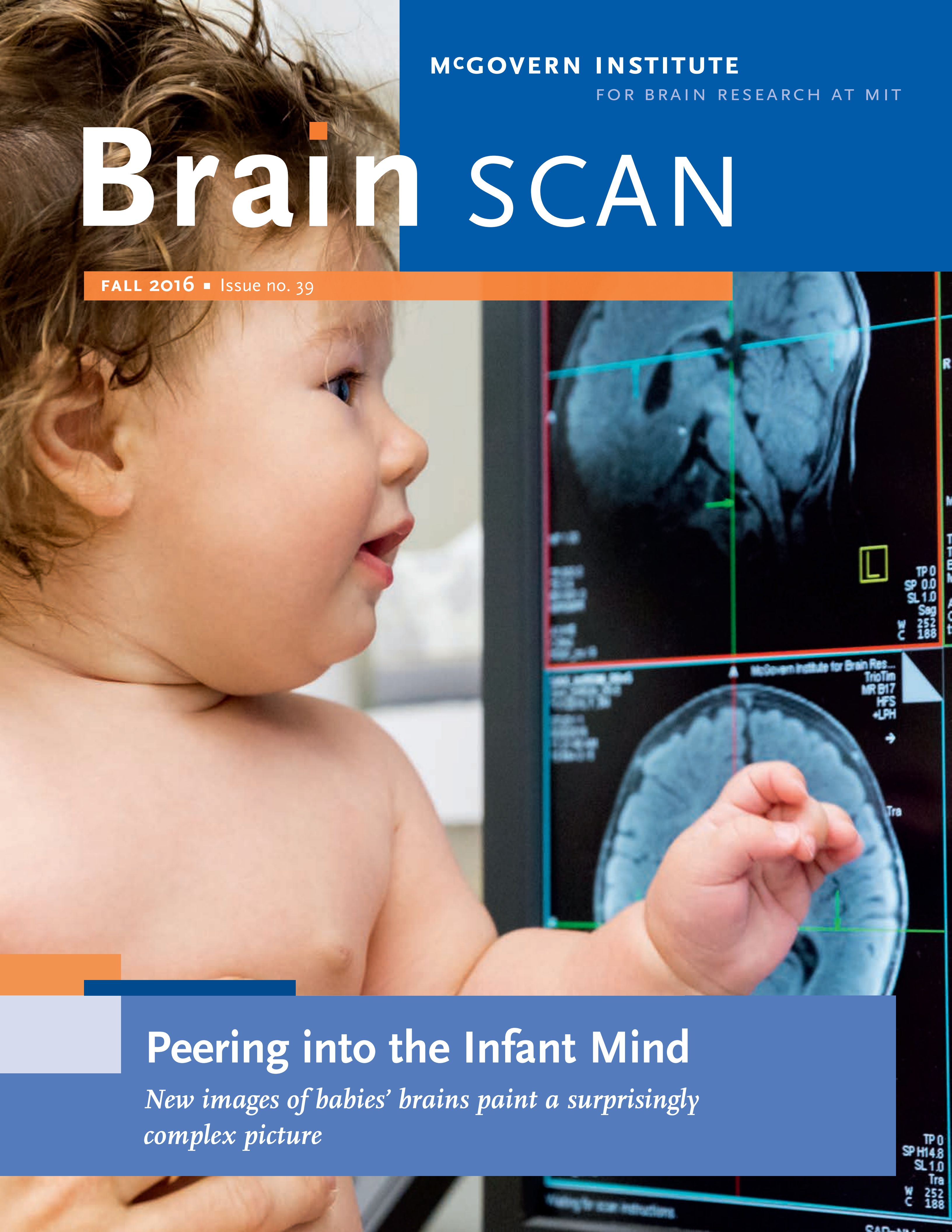
McGOVERN INSTITUTE
FOR BRAIN RESEARCH AT MIT

Brain SCAN

FALL 2016 ▪ Issue no. 39



Peering into the Infant Mind

New images of babies' brains paint a surprisingly complex picture

FROM THE DIRECTOR

Philosophers have long debated the concept of 'tabula rasa' or blank slate—the idea that the human mind is formed without any preconceptions about the world, and is shaped entirely by experience. Most biologists would probably argue that some aspects of human nature are innate, but my colleague Rebecca Saxe is tackling the question head-on, by scanning the brains of young babies. In a technical tour de force, her team has performed functional MRI scans on infants as young as two months—including Rebecca's own sons Arthur and Percy—to identify brain areas that respond preferentially to specific classes of visual stimuli, such as faces and scenes, similar to those found in adults. Although these areas are certainly fine-tuned by subsequent visual experience, Rebecca's findings suggest that the initial preferences for specific categories are already present from birth, presumably based on instructions that are somehow encoded in our genomes.

In addition to its intrinsic interest, this work has important practical implications. Many brain disorders arise very early in life, even if they are not diagnosed until years later. Just as with healthy brain development, these disorders unfold in a sequence of stages, in which early problems can set the developing brain on a trajectory that may be difficult to change later. But this view also provides grounds for optimism that early intervention could help to avoid these outcomes and instead direct development on a better course. By helping to understand how genes and environment shape brain development in the first few months of life, Rebecca's research is laying the groundwork to make this vision a reality.

Bob Desimone, Director
Doris and Don Berkey Professor
of Neuroscience

On the cover:
A baby looks at pictures of her own brain after being scanned for a study at the McGovern Institute.

Photo: Caitlin Cunningham

Photo: Caitlin Cunningham

Rebecca Saxe is discovering that babies' brains are more like those of adults than previously realized.

Mothers often speak with a sense of wonder about seeing their new baby's face for the first time. For McGovern Associate Investigator Rebecca Saxe, an even more wondrous moment came when she first saw her baby's brain.

"I thought, wow, that will be my baby's mind and my baby's self," she says.

