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

Interpreting complex connections

U takes a leading role in the Lifespan Human Connectome Project, phase two of a national brain mapping initiative

More than six years ago, the University of Minnesota spearheaded the technological advances behind the most ambitious brain imaging study ever conducted, the Human Connectome Project. It mapped the vast network of about 90 billion neurons and trillions of interconnections in the brains of young, healthy adults at the millimeter scale.

The U's Center for Magnetic Resonance Research (CMRR) developed the imaging methods and directions on reconstructing the images to make sense of the data. Colleagues at Washington University in St. Louis did the bulk of the brain scanning—in total, 1,200 volunteers—and, together with investigators from Oxford University, developed the image processing pipelines.

Findings from this National Institutes of Health (NIH)-funded project, now complete and celebrated as a success, are publicly available to scientists and anyone else who wants them. The insights gleaned so far are fascinating.

"Our consortium [found] that the brain networks that we can detect very much correlated with behavioral measures, lifestyle measures," says CMRR director Kamil Ugurbil, Ph.D. "For example, they are correlated very strongly with IQ, with education, with drug use or alcoholism, etcetera."

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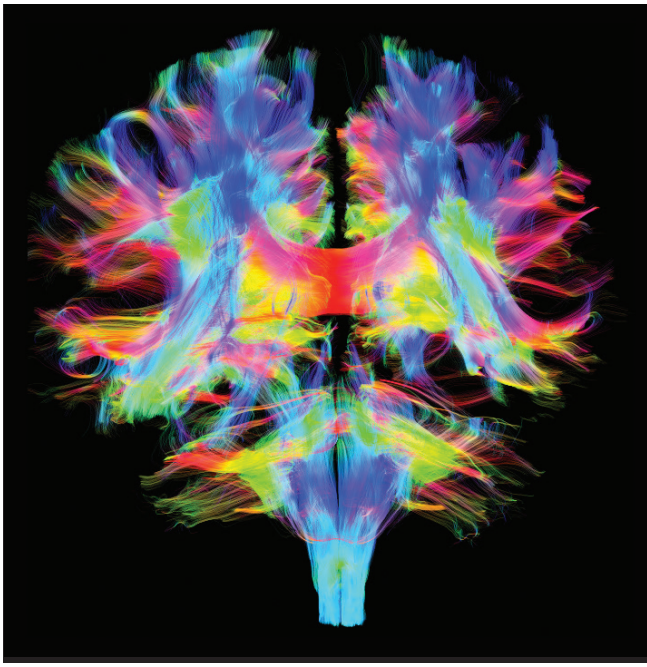


Images derived from Human Connectome Project data give researchers unprecedented views of the brain.

Image: Vu, A.T., Auerbach, E., Lenglet, C., Moeller, S., Sotiropoulos, S.N., Jbabdi, S., Andersson, J., Yacoub, E., Ugurbil, K., 2015. High resolution whole brain diffusion imaging at 7T for the Human Connectome Project. Neuroimage 122, 318-331.

Interpreting complex connections *(continued from cover)*

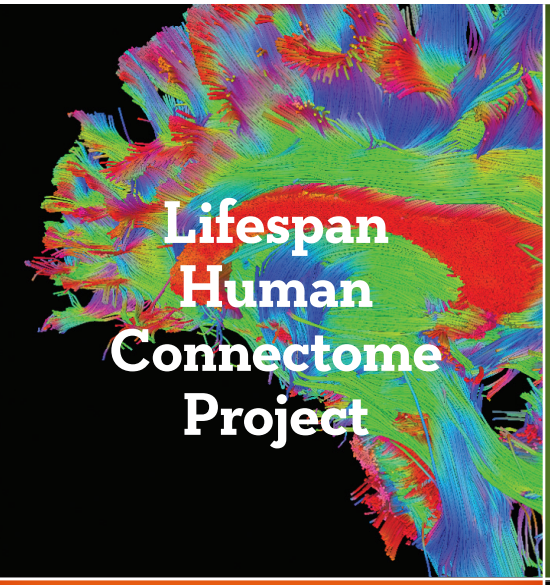
Other researchers used the Human Connectome Project data to show that brain networks are unique to individuals, much like fingerprints. That's encouraging, Ugurbil says, because if researchers can identify networks unique to individuals, they may be able to identify abnormalities unique to individuals as well.

