Brain SCAN

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FOR BRAIN RESEARCH AT MIT

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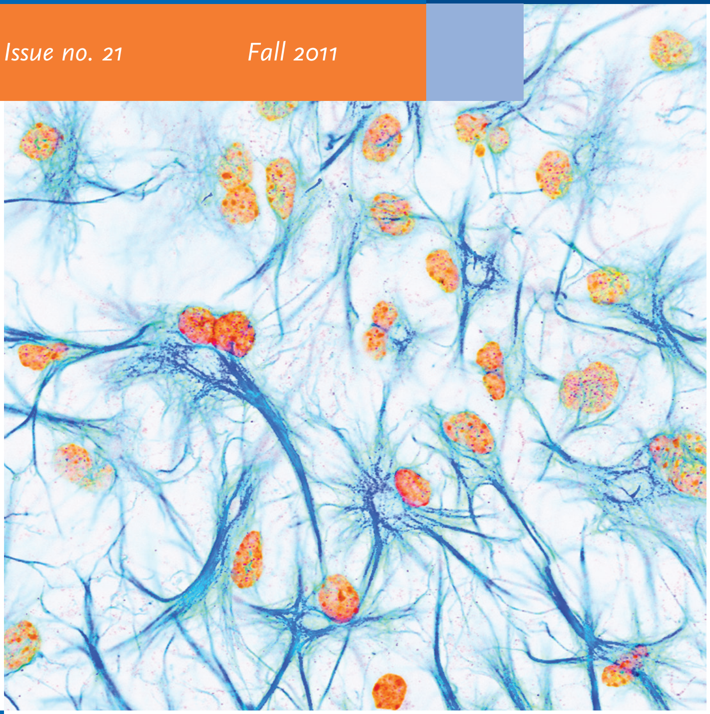


From the director

In this issue we highlight the work of Nancy Kanwisher, a founding member of the McGovern Institute and a leading proponent of the idea that the human brain has specialized structures and circuits for different mental abilities.

Cover image: Cultured neurons and glial cells.

Courtesy of Michael Wells and Guoping Feng.

The brain is often compared to a computer, with its flexible operating system that can be programmed to perform many different tasks. Nancy Kanwisher's work, however, suggests a different metaphor—that of the brain as a 'Swiss army knife' composed of specialized components that have evolved for distinct functions. Nancy has shown, for example, that the brain has specific areas devoted to perceiving faces, places and written words. She is now turning her attention to language and autism, and to developing new ways to image the brains of children at the age when problems often begin to emerge. In addition to being a great scientist herself, Nancy is also an outstanding mentor to our young researchers, many of whom have gone on to successful careers after cutting their scientific teeth in Nancy's lab.

Understanding language is also a major goal for another of our faculty members, John Gabrieli. One of John's central interests is dyslexia, and in the past year alone he has published no less than four papers on the subject. I'm especially pleased to announce that John's dyslexia research will benefit from a new gift from our longtime supporters Jeffrey and Nancy Halis. In the current climate of shrinking federal budgets, philanthropic support is more important than ever, and we are deeply grateful for Jeff and Nancy's support.

We also welcome a new member of our leadership board, Hugo Shong, who is President of IDG Asia. Along with Pat and Lore McGovern, Hugo has been closely involved in planning the IDG-McGovern Institute at Tsinghua University, announced earlier this year. I am pleased to report that two more such institutes are now planned, at Peking University and Beijing Normal University. We look forward to working with Hugo as these plans advance, and to developing many exciting collaborations with our new sister institutes in China.

As 2011 comes to an end, I'd like to thank all of you who have supported us over the past year, and to wish you the very best for the holidays and for the year ahead.

Bob Desimone, Director

Nancy Kanwisher, a founding member of the McGovern Institute.

Photo: Kent Dayton

REVEALING THE MIND'S STRUCTURE

Nancy Kanwisher uses brain imaging to learn about the organization of the mind. Discovering where thoughts are localized within the brain may tell us a lot about vision, language and what it means to be human.

Nancy Kanwisher is working on what she sees as one of the great intellectual quests of our time: understanding the nature of the human mind.

"I became a cognitive psychologist because I wanted to know who we are and what thinking is," she says. "I study the brain because it's the physical organ where mental life happens."