Saxe, who is also a professor in MIT's Department of Brain and Cognitive Sciences, had produced the image as part of an ambitious research program to study baby brains using functional magnetic resonance imaging (fMRI). The program builds on earlier studies of adult brains by McGovern Associate Investigator Nancy Kanwisher, Saxe's former mentor

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who is also a collaborator on the new baby study. Kanwisher had found that the adult human brain has regions that respond specifically to images of faces, scenes, and other classes of visual stimuli.

Kanwisher's findings posed a question: are these specialized brain regions formed by visual experience, or are they already present from birth? The question addresses a fundamental and longstanding debate about human nature: does the human brain and mind start out as a 'blank slate,' waiting to be shaped by experience, or are we pre-wired to perceive the world in ways that are shaped by our biology? Brain imaging could help provide the answer, but scanning the brains of young infants is far more difficult than studying adults, and the question remains unanswered two decades after Kanwisher's original discovery.

Saxe has now taken up the challenge, exploiting new advances in fMRI and functional near-infrared spectroscopy (fNIRS), both of which measure changes in blood flow when particular brain regions become more active. Her findings are providing scientists with the most detailed images ever produced of brain activity in young babies. The results that have emerged so far suggest that baby brains are more specialized than anyone had realized. They also have important practical implications, raising the possibility of identifying developmental disorders early enough to make corrective changes before troubles amplify over time. "There's a very strong push now to intervene early in developmental disorders," says Saxe. "If we want to do that using brain scans, we first need to understand what typical development looks like."

The Long Road to the First Scan

Saxe had been thinking for many years about using brain imaging to study awake babies. As a graduate student with Kanwisher, she had worked at the leading edge of fMRI studies of adults, and she had also done behavioral experiments with babies during her postdoctoral research at Harvard. "From the outside, baby behavior looks unsophisticated and random," she says. "But behavioral research has revealed that there are richer, more elaborated conceptions of the world in their minds that are not obvious from their actions."

