Better together

A U research team hopes that focusing on stroke recovery will bring about ways to help patients regain lost function

Stroke is one of humanity’s most feared medical misfortunes. In the United States alone, it confines 800,000 people every year, has left 6.5 million survivors, and is the leading cause of disability.

Triggered by ruptures or blockages of blood vessels in the brain, stroke kills brain cells and leaves a multitude of long-lasting effects that include weakness in limbs, dizziness and imbalance, and the loss of vision and speech. It kills about 140,000 people annually in the United States.

Because stroke primarily hits older people, some think of it as an inevitable and impossible-to-treat consequence of aging. But not biomedical engineer Bin He, Ph.D., physical therapist James Carey, Ph.D., P.T., neurosurgeon Andrew Grande, M.D., or neurologist Mustapha Ezzeddine, M.D., at the University of Minnesota. Their collective research holds the potential for limiting the permanent damage that stroke leaves behind.

He, for instance, has long been fascinated by the teamworking potential of brains and computers. He and his colleagues have developed technologies to help people with paralysis from spinal cord injuries. In their research, continued on page 2
Subjects have learned how to remotely move and manipulate robotic objects with the help of skull caps that detect electroencephalogram (EEG) brain waves and a brain-to-computer communications interface (BCI) that translates the EEG signals into commands for the robotic devices.

Recently, He and his team have tried their technology with stroke patients, a transition sparked by the experiences of one of He’s colleagues who had a stroke.

“That was a shock to me, and it made me think about how BCIs can help treat stroke,” says He, who directs the U’s Institute for Engineering in Medicine and Center for Neuroengineering and holds the Medtronic-Bakken Chair for Engineering in Medicine.

His team began by training patients to think in a way that generates EEG signals that direct a computer to move a cursor on a screen. With that goal achieved, the next step was even more challenging, a project designed for stroke patients without muscular control of their hand.

Based on the motor-imagination abilities intact in many patients, merely thinking about moving a paralyzed limb could generate useful EEG signals. “We developed a virtual hand, and we trained the subjects to control that virtual-reality hand to grasp a virtual cup,” He says. “They saw that their brain makes them able to do that.”

Using this technology, he says, it might be possible to stimulate and reactivate injured brain tissue to restore function. He hopes it will one day become standard treatment for stroke patients.

Strengthening through inhibition

Carey, a professor in the Medical School’s Program in Physical Therapy, is involved in yet another innovative approach to treating stroke. Carey and his colleagues, which include He and Grande, are investigating the perhaps counterintuitive idea that an effective way to strengthen the areas of the brain injured by stroke is to temporarily inhibit the healthy parts.

The researchers inhibit the healthy brain hemisphere using repetitive transcranial magnetic stimulation (rTMS), a noninvasive and painless technology that applies a weak magnetic pulse directly to a person’s head. Because the healthy side can have a suppressive effect on the stroke-affected side, inhibiting the healthy hemisphere can ultimately excite surviving neurons in the stroke-affected hemisphere. This can help certain patients gain better use of their stroke-affected hand.

After the patient’s exposure to rTMS, “we ask the subject to do a task, such as moving a cursor on a computer screen and using their stroke-affected hand to follow a target over and over,” explains Carey, who has researched this approach since 2006.

“The patient benefits from the rTMS stimulation and the motor learning training at the same time,” he continues, a combination that may be more effective than either approach separately.

This technique appears to help some types of stroke patients. “The location of the stroke is one factor, and the age of the subject is another,” Carey says. “It will take more time and studies to determine what are the other absolute factors. Perhaps genetics and life habits are factors that need to be ferreted out.”

A cell transformation

Grande, an assistant professor of neurosurgery and codirector of the University’s Earl Grande Stroke and Stem Cell Laboratory, is also active in basic science research that approaches stroke recovery from a different direction.
“People have functional impairments after stroke because brain neurons have died in the area of the stroke,” he says. “Our approach is to regenerate neurons that have been lost, and to have those new neurons establish connection with existing brain circuits to lead to a recovery of function.”

Since human stem cells were discovered in the 1990s, neuroscientists have known that stem cells from skin or other sources can regenerate over time to replace damaged cells of many types. More recently, researchers have tried transplanting stem cells into the brain to replace damaged neurons. But these transplants rarely survive, as they can be rejected or form tumors, making them less than ideal.