Kanwisher's goal is to learn how the brain is organized. Should we think of it as a "Swiss army knife," an assemblage of specialized tools for different tasks such as language, math or music? Or is it more like a computer, with a single processor that can run different programs for each task?

The answer to this question will have profound implications for understanding the human mind. It will also be of great importance for understanding brain disorders—whether, for example, conditions such as autism are caused by a general impairment of brain function, or whether they have their origins in the disruption of specific circuits with distinct functions.

It has long been known that the brain has specialized areas for certain functions, including perception—vision, hearing, touch—and the control of movements. Indeed, one of the most recognizable images in neuroscience is Penfield's famous homunculus, depicting how the body is mapped onto the brain. "But it was much less clear whether this was also true for cognition," Kanwisher recalls. "Many people thought that cognition was distributed throughout the brain. I wanted to find out whether that's true or whether the different components of our mental lives can also be mapped onto different brain regions."

For the past 16 years she has been scanning the brains of human volunteers, searching for answers to that question. Her work has revealed a remarkable degree of specialization for diverse functions, from vision to language and abstract thinking. It is also suggesting new ways to study autism and general intelligence.

Wow! That's me!

Kanwisher grew up in Woods Hole, Massachusetts, where her father was a field biologist. She entered MIT, majoring in biology at a time when only 15% of the students were women. She remained at MIT as a graduate student, under the supervision of Molly Potter, a professor of psychology in the Department of Brain and Cognitive Science. "I couldn't have made it without her and all the time and encouragement she gave me."

After receiving her doctorate in 1986, Kanwisher taught at the University of California, Los Angeles and at Harvard University before returning to MIT as a faculty member in 1997. She is a founding member of the McGovern Institute.

Kanwisher began her career by probing the human mind through carefully designed behavioral experiments, which are still essential to her work. But her career took a new direction in 1995, when she became an early adopter of the brain imaging method known as functional magnetic resonance imaging (fMRI). This method, based on local changes in blood flow, allows researchers to see when a particular part of the brain becomes active as subjects lie within the scanner.

The opportunity to look inside the black box was irresistible to Kanwisher, and she started using fMRI to study the brain's visual responses, often using herself as a test subject. Over the years she has spent many hundreds of hours in the scanner, and at one point in her quest for precise measurements, she even had a series of small dots tattooed onto her own scalp, allowing the MRI image to be registered more accurately onto the anatomical shape of her head.

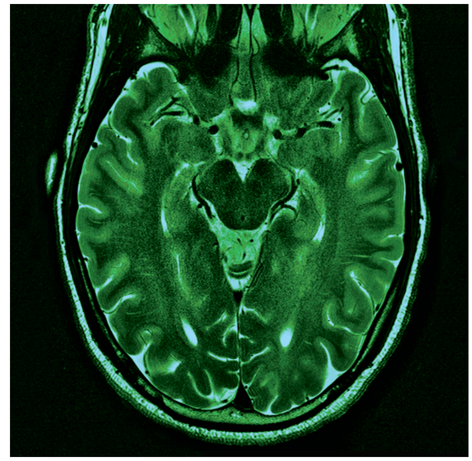
Places for faces

For her first imaging experiments, Kanwisher decided to study face perception. "It seemed like low-hanging fruit," she explains. "We already knew that injuries to the right temporal lobe could cause prosopagnosia (face blindness), and several lines of evidence suggested there might be a brain area specifically involved in perceiving faces." Sure enough, the initial scan results revealed a part of the temporal lobe that responded to faces much more strongly than any other stimuli, and through a careful series of tests she was able to exclude several alternative explanations, and to prove that this small patch of visual cortex, now known as the fusiform face area, is indeed specifically dedicated to seeing faces. "Even though we predicted that it would be there, it was still thrilling to find it," she recalls.

After moving to MIT, Kanwisher soon began to discover other specialized visual areas, with selective responses to images of body parts or places. And recently, in a collaboration with MIT computer scientist Polina Golland (supported in part by the McGovern Institute Neurotechnology Program), she has developed an unbiased statistical method for identifying patterns of brain activation, which yielded the same three categories of responses, to faces, body parts and places—a powerful validation of her earlier work.

Kanwisher attributes her early success to the encouragement of her graduate advisor Molly Potter (left), and she in turn has mentored many other successful scientists, including Rebecca Saxe (right). All three are now on the MIT faculty.

