# Brain SCAN

McGOVERN INSTITUTE
FOR BRAIN RESEARCH AT MIT

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## From the director

**Brain imaging studies tend to focus on adults because it takes special procedures and equipment, not to mention style, to work with children. The Martinos Imaging Center at the McGovern Institute offers those resources for researchers—and a welcoming environment for child volunteers and their families.**

*Above: "Neural Garden"—watercolor by Elizabeth J. Horowitz, Copyright 2008*

Brain imaging allows us to peer inside the human brain in a safe, non-invasive way. But to understand how we develop our human capacities, and also to gain insights into developmental disorders, we need to study the brains of children, not just adults. As you will read in this issue of *Brain Scan*, working with children presents many challenges, not least of which is finding families who are willing to volunteer for these studies. I applaud the staff of the imaging center for meeting these challenges with a level of creativity and technical expertise that few other facilities can match.

Importantly, this remarkable facility is a resource for the entire research community. In addition to McGovern researchers, the center is used by many other researchers from MIT and beyond. With over 3000 hours of use per year, the center is in nearly constant use—a testimony to the importance of neuroimaging in modern neuroscience.

To me, this center exemplifies the significance of core facilities in providing researchers access to technologies that are too expensive for any one lab to procure alone. There is a danger that such large investments can become the province of "big science"—out of the hands of individual researchers. Here at the McGovern Institute, though, we have the best of both worlds, benefiting from a shared resource that supports research projects by individual investigators.

We are all keenly aware of the current economic crisis, but the McGovern Institute is fortunately weathering the storm relatively well—thanks to our founders, Lore and Pat McGovern, and our many generous donors. At this critical time, we are thrilled to announce a new graduate fellowship established by Mark Gorenberg. I can think of no better investment in the future than supporting young researchers in the formative years of their career.

**Bob Desimone, Director**

*Eight-year-old Fiona O'Loughlin practices an fMRI task for a study on dyslexia.*

*Photo courtesy Patricia O'Loughlin, MIT*

# PLAYING FOR SCIENCE: IMAGING THE DEVELOPING CHILD'S BRAIN

**At the Martinos Imaging Center, researchers have the unique ability to explore the developing child's brain and to learn more about disorders that emerge during these early years. Scanning children requires special resources and skills, and having a child-friendly environment is essential to the success of this program.**

Most weekdays, the Athinoula A. Martinos Imaging Center at the McGovern Institute is a place of quiet industry. But on the weekends, the center transforms into a hub of youthful activity, as groups of children arrive to participate in brain imaging studies with parents, siblings, and even grandparents in tow.

The researchers shower the children with praise, surround them with toys, and make the experience engaging and fun—while trying to pack maximum value into the scanning time for these easily distracted subjects. The atmosphere may resemble a trip to the science museum, but the children are helping researchers learn more about how the human brain develops during childhood.

Of the approximately 3,500 people whose brains have been scanned here since the center opened in 2006, almost 200 have been children, some as young as five. The number of children will increase because of a recent $8.5 million award from the Ellison Foundation to study dyslexia and autism—complex brain disorders that first appear in early childhood.

"Our ultimate goal is to look at these disorders as early as possible to understand how they develop," says John Gabrieli, director of the imaging center, who coordinates the dyslexia component of the Ellison project. "We want to discover new ways to identify these conditions at an early stage when they are most treatable, and to understand how different treatment options might influence the brain."

"We are also studying typical brain development," adds McGovern Institute's Nancy Kanwisher, who coordinates the autism work. "That's because to understand how development goes wrong, we must also understand how it goes right. We still have so much to learn about how our human abilities emerge during childhood."

## Not just child's play

"Let's see if you have a brain," teased the father of a 10-year-old boy who was about to enter the scanner for a study on memory led by Noa Ofen, a postdoctoral associate in the Gabrieli lab.

The slightly nervous boy had just rehearsed for Ofen's study in a mock scanner across the hallway. There, in a brightly colored room full of toys, children learn the task they will perform in the scanner. They can also scan Froggy to see if he has a brain. (He does not; he's a stuffed animal.)

"This is not just play," explains Ofen. "It's crucial for our ability to get better results."

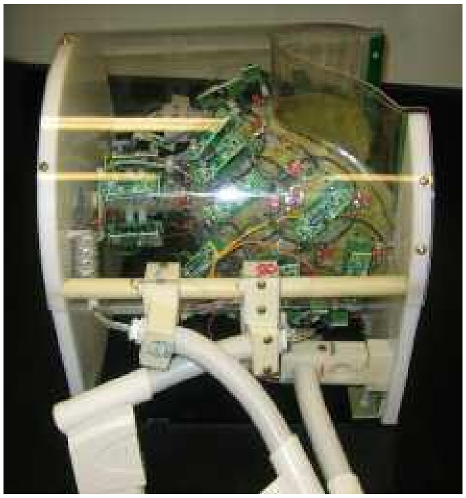
Children tend to fidget, for example, and any movement can blur brain scan images. To help train children to lie still, the mock scanner contains a motion detector and a video monitor. When a child moves, the video stops playing.