So Grande’s lab is trying a new approach. “What we’ve done,” he says, “is to try to change a cell already in the brain into a neuron. We’ve taken glial cells [nonneuronal cells that provide support for neurons in the nervous system] already in the area of the stroke damage, and converted them into neurons.”

Grande’s team achieves that transformation using genetic reprogramming to alter the glial cells so they become immature neurons. From there, the hope is that the immature neurons grow into mature neurons that can connect with already extant neurons.

“It’s like taking an apple and turning it into an orange,” he says of the transformation from glial cell to neuron. “Ultimately, it could provide the means for a recovery of function after stroke.”

In current stroke treatment, patients generally achieve only limited recovery after a critical window of time has passed, Grande notes. “After that, what can you do? That’s where reprogramming for regeneration can help,” he says.

**Critical mass**

The breadth and depth of stroke research at the U isn’t going unnoticed. The University was named one of 25 large medical centers collaborating in StrokeNet, a research network formed in 2014 by the National Institutes of Health in an effort to gain efficiency by creating a national infrastructure that focuses on stroke prevention, recovery, and rehabilitation. StrokeNet partners conduct multiple trials for the network, contribute their own ideas for new trials, create regional research centers, and train the next generation of stroke researchers.

Along with the Neurological Emergencies Treatment Trials (NETT) Network, to which the University also belongs, StrokeNet fosters repeat teams of researchers and administrators, which brings “a much greater degree of efficiency than if every trial had to bring together new physicians, coordinators, and regulatory people,” says Ezzeddine, the medical director of stroke services at University of Minnesota Medical Center and the U’s principal investigator for StrokeNet.

With that efficiency and the innovative approaches University investigators are taking to improve recovery after a stroke, the future looks brighter. Yet much more is possible.

“It is amazing what we can accomplish when there is an intense research focus on a problem,” Grande says. “Look what we’ve done with Ebola and HIV. We need a similar focus on stroke.”

Photo by Scott Streble
Philanthropists’ seed money leads to a major grant focused on why some people battling addiction have more trouble staying sober than others

More than 23 million Americans struggle with addiction to alcohol and drugs—and “struggle” is really an understatement.

“The data tell us that, after treatment, roughly two-thirds of addicts will resume using within a year,” says Kelvin O. Lim, M.D., a professor of psychiatry at the University of Minnesota Medical School and holder of the Drs. T.J. and Ella M. Arneson Land-Grant Chair in Human Behavior. “That’s a really discouraging number.”

Why does one person succeed at sobriety while another two stumble? That’s a question that drives Lim’s research, investigations that recently led to a $2.6 million grant from the National Institute of Drug Abuse (NIDA) to delve more deeply into the differences in the brains of people battling addiction who stay abstinent or relapse.

In the preliminary study, funded by philanthropists Wendy Wells and Norm Cocke, Lim used magnetic resonance imaging to measure the strength of the signal that runs between what he calls “the brain’s reward center—the part that gives addicts such a sense of pleasure—and the prefrontal cortex—the part that says, ‘Hey, slow down, we have to think about this.’” Lim and his team learned that the stronger the signal was, the more likely the addict was to remain abstinent; a weaker signal indicated a higher likelihood of relapsing quickly.

In this work, the technology at the U’s world-renowned Center for Magnetic Resonance Research is his secret weapon. “This is cutting-edge equipment,” he says, “the best in the world, that allows us to do this kind of research. It’s a fantastic resource.”

Now, with the NIDA grant, he’s embarking on a five-year study, in partnership with the Hazelden Betty Ford Foundation, to look at 120 people addicted to stimulants like cocaine or methamphetamine. He’ll take images of their brains three times each, at five, nine, and 13 weeks into their abstinence. He’s looking to identify a marker, that elusive signal, that could allow doctors to one day predict which people in recovery are likely to have the most trouble staying sober.

“If we really can predict relapse,” Lim says, “then our next step is developing strategies that strengthen that brain signal. That’s the kind of personalized medicine we’re working toward.”