Photo: Peter Dizikes/MIT News



Kanwisher often uses herself as a test subject, and a large image of her brain is displayed near the entrance to the McGovern Institute.

Understanding autism

In 2003, Kanwisher's student Rebecca Saxe, who is now a faculty member at MIT, found a brain region that was activated specifically when subjects were thinking about the mental states of other people —including so-called "theory of mind" tasks that require an understanding of another person's beliefs and motivations. "I was astonished," Kanwisher recalls. "Who would have expected that something as abstract as 'thinking about thinking' could have its own specialized brain region?"

Kanwisher and Saxe became intrigued by the idea that this "theory of mind" region might be involved in autism. Little is known about autism, a notoriously complex and varied disorder whose underlying cause is not understood, and for which no physical diagnostic tests are available.

But one of the core features of autism is impaired social interactions, including difficulties understanding other people's thoughts. Autistic individuals also have frequent problems in recognizing faces, and in responding to eye contact or other social signals. "We'd like to know whether any of the brain areas that are specialized for social cognition are affected in autism," says Kanwisher. She and Saxe are both involved in a large project, funded by the Ellison Foundation, to study the biological basis of autism. They are recruiting large numbers of typical and autistic children aged 5 to 12, and giving them a series of

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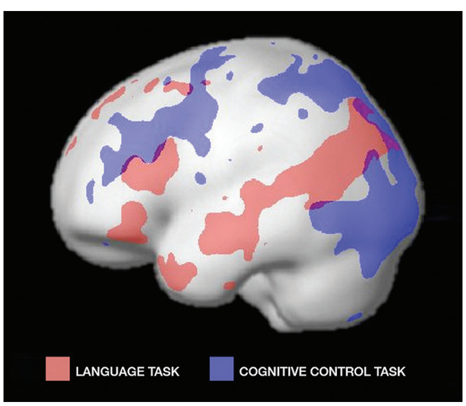
behavioral and brain imaging tests. For Kanwisher, a key goal is to come up with a more precise description of the cognitive deficits in autism, and to relate these to differences within the developing brain. "Almost any therapeutic intervention is likely to be more effective if it's started earlier," she says. "We hope that by studying children at the time when problems are emerging, we will discover things that can help guide the development of better treatments in the future."

Localizing language

Another of Kanwisher's current interests is the brain basis of language, a uniquely human trait that is also a test bed for competing ideas about the nature of the human mind. "There is a long-standing debate in cognitive psychology about whether language overlaps with other non-language cognitive functions such as math, working memory, or music," she explains. Support for the idea that they are distinct comes from studies of brain injuries, which can affect each of these skills independently, suggesting they might depend on different brain regions. Yet this view has not been corroborated by previous imaging studies, which have generally found that language-responsive regions are also activated by non-language tasks.



Different brain areas are activated by a language task (red) and a control task (blue). Some of these areas are adjacent but there is little overlap between the two tasks.

Image: Evelina Fedorenko and Nancy Kanwisher

"We thought maybe this paradox results from flaws in how imaging data are analyzed," says Evelina Federenko, a research scientist in Kanwisher's lab. Most previous studies looked at average patterns obtained by combining data from many subjects. But individual brains are not identical, and if the boundaries between neighboring brain regions are not always in exactly the same place, then the averaging method could blur the maps. This could create the appearance of an overlap even if the regions are in fact sharply separated in each individual.

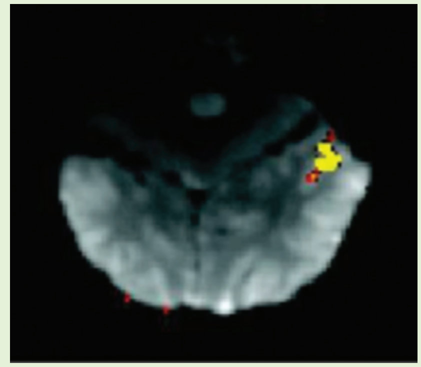
"To avoid this problem, we wanted to analyze each subject individually and compare their patterns of activity as they performed language tasks and other cognitive tasks that don't involve language," Federenko explains. "We looked at seven different tasks and nine brain regions, and we found a striking degree of specialization in almost every subject. Most language regions respond specifically to language and not to any of the other cognitive tasks that have been suggested to overlap with language."