*The staff of the Martinos Imaging Center. From left to right: Steven Shannon, Christina Triantafyllou, Susan Whitfield-Gabrieli, Sheeba Arnold Anteraper.*

*Photo courtesy Patricia O'Loughlin, MIT*

The mock scanner also reproduces the loud clangs and vibrations (mimicked by a subwoofer) of the real scanner. "The noise level is like a rock concert—only without the music," says research scientist Steven Shannon.

Once acclimated to the environment of the mock scanner, children are often enthusiastic to participate in the 'real' thing. "It was fun getting scanned. I was really happy to be chosen. Now I'm telling my friends to try it," said eight-year-old Fiona O'Loughlin, who participated as a typically developing child in a study on dyslexia. Fiona's mother, who is a research assistant in Gabrieli's lab, recruited her daughter for the study.



*The newly developed 32-channel pediatric coil will improve image quality and increase scanning speed.*

*Photo courtesy Larry Wald, Massachusetts General Hospital*

Researchers also recruit volunteers from the local community by advertising on Craigslist, by distributing flyers, and by visiting schools, day care providers, and community centers. While they recently hired a full-time outreach person to coordinate these efforts, they still rely on word of mouth. Ofen's hairdresser, for example, has referred four children to the center.

"It's easy to recruit the children of MIT science nerds," says Gabrieli, himself a father of two children whom he hopes to 'volunteer' when they are old enough to participate in a study. "But we want to discover what's distinctive about dyslexia or autism, not what's distinctive about our colleagues' offspring. Getting a representative sample of the community can be a challenge, but it's an explicit goal of our studies."

## Packing in the data

Another challenge for the researchers is to develop tasks that are entertaining enough to keep children engaged while their brains are being scanned.

"To keep adults motivated and on task, you tell them to do the task and then pay them. With kids, it's not so trivial," said Rebecca Saxe, a former student of Kanwisher's who now runs her own lab in the MIT Department of Brain and Cognitive Sciences.

Saxe, an expert on social cognition, is currently studying autism. She wants to test the hypothesis that people with autism have difficulty imagining what others are thinking and that this impairment contributes to their social deficits.

To test this 'theory of mind' hypothesis, Saxe studies the activity of specific brain regions while children listen to stories and clips of music. These tests can reveal which brain regions specialize in language comprehension and which regions are activated simply by the sound of a human voice. Saxe also looks for patterns of activity that happen specifically when children imagine what other people are thinking.

*continued, page 4*

## A snugger fit

Working with small children also requires specialized scanning equipment. For example, the quality of a brain scan depends on the signal that the scanner receives from elements enclosed within a coil around the child's head. Currently, the imaging center has 12-channel and 32-channel coils designed to accommodate adult heads.

When the center acquired the 32-channel adult head coil last August, the results were impressive. "You can see the difference in image quality because the signal is better in the 32-channel coil, meaning that you can see finer details on the brain images that were previously not clear," explains Christina Triantafyllou, an MRI physicist and associate director of the imaging center.

But the size of the head coil is also important—the closer the fit, the better the image. Although the new 32-channel coil has led to marked improvements in the images obtained from adults, this large coil does not closely fit the smaller heads of children. So, MIT researchers are now collaborating with Larry Wald, a biophysicist at Massachusetts General Hospital, to develop a smaller 32-channel coil for the center—one that is specifically tailored for children.

## Better analysis

New software is also improving imaging technology at the center. Researchers now use a system that compensates for head movements in real-time, explains research scientist Susan Whitfield-Gabrieli, who is the other half of the husband-and-wife team in the 'GabLab' and who directs data analysis for the imaging center.

Whitfield-Gabrieli has developed a software program called ART that detects and rejects false signals or artifacts. ART is especially helpful in pediatric imaging, where so many factors can compromise results.

"In one study on language and dyslexia, investigators were horrified not to find any brain activation in the expected language area," she recalls. "But after using ART they could clearly see the activated regions." Whitfield-Gabrieli now has an NIH grant to further develop and disseminate this software.