Wells, whose two siblings died from addiction-related causes, is thrilled that her seed money resulted in such a successful project. “Honestly, I think the money I gave Dr. Lim might be the best investment I ever made,” she says.

“The propensity to become addicted, why some stay addicted while others transition into abstinence—these are complex questions,” says Lim. “We have hints to the answers, we see a path for exploration, but we still have a lot of work to do.”
Never too early

A University scientist and his wife found their estate planning process fulfilling and even ‘fun’

She has a passion for helping children and families struggling with serious illness; he’s committed to advancing neuroscience research. Together, Katie and Christophe Lenglet crafted an estate plan that honors both priorities and ensures that what they’re earning now will help others when they’re gone.

The Lenglets are young—27 and 35, respectively—and as Christophe says, “we don’t have a lot right now. We’re not going to be able to write a big check tomorrow. But we can do this.”

And they want to spread the word that philanthropy isn’t just for the affluent: Creating an estate plan that nurtures what you value is both simple and rewarding.

Katie Lenglet is a physical therapy student who has long volunteered with children and parents. That, combined with her family’s experiences—Katie’s sister battles a rare form of cancer—has shown her the grueling challenges families face when a child needs ongoing medical care.

“It’s heartbreaking to see what families of very sick children go through,” Katie says. So part of the Lenglets’ estate gift is earmarked to help families of patients who have pediatric neurological conditions. “It’s practical help: Here’s money for dinner. If you have another kid in soccer and you have [a medical] appointment, here’s money for the babysitter. Here’s help with hotel costs, with travel bills.”

The other part of the Lenglets’ gift will support pediatric neuroscience research.

Christophe is a McKnight Land-Grant Assistant Professor at the Center for Magnetic Resonance Research and an Institute for Translational Neuroscience Scholar. Much of his work has focused on developing imaging and analysis methods for brain diseases such as ataxia.

Christophe himself has benefited from philanthropy: “I go through the process of looking for money. I know how hard it is. Philanthropy has helped me a lot. UMF [University of Minnesota Foundation], BAARC [Bob Allison Ataxia Research Center], we’re writing papers now, thanks to them.”

Starting a conversation about wills isn’t always easy, but it ended up being “fun,” Christophe says. “The idea of thinking about what you could do with whatever you have, however much that is, to us that’s fulfilling. You know you’re going to have some kind of impact.”

Katie finds the culture of philanthropy at the U inspiring. “I like being involved in a community like that, of people—including a lot of physicians at the U—who want to give back.”

To learn more about planned giving opportunities at the University of Minnesota, contact Catherine McGlinch at 612-626-5456 or mcgra022@umn.edu, or visit plannedgiving.umn.edu.
Sally Rothmeyer still remembers the day in 1994 when she started feeling a little “off.” The Apple Valley, Minn., resident had recently returned home from a Twins game in Baltimore, so she attributed her dizziness to the previous day’s travel.

But when Rothmeyer tried to get out of her bed that morning, “it was as if someone slapped me back down,” she says.

She immediately went to see her primary care physician, and later a community otolaryngologist and a neurosurgeon, but she kept having dizziness episodes that sometimes included falling. Her friends insisted that she get another opinion.

Rothmeyer wanted to go somewhere “big,” so she chose the University of Minnesota.

“I remember being in the office at the U and calling one of my friends,” she says. “I told her, ‘I think I’ve been shopping at Kmart, and I’ve landed at Saks Fifth Avenue.’”

Her care team at the U included neurosurgeon Stephen Haines, M.D., and otolaryngologist Samuel Levine, M.D. Using fairly new imaging technology for the time, they detected an acoustic neuroma—a tumor that arises in the ear’s internal auditory canal, the tunnel through which balance, hearing, and facial control nerves run.

Because of the tumor’s placement and the nerves involved, there was a chance that if Haines and Levine used the standard procedure to remove it, Rothmeyer could lose hearing in that ear.

Fortunately for Rothmeyer, Haines and Levine had been researching a new neuroma-removal technique.

“When we switched to the new approach, our results immediately improved,” Haines says. “About 70 percent of our patients retained their hearing.”

Rothmeyer would become one of the earliest patients to have surgery using this technique, which is still used today. She came out of surgery with her hearing intact.