What's next? Extensions of this immense undertaking (see below). The NIH is now funding a Lifespan Human Connectome Project, designed to track normal brain changes in humans from infancy to "as old as we can get," Ugurbil says.

The NIH is also funding 13 connectome projects focused on specific neuropsychiatric diseases to identify where and how alterations occur—and potentially to find ways to intervene with disease processes.

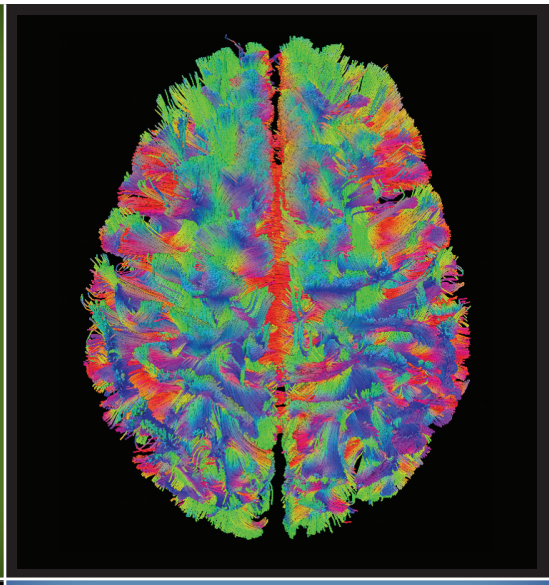
"Predominantly, this drive comes from the hypothesis that all neuropsychiatric diseases are circuitry diseases and you cannot study them with just normal magnetic resonance imaging," says Ugurbil.

U psychiatry professor Scott Sponheim, Ph.D., is leading one such project on schizophrenia (see sidebar on page 3).

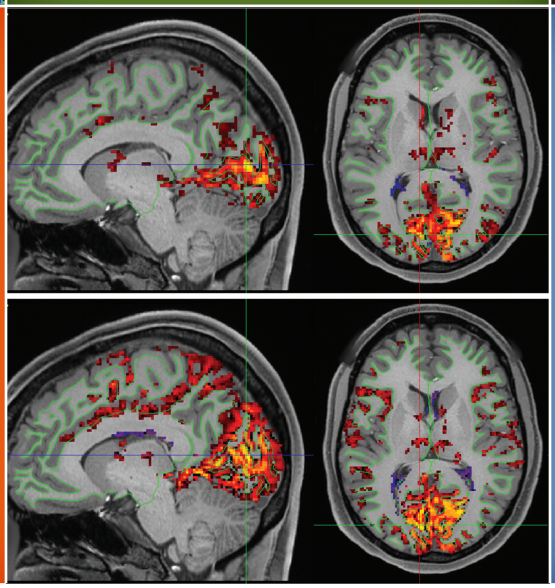


Lifespan Human Connectome Project

The Baby Connectome Project focuses on children from birth to early childhood to map structural and functional changes that occur in the brain during typical development. The U's Jed Elison, Ph.D., McKnight Land Grant Professor, and Ugurbil will lead this effort with partners at the University of North Carolina.



The Lifespan Human Connectome Project: Development targets ages 5 to 21 and will track changes in the brain, behavior, and mood as children move through puberty. The U's Essa Yacoub, Ph.D., and Kathleen Thomas, Ph.D., will lead this arm of the study, which also takes into account physical and mental health, thinking and decision-making skills, and behavioral and emotional regulation.



The Lifespan Human Connectome Project: Aging will characterize several factors that influence cognitive function alongside the comprehensive brain connectivity mapping in healthy volunteers aged 36 and up. This study—led by Ugurbil and the CMRR's Melissa Terpstra, Ph.D.—will track risk factors for Alzheimer's disease, cognitive symptoms associated with perimenopause, and key aspects of socioeconomic and health status.

