, and other areas.

"We are finding amazing cross talk," Chafee says. "Our hope is that we can build a multilab structure and continue connecting the dots, from molecules to cognition."

To make a gift to this research, contact Catherine McGlinch of the University of Minnesota Foundation at 612-626-5456 or mcgra022@umn.edu.

Thanks a BILLION!

The University of Minnesota Foundation's Vision 2017 fundraising campaign to advance medicine and promote health at the University of Minnesota, including brain, nerve, and muscle health, was a huge success. It was so successful, in fact, that we surpassed our $1 billion goal 15 months early. Here are a few reasons we're celebrating:

$131,776,218

total raised for neurosciences-related research, education, care, and outreach at the University of Minnesota during the campaign, including private gifts and private grants

20,309

gifts made to the neurosciences during the campaign

9,250

people gave to the neurosciences at the U during the campaign

$8 million

largest gift made to the neurosciences during the campaign, from an anonymous donor for research into curing macular degeneration and repairing spinal cord injuries

Elite Certification

The University of Minnesota Health Stroke Center joined the ranks of roughly 100 elite stroke treatment centers nationwide in June when it received the Joint Commission's Comprehensive Stroke Center certification.

The certification confirms the M Health Stroke Center's position as a top regional center for acute stroke care with expertise in treating a full range of cerebrovascular diseases. The recognition followed a lengthy evaluation process conducted by the Joint Commission, which includes rigorous standards for patient care, education and research, the expertise of providers and staff, and diagnostic and treatment capabilities.

At the M Health Stroke Center, led by neurologist Mustapha Ezzeddine, M.D., patients can receive care from specialists in stroke neurology, neurosurgery, neurointerventional care, neurocritical care, physical medicine and rehabilitation, and emergency medicine. This multidisciplinary approach also includes coordinated care from speech, physical, and occupational therapists; social workers; care coordinators; nurses; and pharmacists. The center's outpatient clinic provides evaluation, consultation, procedure planning, and follow-up.

The M Health Stroke Center also is the regional coordinating center for the National Institutes of Health–funded StrokeNET, the national research network for the advancement of acute stroke treatment, recovery, and prevention.

Join the Minnesota Twins, the Twin Cities chapter of the Baseball Writers' Association of America, and the University of Minnesota on **Thursday, January 26,** for a celebration of baseball and philanthropy.

Enjoy an evening indoors at Target Field, bid on rare baseball memorabilia, be part of a televised awards dinner featuring current and former Twins, and celebrate 2016 Diamond Awards winners.

Proceeds benefit the University's innovative research and patient care in ALS (Lou Gehrig's disease), ataxia, multiple sclerosis, muscular dystrophy, and Parkinson's disease. For more information or to purchase tickets, visit ***diamondawards.umn.edu.***

The Line Up

News from the Bob Allison Ataxia Research Center

Ataxia is personal for clinic's new physician

Lawrence Schut, M.D., was just a scared 5-year-old when he first heard the word "ataxia." He'd just seen his father's cousin Alice battle through a choking attack. Later, his dad, Henry, gently explained that Alice had a condition called ataxia.

But as Schut would learn, it wasn't just Alice who had ataxia, a neurodegenerative condition marked by a loss of motor coordination, slurred speech, and vision and swallowing problems. A type of deadly, hereditary ataxia called spinocerebellar ataxia type 1 (SCA1) pervaded the extended Schut family; ultimately, it would kill more than 65 of his relatives over five generations.

"We were a close family and had reunions every summer," Schut remembers. "We loved to play baseball, but every year there would be someone else who couldn't run the bases anymore. And always three or four people in wheelchairs. And others missing, who, we'd learn, had died before they even turned 40."

Schut was hardwired to learn more. He became a neurologist, completing his residency at the University of Minnesota in 1966; in 1990, he started the U's first ataxia clinic. And now Schut has "unretired" to once again join the ataxia clinic, seeing patients who carry the same SCA1 gene, traced back in his family to 1915, but also those who have one of the other 40 known types of ataxia.

Minnesota has been called "ground zero" for ataxia research and treatment, and much credit for that goes to the Schut family. Henry Schut and his brother, John Schut, M.D. (a neurologist who developed the disease and died of it), started the National Ataxia Foundation (NAF) at the kitchen table in Henry's Maple Lake farmhouse in 1957. Today, NAF emphasizes education and awareness, though research into the cause and cure of ataxia remains the highest priority.

Pioneering University of Minnesota scientist Harry Orr, Ph.D., who recently became the inaugural holder of the Bob Allison Ataxia Research Center Chair, was the first to identify the gene that causes SCA1, in 1994. He has had a long relationship with the Schut family—several family members have even volunteered in his lab over the years. Orr continues to seek an effective treatment.

"In our family, it was the support of the kinship, and then genetic counseling and intervention, that made a huge difference," says Schut. "There's much work still to be done, but scientists like Harry Orr are really helping this disease."

And let's not forget Schut himself, still dedicating much of his life to the fight against ataxia, even during his "retirement."

Neurologist Lawrence Schut, M.D., is carrying on the quest to advance knowledge about ataxia that his Uncle John and father, Henry (in picture), started nearly six decades ago. Ataxia has claimed the lives of more than 65 members of the Schut family, including John.

Photo by Tim Rummelhoff

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ELECTRONIC SERVICE REQUESTED

A mark of excellence in Parkinson's research

"It's like a pacemaker for the brain." That's how neurologist Jerrold Vitek, M.D., Ph.D., describes deep brain stimulation, a surgical procedure that's used to control the life-altering tremors associated with Parkinson's disease.

Today the University of Minnesota is part of an elite group of eight academic medical centers across the country to be named a Udall Center of Excellence for Parkinson's Disease Research.

With more than $9 million in National Institutes of Health support over five years, the U team is charged with defining changes in brain circuitry that cause Parkinson's and then using that information to improve deep brain stimulation and develop new treatments for the disease. Specifically, they will:

- Study changes in brain circuitry that affect patients with Parkinson's disease using brain imaging and intraoperative techniques that Vitek pioneered;
- Develop new approaches for stimulating the pallidum, a region of the brain that's important for controlling voluntary movement; and
- Explore the effects of stimulation on brain circuitry that mediates movement problems associated with Parkinson's.

"We have the best [deep brain stimulation] program in the country, if not the world," says Vitek, head of the Medical School's Department of Neurology, who will lead the Udall effort at the University. "We have researchers from biomedical engineering to clinical practice to imaging, neurosurgery, neurology, neuroscience, etc. We're a broad, diverse group. We bring a lot to the table."

Watch a video about what sets the University of Minnesota apart at ***udall.umn.edu****.*

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