McGOVERN INSTITUTE
FOR BRAIN RESEARCH AT MIT

Brain SCAN

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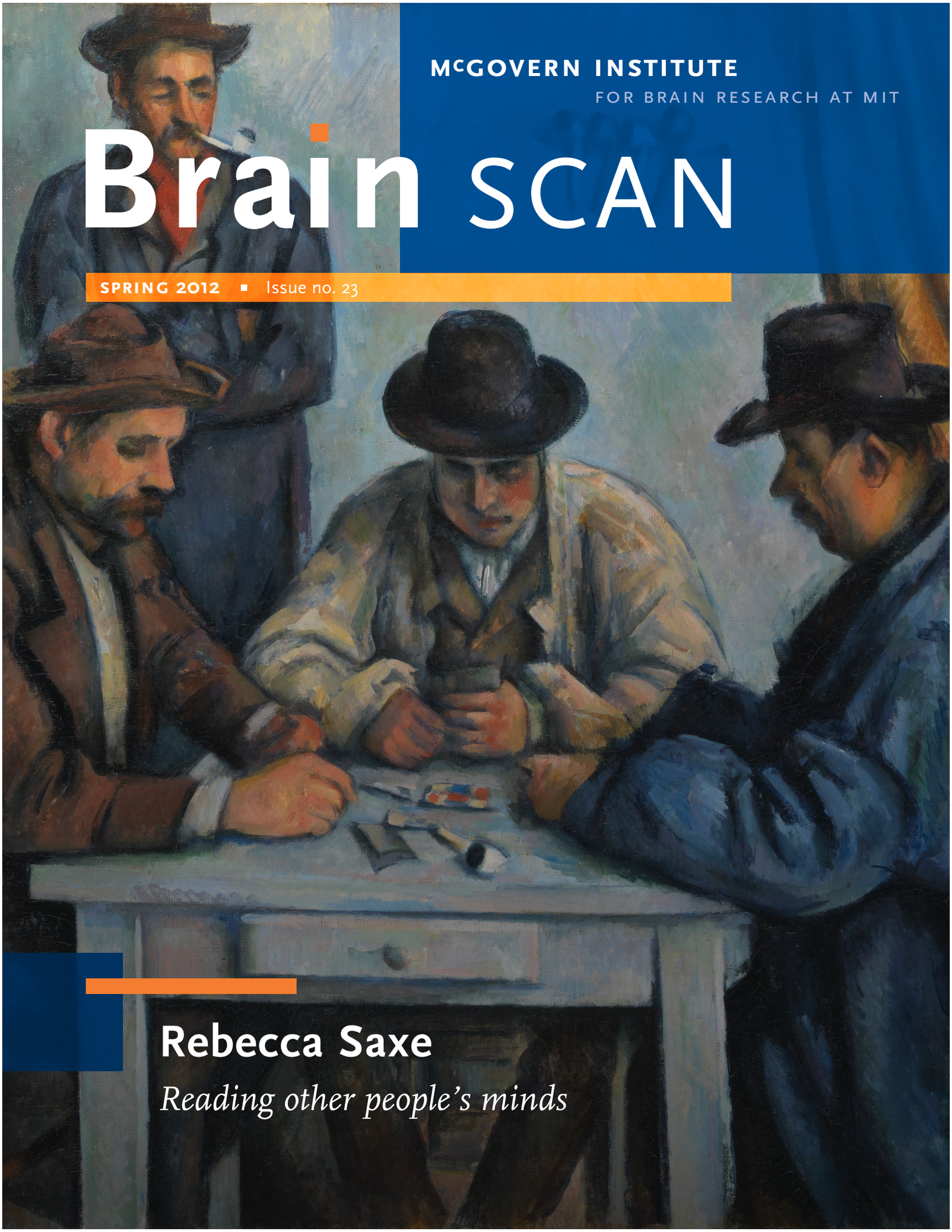


Rebecca Saxe

Reading other people's minds

FROM THE **DIRECTOR**

In this issue we feature the work of Rebecca Saxe, who recently joined the McGovern Institute as an associate member. Rebecca is truly pushing the frontiers of our field, bringing a rigorous scientific approach to some profound questions about human nature, including social communication, moral judgment, empathy, and even conflict between ethnic groups.