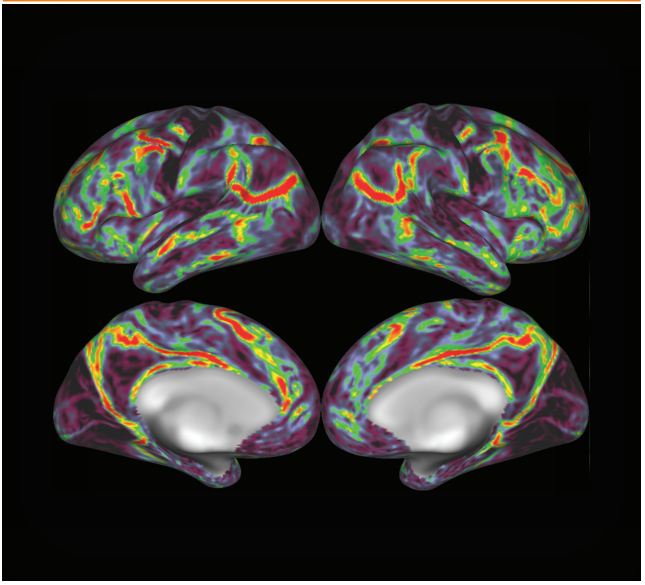
The CMRR's experts will continue to refine and develop the technologies needed for all of the connectome studies—and they're disseminating these techniques to scientists around the world (at nearly 300 sites) in the name of advancing brain science.

"At the expense of sounding immodest, I think there has been a revolution in imaging the brain through the Human Connectome Project," says Ugurbil, adding that anyone who uses functional imaging and diffusion imaging—the two imaging types used in the studies—in their research will benefit. "The technological development has been really fantastic."

Get involved

The University is recruiting healthy volunteers for the Lifespan Human Connectome Project. Study participants will spend one day at the U and will be compensated for their time. Learn more at z.umn.edu/lifespanhcp.

Images: *(Top row) Vu, A.T., Auerbach, E., Lenglet, C., Moeller, S., Sotiropoulos, S.N., Jbabdi, S., Andersson, J., Yacoub, E., Ugurbil, K., 2015. High resolution whole brain diffusion imaging at 7T for the Human Connectome Project. Neuroimage 122, 318-331.* ***(Bottom row)*** *Vu, A.T., Jamison, K., Glasser, M.F., Smith, S.M., Coalson, T., Moeller, S., Auerbach, E.J., Ugurbil, K., Yacoub, E., 2016. Tradeoffs in pushing the spatial resolution of fMRI for the 7T Human Connectome Project. Neuroimage.*



A closer look at the hallucinations of schizophrenia

In the middle of a conversation with his mother, he glimpsed the figure of a man from the corner of his eye. But when he turned his head, the figure was gone.

Minutes later, the figure appeared again in his peripheral vision, creating a debilitating sense of concern. Still, no man was present.

Scott Sponheim, Ph.D., will explore how and why these visual distortions occur.

Scientists don't know exactly what causes the visual hallucinations that some 3 million people with schizophrenia experience, but a new project led by the Medical School's Scott Sponheim, Ph.D., a professor of psychiatry and staff psychologist at the Minneapolis VA Health Care System, will explore why these episodes of visual distortion occur, potentially leading to improved treatments.

Funded by a $3 million grant from the National Institutes of Health and part of the disease arm of the Human Connectome Project, Sponheim will collaborate with the University's Center for Magnetic Resonance Research to obtain detailed brain images of 150 people who have schizophrenia while they perform tasks that prompt activity in the brain's visual and prefrontal cortexes. He will also scan the brains of 100 of their immediate relatives and 50 other healthy people who are not related to someone with schizophrenia.

Sponheim expects that people with schizophrenia will have abnormal activity in both the prefrontal and visual cortexes, while healthy relatives who carry genetic vulnerability for the disorder will have only abnormal activity in prefrontal areas. He thinks the interplay between both abnormalities in the brain causes the hallucinations and represents problems with brain connections that result in schizophrenia.

"By identifying mechanisms for the hallucinations, we can eventually develop more targeted treatments that might improve compromised portions of the brain," Sponheim says.

Illustration by Lisa Haines

Inside *the* mind *of* neuroscientist David Redish, Ph.D.

What does it mean to imagine something? What drives memory and recognition? What is regret? What is fairness? These are some of the questions that occupy the mind of University of Minnesota neuroscientist A. David Redish, Ph.D. He's also an accomplished poet, author, and playwright.

As both a scientist and a writer, Redish says it's the human condition that has always intrigued him.

Q: What is your play "In the Balance," which premiered on the West Coast last fall, about?

A: One of the things it's about is the imposter syndrome, about not knowing how you fit in. It's also about postpartum psychosis, which I find fascinating because I knew nothing about psychiatry at the time I wrote the play. I'd been reading biographies of Sylvia Plath and Ted Hughes, who were an amazingly interesting couple, and I kind of riffed off them.

Q: How do you account for your writing prowess?