And now, more than 20 years later, Rothmeyer is helping the University team gather evidence to answer another important question: Do patients whose hearing was preserved using this technique undergo a natural age-based hearing decline, or do they lose their hearing more rapidly?

Haines and Levine had initially published the improved results they were getting using the new surgical technique in 1993. As more patients had the procedure, Levine kept adding them to a database he’d started. “The thing that’s powerful is when you get 25 to 30 years’ worth of data,” he says.

As part of the current study, Rothmeyer went back to the U to have her hearing and facial control evaluated. Her information was added to Levine’s database.

“If it turned out that we preserved hearing right after surgery, but it was all gone in five years, that wouldn’t be a strong reason to have the operation,” says Haines. “But if it’s going to last the rest of their lives, it would make a huge difference in indication for the surgery. It made a big difference for Sally.”
Hear ye, hear ye

Governor proclaims Sept. 12 as Dr. Harry Orr Day in Minnesota

Renowned ataxia researcher Harry Orr, Ph.D., has received many awards throughout his decades-long career at the University of Minnesota, but this was a first.

Gov. Mark Dayton's office declared September 12, 2015, Dr. Harry Orr Day in Minnesota.

The Minnesota-based National Ataxia Foundation (NAF) nominated him for the honor. NAF President Bill Sweeney presented Orr with the official proclamation at Wolfe Park in St. Louis Park that day as part of the organization’s annual Minnesota Walk, Stroll, ‘n’ Roll for Ataxia Awareness event before a crowd of more than 400 supporters.

The proclamation reads:

Whereas: Dr. Harry T. Orr has taught and performed important, award-winning research for many years at the University of Minnesota and its Medical School; and

Whereas: Dr. Orr is the Tulloch Professor of Genetics, and directs the Institute for Translational Neuroscience at the University of Minnesota; and is a Professor of Pathology at the University of Minnesota Medical School; and

Whereas: Dr. Orr was jointly responsible for first identifying the defective gene causing a type of Spinocerebellar Ataxia in 1993; and

Whereas: Dr. Orr has authored/coauthored more than one hundred studies and medical/scientific articles relating to the genetics and pathology of ataxia; and

Whereas: Dr. Orr has overseen the work of a generation of researchers and Ph.D. candidates who have gone on to work in ataxia research; and

Whereas: Dr. Orr is the Director of the Research Advisory Board and serves on the Board of Directors of the Minnesota-based National Ataxia Foundation; and

Whereas: In 2014, Dr. Orr was elected to the prestigious Institute of Medicine of the National Academies (IOM); and

Whereas: With the potential of clinical studies looming, Dr. Orr’s contributions may accelerate progress in treating ataxia by years.

Now, therefore, I, Mark Dayton, Governor of Minnesota, do hereby proclaim Saturday, September 12, 2015, as Dr. Harry Orr Day in the state of Minnesota.
A new device is designed to reset the brain when it detects an oncoming seizure

For people who have difficult-to-control epilepsy, there’s a new treatment option available through University of Minnesota Health.

The NeuroPace® RNS® System uses electrodes implanted in the brain to monitor brain wave activity and detect seizures before they take hold. The device is programmed to administer electric stimulation to the brain to stop the seizure and restore normal brain function. It’s the most advanced FDA-approved neurostimulation device available in Minnesota.

“I think it’s exciting from many perspectives,” says neurologist Thaddeus Walczak, M.D., director of M Health MINCEP Epilepsy Care, a national Level 4 Epilepsy Center. “It will allow us to help a lot of patients who didn’t benefit from surgical treatment in the past.”

Traditional epilepsy surgery is not an option of the brain or start in areas critical to normal function, Walczak says. But the RNS can help in these situations.

Because the device continuously records brain wave patterns—including activity that occurs leading up to and during a seizure—physicians will have a better understanding of how many and what types of seizures patients are having, Walczak says. “In that sense, it’s revolutionary.”

Walczak hopes that improvements to the device will eventually allow precise, on-demand treatment for seizures.

“Using medications to treat seizures requires continuously treating the brain to prevent something that only occurs occasionally,” he says. “It would be really nice to treat the brain only when it needs to be treated.”