One recent highlight has been our annual symposium, which this year featured magnetoencephalography (MEG), a method for measuring human brain activity that was developed at MIT by David Cohen 40 years ago. It was especially gratifying that David was able to join us at this event; his talk on the origin of MEG offered a fascinating example of how new technologies are invented. Many students and faculty are now using our new MEG scanner at the McGovern Institute.

And on the subject of innovation, I am delighted to report that my colleagues Ed Boyden and Feng Zhang have recently been honored with the UNC Perl Prize for their role in the development of optogenetics, along with Karl Deisseroth of Stanford University. This technology, which enables us to control brain activity with light, is having a profound impact on many areas of neuroscience, and I congratulate Ed and Feng on their well-deserved recognition.

Bob Desimone, Director
Doris and Don Berkey Professor of Neuroscience

On the cover:
To win at cards, players must understand the beliefs and intentions of their opponents, an ability known as "Theory of Mind." Rebecca Saxe studies the brain mechanisms that underlie this quintessentially human ability.

Paul Cézanne, "The Card Players," 1890–92. Metropolitan Museum of Art, New York.

Photo: Justin Knight

Rebecca Saxe is a philosopher-turned-scientist who wants to understand the neural basis of social cognition

Rebecca Saxe jokes in her talks that she uses "normal human brains" in her neuroimaging research. "Normal," she explains, "meaning MIT undergraduates." She gets a laugh every time.

Many brain researchers recruit students and colleagues for their studies. They sometimes even run experiments on themselves. But this doesn't work for Saxe, who uses functional magnetic resonance imaging (fMRI) to study Theory of Mind, the human ability to understand other people's thoughts.

When Saxe is in the scanner, she has a proverbial elephant in her brain. "I know when I'm not supposed to be thinking about what people are thinking, but I can't

Rebecca Saxe

Reading other people's minds

help myself. I start wondering, am I thinking about thoughts? As a consequence, I am—I'm thinking about *my* thoughts," says Saxe, a newly-appointed associate member of the McGovern Institute and an associate professor in the Department of Brain and Cognitive Sciences. "It's very demoralizing."

But certainly not in any way that slows her down. Saxe completed her PhD in less than three years and received tenure at the exceptionally young age of 31. Her chosen field, social cognitive neuroscience, has also grown rapidly, from about half a dozen papers when she entered graduate school to thousands of papers today.

Saxe applies the tools and theories of neuroscience to understand human social behavior, including moral judgments, identification with groups, and feelings of empathy. Ultimately, she says, society is built on such social reasoning. By understanding the nature of social cognition as it manifests itself in the brain, she hopes that science can help build a better society for everyone.

Beyond her academic credentials, Saxe's work has attracted wide public attention. *Popular Science* magazine listed her as one of their "Brilliant 10" in 2008, the World Economic Forum recently named her a Young Global Leader, and her 2009 TED talk has been viewed over a million times.

A Social Mind

Originally drawn to science after learning that life is made of molecules, Saxe began —at the young age of 17—to wonder about the nature of thought. "The human mind and human self are represented in the firing of cells in the brain," she says. "The idea that you could study the basis of our humanity in scientific terms was very appealing to me."

She went to Oxford University to study Psychology, Philosophy and Physiology. As an undergraduate there, she became involved in two research projects, one exploring a philosophical question about self-deception, the other trying