A: A lot of practice. And poetry has given me a taste for metaphor that helps a lot in academic writing. You know, an extra line in a poem can ruin it. Getting that precision right is something I think is important. I try to do it in my academic writing, and in my academic talks, too.

Q: What's the goal of your neuroscience research?

A: We're trying to understand the two sides of decision-making. What is it that makes you make a decision? What is the process? And then, on the other side, what are the failure modes? If we understand the mechanisms—of self-destructive behavior, for example—we can find those failure modes and where they break. And if we know where they break, we'll know where to treat them.

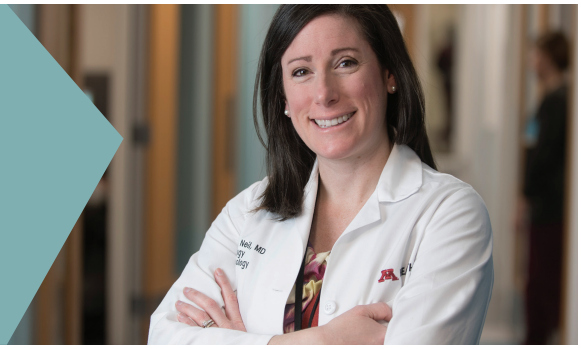
Q: You were recently named the Department of Neuroscience's J. B. Johnston Land Grant Chair. How will that support make a difference in your work?

A: First, it provides stability to my lab, which is especially important for my technicians, who are fantastic; they are my lab knowledge base.

Second, it provides us flexibility. One of the most important things about science is that we are explorers. As Isaac Asimov said, "The most exciting phrase to hear in science is … 'That's funny.'" Discovering a new direction and following that new discovery is both expensive and important. The Johnston Land Grant Chair provides us the flexibility to chase those new discoveries. I am deeply grateful for that opportunity.

Invested and focused

Among dedicated, collaborative colleagues, a new addition to the University's neuro-oncology team finds herself right at home



Elizabeth Neil, M.D., joins a U of M team that's gearing up for a Phase I clinical trial to evaluate a new immunotherapy for brain tumors. Photo by Scott Streble

You can sense the passion when Elizabeth Neil, M.D., talks about working with people who have brain cancer who come to the University of Minnesota seeking help.

"A diagnosis of cancer, especially brain cancer, is a scary and traumatic event for anyone," she says. "I focus on understanding their concerns, answering their questions, and working to structure the best treatment that coincides with their goals of care."

What most excites Neil, an assistant professor in the Medical School's Department of Neurology who arrived at the U last August, is the opportunity to work closely with the cadre of scientists who are developing new therapies to treat the devastating cancers she sees in the clinic. Right now, she's preparing for a Phase I clinical trial for people diagnosed with the most aggressive form of brain cancer, glioblastoma, with colleagues Christopher Moertel, M.D., and Michael Olin, Ph.D., who have already finished a smaller study of a promising new immunotherapy designed to fight brain tumors.

"Immunotherapies, like the one Moertel and Olin have developed, are the next frontier in cancer treatment," Neil says. "They harness the body's own immune system to attack and kill the cancer."

As she settles in at the U, Neil gets daily confirmation that she has come to the right place.

"Everyone here is so invested, so devoted and focused on collaboration," she says. "And I think we're on the verge of major breakthroughs here because of our amazing researchers. I'm so proud to be a member of this team."

To find out how you can support this work, contact Eva Widder at 612-624-8650 or ewidder@umn.edu.

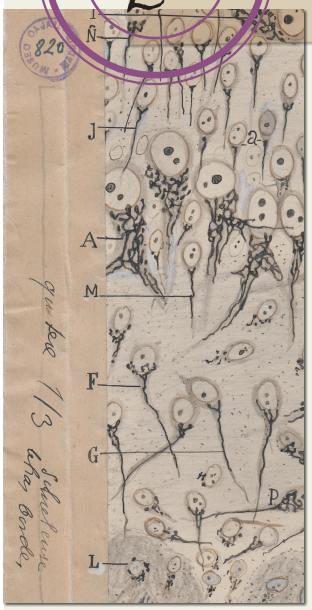


Image courtesy of Weisman Art Museum and Instituto Cajal (CSIC)

Last call: The Beautiful Brain exhibit

Don't miss your chance to see the intricate drawings of Santiago Ramón y Cajal (1852–1934) up close at *The Beautiful Brain* exhibit, free and on display at the University of Minnesota's Weisman Art Museum through May 21.