*An artistic thank-you note sent by one young study participant to a team of researchers in the Gabrieli lab.*

*Image courtesy John Gabrieli and colleagues*

## Complementary pictures

Other imaging methods are also enhancing the capabilities of the center. For example, the recently acquired electroencephalography (EEG) machine detects electrical activity in the brain without the time-delay inherent in an fMRI signal. This speediness makes EEG valuable in studying fast-paced cognitive and perceptual processes.

But although EEG can reveal the timing of brain activity with great precision, it is much less accurate than fMRI for localizing the source of the signal.

"There are methodological limits with every technology for studying the brain," Gabrieli reflects. "So the most improvement will come from combining these different methods in each subject. The direction we're going is to have a single center with all the best measures of the human brain structure and function so that we can gain a better understanding of the brain in health and disease." ■

## By The Numbers

The MRI scanner logged almost 3000 hours in 2007 and over 3500 hours in 2008, according to Sheeba Arnold Anteraper, the programmer for the imaging center. "With new facilities like the EEG coming online, it's only going to get busier," she says.

More than 30 groups of researchers use the center, and the machines are usually booked well into the night. Most subjects are healthy adults volunteering for basic research studies on normal brain function. But a growing number of subjects are children and clinical patients with a wide variety of brain disorders, including schizophrenia, depression, bipolar disorder, Alzheimer's disease, and macular degeneration.

"Every participant understands that our work is purely for research rather than therapeutic purposes," Gabrieli stressed. "Patients are not being treated here, but even the children realize they are helping scientists so that one day, scientists may help others in need."

## Mark Gorenberg Establishes Graduate Student Fellowship

Mark Gorenberg '76, a member of the McGovern Institute Leadership Board, has established a new graduate student fellowship at the McGovern Institute with the hope that others will be encouraged to do the same.

A dedicated volunteer for and donor to MIT, Gorenberg serves as a member of the MIT Corporation and co-chairs MIT's $500-million Campaign for Students. Part of that campaign involves undergraduate scholarships, as well as fellowships for graduate students who must otherwise rely on private funding to complete their research once NIH funding runs out.

"MIT is a meritocracy that admits the best and the brightest students regardless of financial need. But to compete for the very best graduate students, we need fellowships so students can really devote themselves to their research," says Gorenberg, who is a Managing Director at Hummer Winblad Venture Partners in San Francisco. In addition to earning a degree in electrical engineering from MIT, he holds master's degrees from University of Minnesota and Stanford University, and was a member of the original SPARCstation 1 team at Sun Microsystems.

"Fellowships can help drive a cycle that begins with amazing students who attract great faculty," Gorenberg says. "As they work on important projects together, their research attracts more excellent students."

He credits McGovern Institute director Robert Desimone with the motivation for the Gorenberg Fellowship. "Bob told us

*Mark Gorenberg, a partner at Hummer Winblad Ventures and a member of the McGovern Institute Leadership Board.*

*Photo courtesy Hummer Winblad Venture Partners*

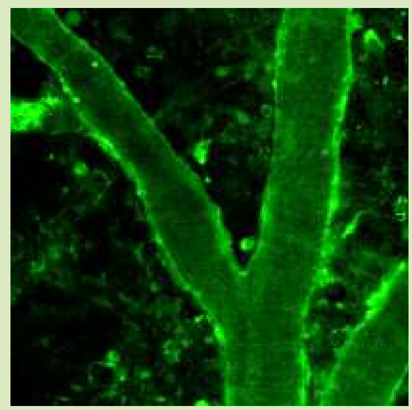
about when he was a graduate student and how critical it was to have fellowship support to complete his training after NIH funding ran out. I hope one day a McGovern graduate student will be the next generation's Bob Desimone, working to solve the many brain disorders that plague humankind."

Gorenberg says he was also inspired by the generous examples set by other donors to the institute. The Gorenberg Fellowship joins other fellowships that are supported by Shelly and Janet Razin, the Schoemaker Foundation, and the Friends of the McGovern Institute.

"The young researchers who are granted these fellowships are exceptional people, and the ability to support them at the start of their careers is part of our core mission," says Desimone. "We're very grateful to Mark for this new opportunity to attract and support students in these hard economic times." ■

## Glowing Reports

Christopher Moore's research is benefiting from the new two-photon microscope that he recently acquired with the help of a gift from Tom Peterson '57, a member of the McGovern Institute Leadership Board. "With this machine, we can now see the small neurons and smooth muscle cells that control blood flow within the brain," says Moore.