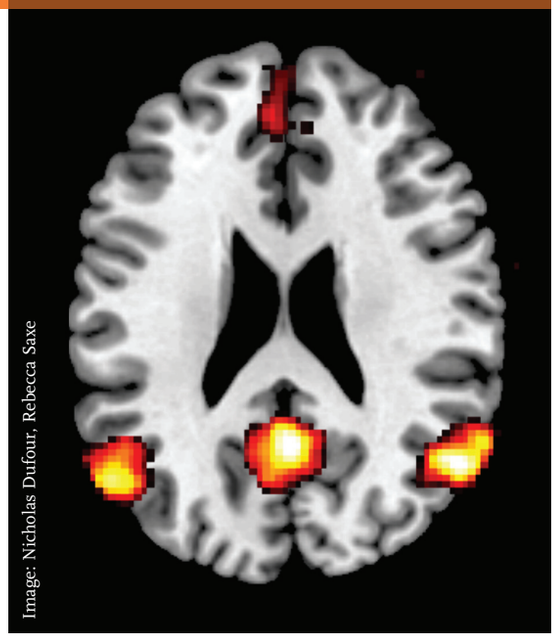


Image: Nicholas Dufour, Rebecca Saxe

Saxe uses MRI to identify human brain regions that are activated by social tasks.

to answer a narrow scientific question about attention that, she says, "didn't make good dinner party conversation." It did, however, involve gathering data on human brain activity, using a method known as electroencephalography (EEG).

Facing a decision between philosophy and science, her future could have gone either way, but the data tipped the scales. "While the philosophical question I was working on seemed more urgent, I couldn't give up on the data," she says. Neuroscience had her hooked.

Saxe came to MIT for graduate school to work with McGovern Investigator Nancy Kanwisher, who uses neuroimaging to study the organization of the human brain. At that time, scientists were just beginning to probe the social mind using fMRI, and Kanwisher helped Saxe devise her own approach.

In 2003, Saxe published her first major discovery, defining a region of the brain, the right temporo-parietal junction (rTPJ), that becomes activated only when we think about other people's thoughts. Others had previously associated this region with Theory of Mind, but Saxe was the first to show that this region is highly specialized for it. Few people had expected this, and in Kanwisher's words, Saxe's finding was "one of the most astonishing discoveries in the field of human cognitive neuroscience."

Right or Wrong

Saxe has continued to study the rTPJ ever since, often by scanning volunteers as they read simple stories that require understanding the thoughts and motives of the characters. One current interest is the basis of moral judgments, and Saxe has developed a collection of stories that probe this question by pitting intentions against outcomes. In one example, the main character intentionally kills her friend by putting poison in her coffee. Then, in different versions, she tries to kill her friend but fails because she mistakes sugar for poison, or else she accidentally kills her friend by mistaking poison for sugar.

While everyone agrees intentional killing is morally wrong, people vary in how harshly they judge an accidental death relative to an unsuccessful murder attempt – in other words how much weight to place on the character's intentions relative to the actual outcome.

If the rTPJ is involved in understanding intentions, then interfering with this brain region should alter people's moral judgments. Saxe was able to test this hypothesis using transcranial magnetic stimulation, a method for temporarily disrupting brain function with a powerful magnetic pulse. She found that when the pulse was aimed at the rTPJ, people tended to be more forgiving of the unsuccessful attempted killing.

Individuals with autism also show a similar effect; in collaboration with McGovern Investigator John Gabrieli, Saxe found that adults with autism were less forgiving of the accidental killing scenario than adults without autism. As with the magnetic pulse experiment, autistic subjects tended to base their judgments more strongly on actual outcomes, with less emphasis on the actors' intentions. The findings suggest that the rTPJ may be impaired in people with autism, an idea that Saxe is continuing to explore.

Photo: TED / James Duncan Davidson

Saxe speaking at the TEDGlobal conference in 2009. Her talk has been viewed over a million times.