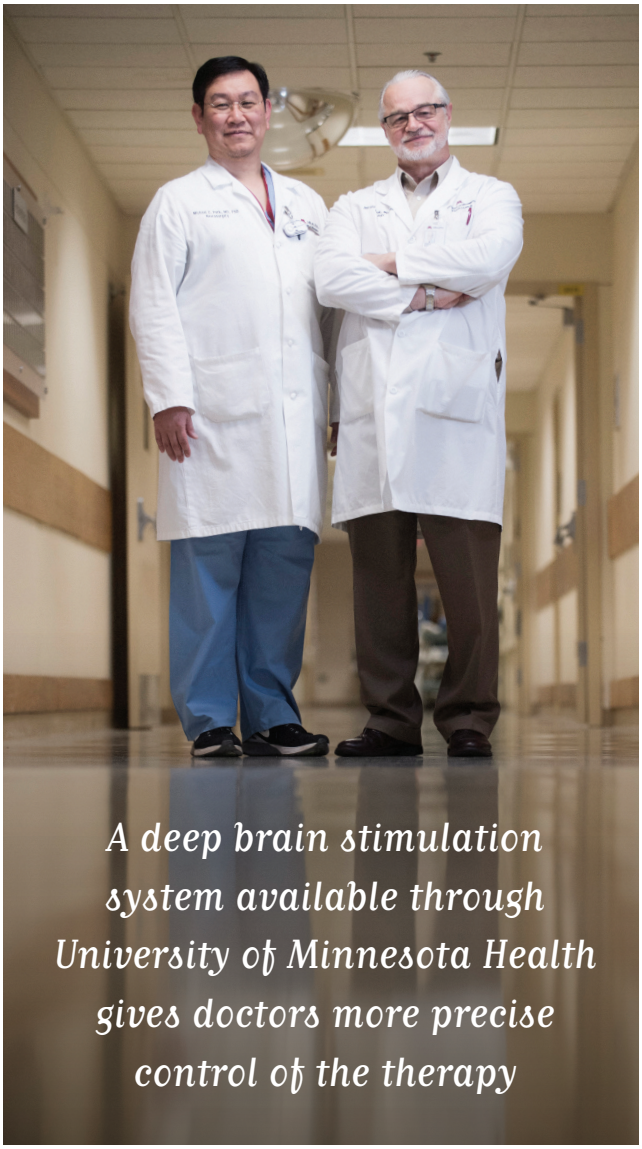
Considered the father of modern neuroscience, Cajal studied thin slices of human and animal brains under a microscope and recorded his discoveries on paper with pencil and ink. Combining his scientific and artistic skills, he showed that the brain is composed of individual cells—a new idea in his time—and received the Nobel Prize for his work in 1906.

In this exhibit, made possible by presenting sponsor Beverly N. Grossman, Cajal's drawings are accompanied by contemporary visualizations of the brain, along with photographs, historic books, and scientific tools.

The traveling exhibition was organized by the Weisman Art Museum in collaboration with U neuroscientists Eric Newman, Ph.D., Alfonso Araque, Ph.D., and Janet Dubinsky, Ph.D. Araque was formerly at the Instituto Cajal in Madrid, where Cajal worked and where his drawings are housed.

NEW & *improved*

Photo by Scott Streble



A deep brain stimulation system available through University of Minnesota Health gives doctors more precise control of the therapy

Neurosurgeon Michael Park, M.D., Ph.D., and neurologist Jerrold Vitek, M.D., Ph.D., believe the Infinity system will offer patients better control of their symptoms.

A new medical device available through University of Minnesota Health could provide improved symptom relief for people living with Parkinson's disease and other movement disorders.

Called the Infinity Deep Brain Stimulation system, the implantable brain device delivers targeted electrical stimulation to specific regions of the brain in order to treat symptoms associated with Parkinson's. M Health care teams are the first in Minnesota to make this new technology available to patients.

"We believe that this next-generation device offers our physicians a technical advantage," says M Health neurologist Jerrold Vitek, M.D., Ph.D., who leads the Department of Neurology at the University of Minnesota Medical School. "The ability to directionally steer stimulation will benefit our patients through better control of their symptoms."

Deep brain stimulation has been used to treat symptoms of Parkinson's and movement disorders for decades. To administer the therapy, surgeons implant a thin wire—called a lead—deep into a patient's brain to modify the abnormal activity that leads to tremors, stiffness, and slow movement associated with their disease.