*Blood vessels and surrounding neurons as revealed by two-photon microscope.*

*Photo courtesy Bryan Higashikubo, McGovern Institute*

## Viral Vectors that Rock

*Rachael Neve (left), director of the viral core facility at the Picower and McGovern Institutes, creates specialized vectors that deliver genes into the neurons of living animals. In vivo image of pyramidal neurons in mouse visual cortex (right) expressing a gene for a fluorescent protein. The gene was delivered by one of Neve's viral vectors.*

*Images courtesy Patricia O'Loughlin, MIT; Jason Coleman, Picower Institute*

Just a few months after the opening of the viral core facility at the Picower and McGovern Institutes, researchers are already using a powerful new neuroscience tool, thanks to the fast work of the facility director, Rachael Neve. She produces viral vectors that deliver genes into the neurons of living animals so that researchers can, for instance, test the effect of specific genes on behavior.

To produce these viruses, she cripples them so they cannot reproduce, strips out their disease-causing genes and replaces them with a gene of interest. When injected into an animal's brain, the viruses are taken up and the genes are expressed by neurons, explains Neve, who has a reputed green thumb when it comes to handling these tricky reagents.

Viral vectors are a staple of cancer research, but neuroscience applications have proved more difficult. This is partly because most viruses target only dividing cells, but neurons do not divide. Also, the original vectors were developed with a view to clinical gene therapy—something that has until recently seemed too far-fetched to apply to the brain.

Neve, however, conceived of using viral vectors as experimental research tools rather than for gene therapy. So she worked on herpes simplex viruses (HSVs), which unlike many viruses do infiltrate neurons. It took 10 years but she developed a unique way to produce viral particles that are nontoxic yet still effective at delivering genes into the living brain.

"Every researcher who has used my vectors has gotten results," Neve says. "It's a very robust system. I get emails saying 'Your virus rocks!' It's been really satisfying."

Neve sees part of her role as spurring the imagination of researchers. "I meet with investigators to learn about their studies and I suggest how they could use viral vectors to achieve their goals." These ideas are starting to stimulate new collaborations, often involving researchers from several different fields.

Neve's own goals include creating vectors from adeno-associated viruses and lentiviruses, in addition to the HSV that she is already using. "When you inject HSV into the brain, it only works for about a week. That's ok for some experiments, but it would also be nice to get more permanent expression, especially for behavioral studies. These other viruses can be expressed for much longer periods, but I need to make them more efficient." She hopes to be able to offer these new vectors soon. ■

# Public events

## Scolnick Prize Lecture

*Monday, April 27, 2009, 4 p.m.*
The McGovern Institute awarded the 6th annual Scolnick Prize in Neuroscience to Jeremy Nathans, a professor at the Johns Hopkins School of Medicine and a Howard Hughes Medical Institute Investigator.

*Jeremy Nathans of Johns Hopkins Medicine will receive the McGovern Institute's 2009 Scolnick Prize for Neuroscience.*

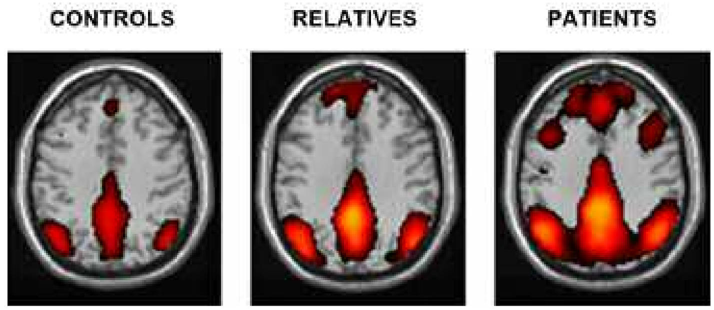
*Photo courtesy Johns Hopkins Medicine*

## Annual Symposium

*Thursday May 7, 2009*
In this one-day symposium, leading international experts in basic and clinical research discussed the biological functions of the basal ganglia in health and disease. The basal ganglia are involved in many aspects of behavior and are also implicated in Parkinson's disease, Huntington's disease, drug addiction, and many psychiatric conditions.

*Details are available on our website.* ■

## In the News




*Schizophrenics and their relatives show altered activity in the default network of the brain.*

*Image courtesy Susan Whitfield-Gabrieli, McGovern Institute*

The *Boston Globe* covered an fMRI study by **John Gabrieli** and colleagues, which found that people with schizophrenia have an overactive default network of the brain that is normally involved in self-reflection (see image). The study was supported in part by the Poitras Center for Affective Disorders Research.

The *Boston Globe* and *US News & World Report* covered a study in *Science*, coauthored by **H. Robert Horvitz**, that identified a new gene involved in the inherited form of amyotrophic lateral sclerosis (ALS) or Lou Gehrig's disease. The discovery could lead to new animal models for the disease.