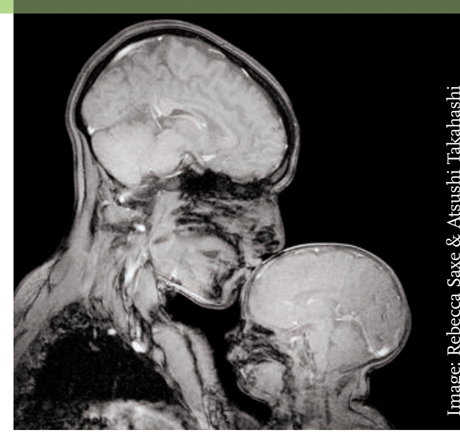


Image: Rebecca Saxe & Atsushi Takahashi

Magnetic resonance image of Rebecca Saxe with her son Percy at the age of two months.

After returning to MIT in 2007 to set up her own lab, Saxe and her then-graduate student Ben Deen began to plan a program to study young infants using fMRI. They first needed to obtain formal approval based on a safety evaluation. The scans themselves were deemed safe for babies, but there were concerns about noise, given that some scanning protocols can be as loud as a rock concert, around 125 decibels.

The Saxe Lab developed an MRI head coil specifically designed for baby-sized heads.

So Deen worked with Atsushi Takahashi, the MRI physicist at the Martinos Imaging Center at MIT, to develop new scan sequences that would soften the potentially ear-damaging sounds inside the scanner. Deen also had to build a new head coil specifically designed for baby-sized heads. Solving these technical problems took several years of work, but finally, in 2013, the team was ready to do their first scan. They also had their first subject—Saxe's first son, Arthur, who was then four months old.

They put him in the scanner and showed him movies of faces and scenes. No one knew if the images would reveal a functionally organized visual cortex or an unstructured blank slate. "I genuinely had no idea what to expect," says Saxe.

The images of her son's brain revealed an area of cortex that responded to images of natural scenes. That area was in the exact same place as in adults. "It was amazing to see," says Saxe.

That first scan unleashed a wave of questions and ideas about how to answer them. Was part of the brain pre-wired to recognize scenes, or had her son's scant visual experience already shaped this region? If experience had caused this region to develop, why didn't the data show a similar region for faces? Her son had certainly seen more faces than forests and mountains.

"It was like the early days of fMRI," Saxe says. "We'd get a day's worth of data and by midnight we'd be emailing each other with new ideas for experiments."

Burping, Sleeping, Crying, Scanning

After the initial excitement, though, progress was slow. fMRI scans, like photos, are very sensitive to motion, and head movements as small as a tenth of a millimeter can blur the data. Unlike earlier studies, in which babies were scanned while sleeping, Deen and Saxe needed them to lie still while remaining awake and watching a movie. Babies seldom remain still for long, and the researchers had to hope that their subjects would not burp or start crying or need a diaper change half way through the scan.

Heather Kosakowski, manager of the Saxe Lab, prepares to scan an infant subject.

Eventually, by the end of the study, they had managed to scan 17 babies. All told, the team booked 126 hours in the scanner and obtained 23 hours of actual scan data. Much of it was corrupted by motion and had to be discarded; ultimately the researchers were left with just 4.3 hours of usable data, from 9 subjects.

As they analyzed the results, Saxe and her colleagues realized that the initial picture from her son's first scan was incomplete. His brain showed responses to scenes but not faces, but with more subjects it became apparent that by 4 to 6 months, babies already have specialized visual areas that respond preferentially to faces or scenes. The responses are not as finely tuned as in adults, suggesting that later experience is also important, but the overall organization was remarkably similar to that of adults. "It's lovely to see," says Lindsey Powell, a postdoc in the Saxe Lab who is also scanning babies. "It's not just a single region, but a whole network of brain regions seen in adults."

Saxe now hopes to untangle how experience shapes these specialized regions. Lab manager Heather Kosakowski has started scanning individual babies repeatedly over time as they mature from three to six months. She is using a method known as multi-voxel pattern analysis to discover how the brain's response to different types of images changes over the first few months of life.