Kanwisher and Federenko now hope to discover whether these different language regions have different functions—for example whether some are specialized for processing the grammatical structure of a sentence while others are involved in understanding its meaning.

Why these and not those?

While working on the language project, Kanwisher and her colleagues identified brain regions that appear to be specifically activated by other functions such as pitch perception, which they are now investigating. But they also found other regions that were activated by any difficult task. Other researchers had also described similar findings, and it has been suggested that such areas may contribute to general intelligence, perhaps analogous to the way a computer's CPU underlies its ability to perform multiple tasks. But as with language, these effects had previously been detected only in group averages, making it difficult to be sure that the overlapping activations were real rather than artifactual. "We can now identify these candidate 'general purpose areas' in individual subjects," says Kanwisher. "That means we're in a great position to study what they do, and how the brain's general-purpose machinery works together with other areas that are specific to particular cognitive tasks such as language."

"We don't understand why the brain compartmentalizes some functions but not others. There must presumably be some computational advantage, but we don't yet understand it. That's the question I'd most like to answer in the next ten years." ■



Why here and not there?

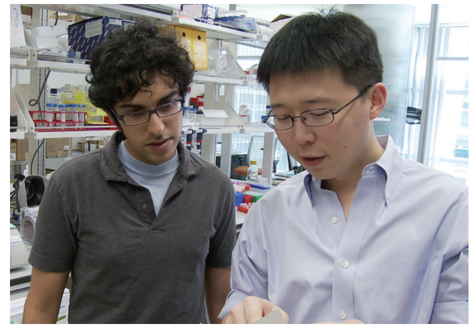
Several years ago, Kanwisher identified a tiny brain region that recognizes written letters. Unlike other mental functions with specialized brain areas (such as face recognition or spoken language), writing is a recent cultural invention, and it seems implausible that the human brain could have evolved a new region for an ability that is only a few thousand years old. "So if it's not hard-wired into our genes, why does writing always end up in the same brain region in every person?" she asks. She hopes to discover whether the other cognitive areas she has identified are hard-wired or develop through early experience with the world. ■

New Gifts Support Faculty, Innovative Research

Over the past few months, three longtime supporters of the McGovern Institute made generous new contributions that will fund research ranging from molecular engineering to dyslexia.

Faculty member Feng Zhang, who is designing new molecular tools to manipulate the living brain, will benefit from a new gift by Robyn and Robert Metcalfe '68. "We are supporters of the McGovern Institute because we share the vision of Lore and Pat McGovern for brain research," said Bob Metcalfe, who formerly chaired the McGovern Institute Leadership Board and whose family members have been personally affected by brain disease. "We believe in the McGovern Institute's fine faculty, whom we've gotten to know up close for several years."

Longtime Friend of the McGovern Institute, Ira Jaffe '61 is continuing his support for Ann Graybiel, who studies the basal ganglia, brain structures implicated in Parkinson's disease, Huntington's disease, obsessive-compulsive disorder, and addiction. Jaffe, an attorney at Jaffe Raitt Heuer & Weiss in Southfield, Michigan, has supported Graybiel's research since 2006. "An in-person visit exposed me to the combination of cutting edge research, inspiring young researchers, and the intellect and dynamic energy of Ann Graybiel," said Jaffe.



Feng Zhang (right) with postdoc Neville Sanjana

The work of John Gabrieli, whose research interests include language learning and dyslexia, will be supported by a substantial new gift from the Halis Family Foundation to fund further dyslexia and early intervention research. Jeffrey Halis '76, President and Partner at Tyndall Management LLC in New York, cites a family history of dyslexia and Alzheimer's disease as key factors in his decision to support the Gabrieli lab. ■

McGovern Institute Welcomes New Development Director

We are delighted to welcome Kara Flyg, Director of Development at the McGovern Institute. Kara will be working with director Robert Desimone and McGovern board members to promote the institute's vision and long-term fundraising strategy.

Kara comes to the McGovern Institute with a strong record of expanding philanthropic support for non-profit institutions; most recently as Associate Director of Philanthropy at The Nature Conservancy, and previously as a fundraiser for the Joslin Diabetes Center in Boston.

Kara's interest in neuroscience is rooted in her experience caring for a family member with a brain disorder. "I recognize the impact that new discoveries can have on millions of families like my own," she says. "We need a better understanding of brain disorders in order to develop better therapies, and I am excited by the challenge of linking the McGovern Institute's outstanding researchers with the resources to make them possible."