Brain Patterns

To further dissect the working of the rTPJ, Saxe and her graduate student Jorie Koster-Hale are applying a novel approach to analyzing fMRI data. As with all fMRI scans, they record brain signals in "voxels," or 3-dimensional pixels. They then apply a statistical method called "multivoxel pattern analysis" to examine the patterns of brain

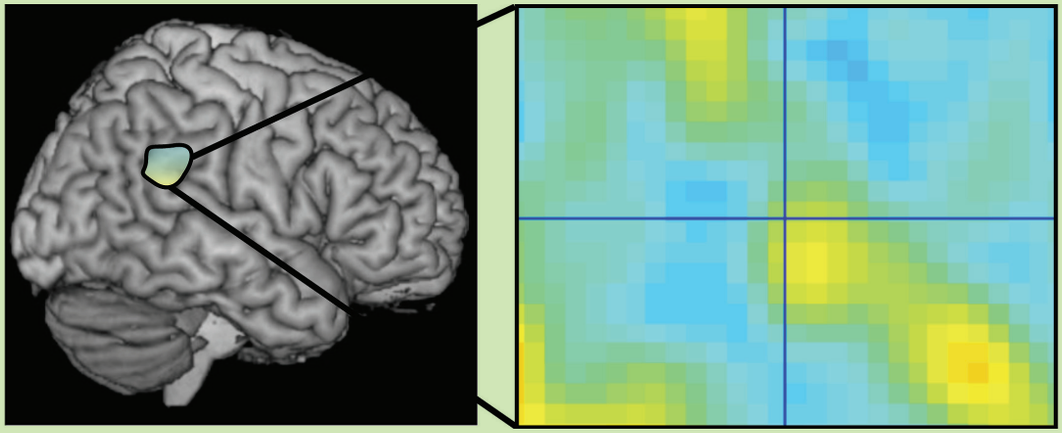


Image: Jorie Koster-Hale, Rebecca Saxe

Pattern of neural activation in the rTPJ in response to reading a story with a moral violation. Yellow signifies more activation, blue is less activation.

activity that are evoked by their stories. The technique has been applied to visual object recognition, but never before to high-level cognition.

Koster-Hale's preliminary results show that as subjects read the stories, different patterns of voxels within the rTPJ are activated by different types of scenarios. Thus, one pattern is associated with reasoning about accidental actions, while a different signature is seen for intentional actions. "But in people with autism, we don't see that distinction,"says Koster-Hale. "We see a strong response to both kinds of actions, but it's the same response, as if the rTPJ was less able to differentiate the two kinds of stories."

The work is still in progress, and clearly there is plenty more to be learned about the rTPJ. "The results are super-exciting," says Saxe. "But they're still at the level of voxels. Each voxel represents hundreds of thousands of neurons. The approach is incredibly promising, but still, it can only take us so far."

As technology continues to advance, Saxe welcomes the prospect of being able to measure human brain activity at higher resolution and faster time scales in the future. But she also emphasizes the importance of having a strong conceptual framework. "In the absence of theory, you just try a lot of stuff and work backwards," she says. "But I like having a hypothesis. I like designing an experiment."

Image: Rashaun X. James, U.S. Marine Corps, DoD

Saxe hopes that her work will provide new insights into the origins of ethnic conflict.

Photo: Justin Knight

Members of the Saxe lab: Jorie Koster-Hale (left), Emile Bruneau (center), and Mina Cikara (right).

To the Moon

Saxe's work delves deeply into what it is to be human, and her laboratory attracts young investigators who are turning to science to understand their own deepest experiences. As an example, postdoctoral fellow Emile Bruneau, trained in cellular and molecular neuroscience, came to Saxe with an idea to study the neurobiology of ethnic conflict.

Bruneau had traveled widely and witnessed violent conflicts first-hand, including a near-miss during the Sri Lankan civil war when he saw a plane blow up shortly after deboarding it. He decided that, if he was to be a scientist, his research needed to align with his real-life concerns about group conflict. Saxe agreed to work with him, despite his lack of neuroimaging experience, he says, "in part because there could be some potential social utility to this science."

By studying people drawn from conflicting groups such as Arabs and Israelis, Saxe and Bruneau have used neuroimaging to identify distinct brain regions associated with empathy for another's physical and emotional pain. In later work with postdoctoral fellow Mina Cikara, they found that the moral calculus in people's minds changes when they identify with a group. "Levels of empathy tend to flip when there's an out-group," says Saxe. "We find that the same people who are more empathetic to the in-group are more likely to be willing to harm an out-group member."