Typically, these wires have electrodes that wrap around their entire circumference, sending electrical stimulation in a 360-degree pattern. This remains a successful approach. However, that 360-degree electrical stimulation sometimes reaches parts of the brain that have not been targeted for the therapy, which can cause temporary side effects.

The Infinity system, manufactured by Abbott (formerly St. Jude Medical), is equipped with improved electrodes that do not wrap around the entire lead. This lets neurologists direct the stimulation toward areas of the brain affected by disease while leaving the unaffected parts untouched. Doctors believe this targeted approach will reduce side effects and potentially improve treatment results.

M Health neurosurgeon and MnDRIVE Neuromodulation Scholar Michael C. Park, M.D., Ph.D., specializes in performing deep brain stimulation procedures and conducts research.

"Our team believes that the Infinity device creates new options for our patients and will translate to superior care," Park says.

The Line Up

News from the Bob Allison Ataxia Research Center

About perspective

This physician with ataxia doesn't know the word "quit"

When Linda Snider was 10 years old, her dad starting showing symptoms of spinocerebellar ataxia type 1 (SCA1), a disease that would ultimately claim his life.

"He slowly lost his identity," Snider recalls. "He went from not being able to dress himself, to not being able to walk or feed himself. In the end, he couldn't talk."

Snider knew she had a 50/50 chance of developing the hereditary form of ataxia. When University of Minnesota scientist Harry Orr, Ph.D., a professor in the Department of Laboratory Medicine and Pathology and holder of the Bob Allison Ataxia Research Center Chair, discovered the gene that causes SCA1 in 1994, Snider was one of the first to be tested; at 21, she was told she had inherited the gene.

"I had just started medical school," she says, "and they were telling me I'd be in a wheelchair by the time I was 40. Suddenly my whole future was about having this disease."

Or not. Snider, now 45 and not in a wheelchair, says she lives a "full and meaningful life." She chose radiology, a specialty she felt she could manage from a wheelchair, and practices in Omaha, Nebraska, where she lives with her partner, Mark Sidwell. She travels. And she stays enthusiastically positive.

"Everything to me is about perspective," she says, "and living a healthy lifestyle, with regular massage, acupuncture, and yoga, which I think has slowed the progression of my disease."

She fights back not only for herself but also for others touched by ataxia. It was Sidwell's idea to start an ataxia support group in Omaha, a concept that's blossomed into regular monthly meetings that alternate between social outings and educational sessions.

Next came the nonprofit Nebraska Ataxia and its fundraiser, which brought in $100,000. Part those proceeds supported Orr's research at the University of Minnesota.

While she loves her home state, Snider heads to the U for health care. She's a regular at the Ataxia Center, where she sees neurologist Khalaf Bushara, M.D., and, occasionally, her distant relative Lawrence Schut, M.D., whose Minnesota family is inextricably linked with SCA1. But why travel to Minnesota when she's well connected in the Omaha medical community?

"Because it's the best," Snider says. "The doctors and support staff there understand this disease better than anyone else in the world. I've been going to the U since I was 16, and I'll always go there because both the care and the research are cutting edge."

Mark Sidwell and Linda Snider, M.D., are the driving forces behind the nonprofit Nebraska Ataxia and its fundraising event, which benefited in part research at the University of Minnesota.

Photo by Jon Pearson

University of Minnesota

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A nondrug approach to beating addiction

In 40 years of research, Marilyn Carroll, Ph.D., has worked to show how substituting healthier forms of gratification can curb drug addiction.

As a postdoctoral student, Carroll, along with her adviser, discovered evidence that less food availability boosted opiate abuse while increased access to palatable food and liquids reduced it.

"There is an inverse relationship between food- and drug-rewarded behavior," says Carroll, who is now a professor in the Department of Psychiatry at the University of Minnesota Medical School. "Food and drugs can substitute for each other."

More recently, Carroll and her U team found that the "reward" of exercise could prevent and reduce drug-seeking behavior. Based on this discovery, researchers at the University of California, Los Angeles employed exercise as a way to treat addiction to methamphetamine. Sure enough, exercise during recovery reduced relapse rates compared with the control condition, under which the study volunteers received only general health education.

Clinical studies at the U of M are planned or under way to employ exercise to help people reduce or stop using nicotine, marijuana, and heroin, and also to test the effectiveness of progesterone (a natural female hormone)—alone and in combination with exercise—to reduce drug-seeking behavior and cravings.

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