Kara can be reached at 617-324-0134, or by email at kflyg@mit.edu. ■

Kara Flyg, Director of Development at the McGovern Institute

Photo: Justin Knight

NIH's Hikosaka to Give Inaugural Sharp Lecture

The inaugural lecture in honor of McGovern Institute founding director Phillip Sharp will take place on Thursday March 1, 2012. The speaker will be Okihide Hikosaka of the National Institutes of Health, a leading expert on brain mechanisms of motivation and learning. The annual lecture is endowed by Biogen-Idec, a biotechnology company that Sharp helped to found (see *Brain Scan* Issue No. 19). ■

McGoverns, IDG to Establish New Institutes in China

Following the decision to establish the IDG/McGovern Institute for Brain Research at Tsinghua University (*Brain Scan*, Issue no. 20), two more such institutes are now planned, at Peking University and Beijing Normal University. "We're sometimes asked 'Why China?'" says Bob Desimone, who spoke at the signing ceremony for the brain research institute at Beijing Normal University in November. "My answer is that there is a global need to better understand the brain and to develop better treatments for brain disorders, and the way to maximize progress is through international cooperation. China is devoting enormous resources to scientific research and we fully expect to benefit as much as our Chinese colleagues from working together in the future." ■

The signing ceremony at Beijing Normal University was attended by (left to right) Qi Dong, vice-president of BNU; Hugo Shong, president of IDG Asia; Binglin Zhong, president of BNU; Pat McGovern; Lore Harp McGovern; Chuansheng Liu, chair of academic council at BNU; and Robert Desimone.

Photo: Beijing Normal University

Meet the researcher

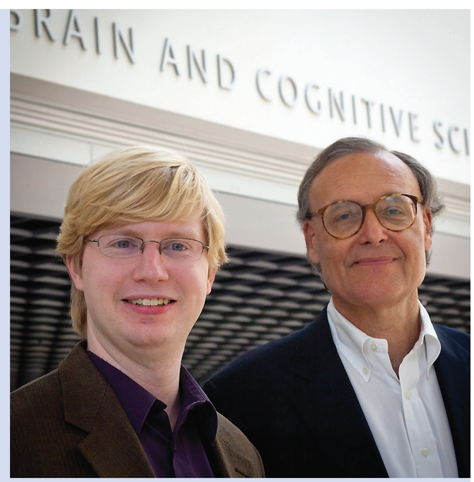
Tyler Perrachione
PhD Candidate
Gabrieli Lab

What is the big scientific question you're trying to answer?
I want to know how we understand what other people are saying when they talk to us. Human language is this remarkable system that lets us take ideas out of our own heads and put them into the heads of other people. I want to know what it is about our brains that lets us do this so easily.

Why the McGovern Institute?
It is an amazing place to do science; the diversity of intellectual and technical talent I get to interact with every day is energizing. John Gabrieli brings a remarkable kind of clarity to scientific questions and pursuits.

What problem are you working on now?
I want to know if there is something fundamentally different about the way the dyslexic brain processes information. Dyslexia is an interesting disorder for evaluating our models of language processing in the brain. The consensus in the field is that the reading difficulties experienced by people with dyslexia aren't a problem with vision, but rather a problem with language—specifically phonology, the knowledge of how the sounds of a language work. Here at MIT, I hypothesized with John Gabrieli that if phonology is impaired in dyslexia, then individuals with that disorder should also have trouble recognizing voices—a result we confirmed and recently published.

What's next?
Now we want to understand how the dyslexic brain manages to handle speech perception so well despite a phonological impairment, with the hope that such a discovery might help identify new ways to overcome reading difficulties.



Tyler Perrachione (left) with John Gabrieli

Photo: Patrick Gillooly/MIT News

RESEARCH NEWS

Some brain regions can distinguish between a scene and its mirror-image, suggesting a role in navigation. Other brain regions make no such distinction, and may be involved in categorization of scenes.

Photo: Brittany G. via www.flickr.com

John Gabrieli and graduate student Tyler Perrachione found that people with dyslexia have a harder time recognizing voices than non-dyslexics, adding to the growing body of evidence that dyslexia is not simply a visual disorder. The study was picked up by the *New York Times*, MSNBC, CBS News, and the *Boston Globe*. Another study out of the Gabrieli lab found that activity in a specific part of the brain predicts how well people remember a visual scene, adding a new element to the longstanding question of why we remember some things better than others.