Bruneau is now working to develop an evidence-based way to evaluate conflict resolution programs. He also tries to apply his scientific insights to his own self-improvement, recognizing that he too has unconscious biases against people different from himself. "I know now that these biases are built into my mind," he says. "But I also know I have a responsibility to work on changing them."

"I think that human neuroscience provides an urgent form of self-knowledge to people."

— Rebecca Saxe

Taking the long view, Saxe believes that with a deeper understanding of our minds and how we think about and judge others, people will also be able to change society for the better. "We run our societies on intuitive psychology," she argues. "Imagine trying to go to the moon on intuitive physics. You would miss."

Saxe is quick to add perspective. "I don't think I'm doing the equivalent of building the Apollo program," she says. "But I really do think that human neuroscience provides an urgent form of self-knowledge to people. I feel privileged to have some of that knowledge and would like to give it to anyone who wants it." ■

New Gifts Support Neurodegenerative and Autism Research


Photo: Kent Dayton

Ann Graybiel

Rae Pourian and Julia Madidi Pourian made a generous gift to support the laboratory of Institute Professor Ann Graybiel. The Pourians have been inspired by Graybiel's efforts to understand the basis of neurodegenerative and developmental brain disorders. They also wished to support Graybiel's role as a mentor to undergraduate and graduate students researching the complexities of the brain.

Bruce Dayton, former CEO of Target Corporation, recently made a generous commitment towards the acquisition of a new MRI scanner for human brain imaging. A philanthropic leader and major supporter of arts organizations in Minnesota and China, Dayton made the gift in honor of his grandson Henry Buxton. The new MRI scanner will be used for many studies, including those designed to understand the biological origins of autism. ■

UCSF's Roger Nicoll Delivers Scolnick Prize Lecture


Photo: Justin Knight

Robert Desimone (left) with Scolnick prize winner Roger Nicoll.

Roger Nicoll of the University of California, San Francisco delivered his Scolnick Prize lecture, "Deconstructing and reconstructing a synapse" to a packed auditorium on April 19. Nicoll was awarded the prize for his pioneering work on synaptic plasticity, the process by which the brain's connections are modified in response to experience. In his opening remarks, Institute director Robert Desimone congratulated Nicoll on his distinguished career, describing Nicoll's discoveries on the mechanism of long-term potentiation as "one of the cornerstones of modern neuroscience." ■

Annual Symposium Features Brain Scanning Technology

Photo: Justin Knight

Robert Desimone (right) presents David Cohen with a plaque commemorating the 40th anniversary of the invention of MEG.

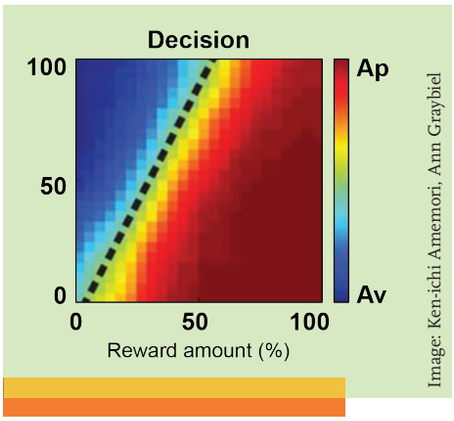
The theme of our annual symposium, held on April 27, was magnetoencephalography (MEG) and its applications to cognitive neuroscience. MEG is a powerful method for imaging human brain activity, and the symposium featured many of the world's leading MEG experts, including speakers from Finland, Germany, Canada and the US. The speakers discussed how MEG is contributing to our understanding of human brain function and disease, including language, movement control and the basis of psychiatric disease.