**Ann Graybiel** was cited as a key expert in a *Los Angeles Times* feature article about habit formation. "Once you have a habit, you may break it," Graybiel told the *Times*, "but you don't forget it." The article cited her 2005 *Nature* study, which found that forming new habits—and resuming old ones—are linked to patterns of activity in the basal ganglia.

The *Canadian Broadcasting Corporation (CBC)* and *US News & World Report* covered a paper by **Nancy Kanwisher** and colleagues exploring how the brain adapts to macular degeneration, the most common form of adult blindness. A *Boston Globe* feature article on facial recognition described Kanwisher as "prominent among scientists whose research suggests there is a specific 'sweet spot' in the brain—called the fusiform face area—that has evolved to recognize faces." Kanwisher also discussed her view that fMRI cannot serve as a lie detector in the French publication *L'Express*.

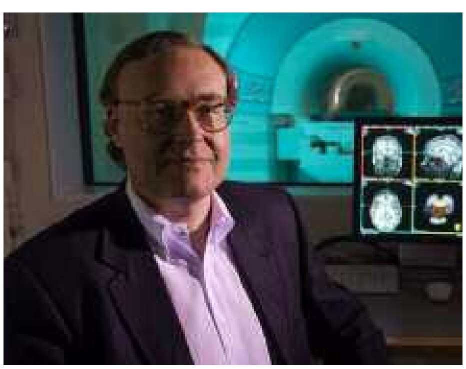
Calling him "one of the fathers of neuroscience," the Italian newspaper, *La Stampa*, interviewed **Tomaso Poggio** about future possibilities for intelligent robots.

*Wired* magazine ran a two-part article featuring **Ed Boyden**'s mission to engineer brains for the better. It also described Boyden's prototype for an affordable, wearable transcranial magnetic stimulation (TMS) unit for treating depression and other conditions.

**Ed Vul**, a graduate student in **Nancy Kanwisher**'s lab wrote a paper with his former colleagues at the University of California, San Diego criticizing statistical methods used in many brain imaging studies. Despite the technical subject matter, their critique was widely reported, including in *Newsweek* and *Scientific American*. ■

*For links to media coverage, go to http://web.mit.edu/mcgovern/html/News_and_Publications/media_coverage.shtml*

## AWARDS AND HONORS



*John Gabrieli, Director of the Martinos Imaging Center at MIT*

**John Gabrieli** was elected fellow by the American Association for the Advancement of Science. The association honored him for "penetrating analyses of the nature of human memory, its neural substrates, its development and its problems." ■

*H. Robert Horvitz (far left) watches President Obama sign the executive order on stem cell research.*

### Lifting the Stem Cell Ban

**H. Robert Horvitz** was among a group of Nobel laureates, scientists, and doctors who stood alongside President Obama on Monday, March 9, as he signed an executive order reversing federal opposition to embryonic stem cell research. Obama's order lifts eight years of funding restrictions on this kind of research, making hundreds of stem cell lines eligible for NIH funding. Horvitz, who shared the 2002 Nobel Prize for medicine, was a member of the committee established by the National Academy of Sciences to develop guidelines for stem cell research. ■

## Beijing Neuroscience Symposium

More than 200 researchers attended the symposium "New Frontiers in Brain Research" organized by the McGovern Institute and Chinese collaborators at Tsinghua University in Beijing on February 24-25. The symposium was part of an ongoing effort to establish cooperative research programs with Chinese research institutions. McGovern faculty members Ed Boyden, Bob Desimone, Michale Fee, Ki Ann Goosens, and Yingxi Lin gave presentations. Also attending were Charles Jennings, Director of the McGovern Institute Neurotechnology Program (MINT), and Gayle Lutchen, McGovern's Director of Administration.

The program was supported by a grant from Hugo Shong, Executive Vice President of International Data Group and founding General Partner of IDGVC Partners, who has a long-standing interest in promoting international neuroscience research.

"The problems we work on are global problems, and they will only be solved with global collaborations," comments Bob Desimone, the director of the McGovern Institute. "China has a lot to contribute to the solution, with its huge talent pool and strong commitment to scientific research. This is a very exciting cooperative program between our two countries." ■


*Members of the McGovern Institute and Chinese colleagues at the joint brain research symposium at Tsinghua University.*

*Photo courtesy Lixia Huang*

## Eric Kandel on Memory

On February 2, Eric Kandel, Nobel laureate and member of the McGovern Institute Scientific Advisory Board, gave a lecture at the institute prior to screening a new documentary about his life and his research on memory. The McGovern Institute co-sponsored the screening of the documentary *In Search of Memory* at the American Academy of Arts and Sciences. ■

***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://web.mit.edu/mcgovern/***

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