Using an innovative technique developed in **Nancy Kanwisher**'s lab, research scientist Evelina Fedorenko identified parts of the human brain dedicated exclusively to language, marking a major advance in the search for brain regions specialized for specific mental functions. In a separate study from Kanwisher's group, research scientist Daniel Dilks found that some brain regions respond differently to a scene and its mirror-image, whereas other regions make no such distinction. The former structures are likely to be concerned with navigation whereas the latter are involved in categorization of scenes.

A paper by **Robert Desimone** described how different brain areas work together to guide the eyes toward a searched-for visual target.

Brain waves shift frequency as a new task becomes routine, according to a new study out of **Ann Graybiel**'s lab, providing a new clue to how the brain reorganizes itself during learning.

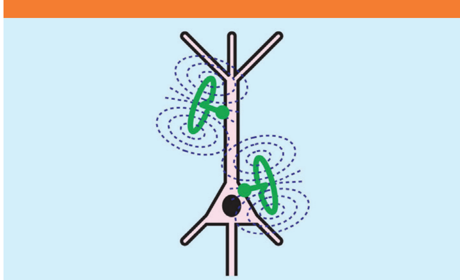
Video Spotlight

In a five-minute video available on our website, Nancy Kanwisher talks about her pursuit to understand the organization of the brain and why this information may reveal clues about autism, language, and what it means to be human. ■

Guoping Feng, **Ann Graybiel** and colleagues have made several new strains of mice, genetically engineered so that different types of neurons can be activated by light. These strains, likely to be widely useful, will be publicly shared via the Jackson Laboratory.

Martha Constantine-Paton described a synaptic mechanism that allows the developing brain to form well-aligned visual maps of the external world. ■

AWARDS AND HONORS

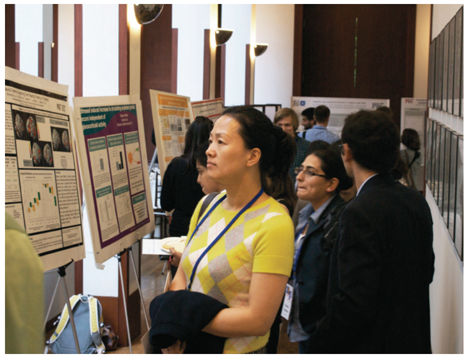


Alan Jasanoff plans to build microscopic devices that will convert neural currents into magnetic fields that could be detected using methods such as MRI.

Alan Jasanoff is among 17 scientists nationwide to receive the NIH Director's Transformative R01 (T-R01) award designed to encourage scientists to explore high-risk projects with the potential to dramatically transform their field.

Yingxi Lin has been named the Fred and Carole Middleton Career Development Professor at MIT.

Guoping Feng and **Feng Zhang** are both among the winners of the 2011-2012 McKnight Technological Innovations in Neuroscience Awards for using new technologies to monitor, manipulate, analyze and model brain function. Only three scientists were selected this year for this prestigious award, which includes a $200,000 prize distributed over a two-year period. ■



Left: Bob Desimone, Lore Harp McGovern and Guoping Feng. Center, Right: Almost 150 people attended this year's retreat, held at the American Academy of Arts and Sciences in Cambridge, MA.

9th Annual McGovern Institute Retreat

McGovern Institute faculty, researchers and staff gathered at the American Academy of Arts and Sciences for a full day of talks at the ninth annual McGovern retreat. Institute co-founder Lore Harp McGovern joined members of the McGovern Institute to hear students and postdocs give thirteen talks on topics ranging from genetic engineering of brain cells to the perception of social interactions by children with autism. The talks were followed by a poster session, reception, and dinner at the Academy.

The McGovern Institute for Brain Research at MIT is led by a team of world-renowned neuroscientists committed to meeting two great challenges of modern science: understanding how the brain works and discovering new ways to prevent or treat brain disorders. The McGovern Institute was established in 2000 by Patrick J. McGovern and Lore Harp McGovern, who are committed to improving human welfare, communication and understanding through their support for neuroscience research. The director is Robert Desimone, formerly the head of intramural research at the National Institute of Mental Health.

Further information is available at: http://mcgovern.mit.edu

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