The symposium also marked the opening of our new MEG lab at MIT, and the anniversary of the 1972 paper by David Cohen describing his pioneering work – much of it conducted at MIT – on the development of MEG technology. Cohen, now a faculty member at Massachusetts General Hospital, gave a historical talk about his invention. Cohen's lecture and other talks from the symposium are now available on our website. ■

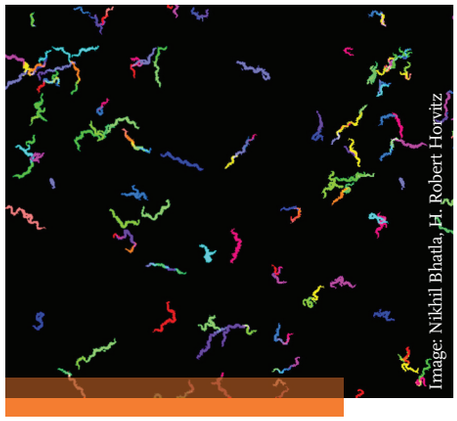
RESEARCH NEWS

Ed Boyden and collaborators at Georgia Tech have developed a robot that can record electrical activity from individual neurons within the living brain, using a method known as whole cell patching. With the new approach, a glass electrode is controlled by a robotic device that can sense automatically when it has made contact with a neuron. The method promises to greatly accelerate many areas of neuroscience research.

Ann Graybiel and postdoc Ken-ichi Amemori study how the brain balances rewards against costs. Recording from the brains of macaque monkeys, they identified different groups of neurons that signal costs and benefits. Psychiatric disorders such as anxiety and depression can bias these cost/benefit calculations in humans, and the researchers found that anti-anxiety drug treatment shifts this balance by blocking the negative signals.



Ann Graybiel and colleagues study how the brain balances rewards against costs.



The Horvitz lab uses a computerized tracking system to study how worms respond to oxygen.

H. Robert Horvitz and colleagues have identified new components of a molecular pathway involved in detecting low oxygen levels in worms. The equivalent pathway in humans is implicated in ischemic stroke and reperfusion injury, and the latest findings may lead to new treatments for these conditions.

Shifts in visual attention are typically accompanied by eye movements toward the attended target, and both are controlled by "top-down" signals from the frontal eye field (FEF). **Robert Desimone** and colleagues show these two aspects of visual behavior depend on different populations of neurons within the FEF. ■

IN THE MEDIA

The CBS television show *60 Minutes* ran a 2-part series on prosopagnosia—the inability to recognize faces—on March 18. **Nancy Kanwisher** was featured in the second segment. The program, "Face Blindness," is available in its entirety on the *60 Minutes* website.

McGovern Institute co-founder, **Patrick J. McGovern**, was featured in *Korn/Ferry Institute's Briefings Magazine*. The article, "Investing in Brains: Pat McGovern's Philanthropic Quest," discusses McGovern's motivations for establishing the institute. A link to the article can be found on our website.

Ann Graybiel's research was featured in a *New York Times Magazine* article about how companies seek to alter consumer habits. The magazine article is based on "The Power of Habit," a new bestselling book by *Times* writer Charles Duhigg. ■

Nancy Kanwisher (right) with 60 Minutes correspondent Lesley Stahl.

AWARDS AND HONORS


Photo: Kent Dayton


Photo: Kent Dayton


Photo: Kent Dayton


Photo: Dominick Reuter

Clockwise from left: Lore Harp McGovern, Feng Zhang, Michale Fee, and Ed Boyden

Institute co-founder **Lore Harp McGovern** received the Distinguished Alumnus award and delivered the 2012 commencement address at Pepperdine University's Graziadio School of Business and Management.

Feng Zhang is one of fifteen researchers to be named a 2012 Searle Scholar. Zhang, who designs new molecular tools to manipulate the living brain, will receive $300,000 over three years to support his research.

Michale Fee received Duke University's Katz Prize, named for neuroscientist Larry Katz, who died in 2005. The prize is given annually to a neuroscientist "whose work reflects Katz's openness to new ideas, creativity, and enthusiasm for technical and conceptual innovation."

Ed Boyden and **Feng Zhang**, along with Karl Deisseroth of Stanford University, have been awarded the Perl/UNC Neuroscience Prize for developing a way to control brain activity using light. ■

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, who is the Doris and Don Berkey Professor of Neuroscience at MIT and former head of intramural research at the National Institute of Mental Health.

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

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