She is also using images designed to test babies' visual sophistication. For example, she presents babies with images of faces looking directly forward and faces in profile. For very young babies, sideways views may be categorized as objects, but a few months later, they are recognized as faces.

The biggest challenge will be working with the babies under time pressure to capture data during what is often a very short window of opportunity. If anyone has the patience and persistence to do this, it's Kosakowski, who emerged from a childhood in foster homes, worked through 5 years of service in the US Marine Corps, put herself through Wellesley College as a single parent, and now is preparing for graduate study in neuroscience. "Allowing myself to

Photo: Caitlin Cunningham

The Saxe Lab uses functional near-infrared spectroscopy (fNIRS) to detect changes in blood flow during brain activity.

believe I can go to graduate school is also allowing myself to believe that the questions I find interesting matter," she says. "It matters that we understand how the infant brain develops."

Attention Seekers

In addition to understanding how experience shapes the infant brain, Saxe and her colleagues also want to learn how the infant brain shapes its experiences. "Babies are active learners in their world," says Saxe. "They choose what to pay attention to. But we don't know what motivates these choices."

Powell, who is leading this project, spent overlapping time with both Saxe and Kosakowski in the Harvard lab of Elizabeth Spelke, one of the world's foremost experts on babies' cognitive development. "In behavioral research, the main thing we can measure is where they're looking and for how long," says Powell. "We can't ask babies what's going on in their heads."

But now, thanks to a new technology known as fNIRS, Powell can measure what is going on. Like fMRI, fNIRS detects changes in blood flow during brain activity, but instead of lying inside a MRI scanner, babies can move around freely during fNIRS scans. They simply wear a fitted cap with an array of light sources that shine light through the skull into the brain—"just like flashlights," says Powell, the first researcher at MIT to use the technology. Sensitive detectors record the small amount of light that is scattered back through the skull, giving researchers a picture of the activity in the underlying brain regions.

Powell is focusing on two areas in particular: the medial prefrontal cortex, which is active when babies pay attention to a friendly face over an unfriendly face; and the dorsolateral prefrontal cortex, which becomes more active when babies pay attention to something informative, such as a person speaking a sentence over a person speaking gibberish. Babies tend to prefer friendly faces and informative speech, and the brain signals that Powell is recording may provide clues to how babies make these choices, which determine what they experience and perhaps shape the further development of their brains.

The work may also shed new light on the origins of autism. For instance, it could be that babies with ASD pay less attention to faces because they are less socially motivated and less interested in faces than typically developing babies. Alternatively, they could find faces uninformative or overwhelming.

"Our experiences shape our brains, but our brains also determine our experiences," says Saxe. "It's a back-and-forth that continues throughout development. My hope is that as we understand it better, we can start to ask how it goes wrong in developmental disorders, and how we might intervene to produce better outcomes."

To learn more about volunteering as a research subject, please visit our website or email the Saxe Lab at mit.kids.brains@gmail.com.

Photo: Caitlin Cunningham

Members of the Saxe Lab from left to right: Lindsey Powell, Heather Kosakowski, Lyneé Herrera, Rebecca Saxe and Hilary Richardson.

New Sculpture Transforms McGovern Institute Entrance

Photo: Justin Knight

MIT's newest piece of public art is located at the Main Street entrance to the McGovern Institute in Kendall Square, Cambridge.

The newest addition to MIT's Public Art Collection is now on permanent display at the entrance to the McGovern Institute. "SCIENTIA," a towering bronze sculpture by Ursula von Rydingsvard, is a gift from Lore Harp McGovern to MIT and represents the 52nd piece of public art on campus.

"SCIENTIA represents that art and science are not separate entities," says McGovern, co-founder of the McGovern Institute and a member of the Council for the Arts at MIT. "Art defines our humanity, advances our curiosity, and forces us to ask big questions—questions the McGovern Institute for Brain Research is trying to answer. 'SCIENTIA' invites you in."

Von Rydingsvard's SCIENTIA is among her most ambitious sculptures to date, at approximately 25 feet tall and weighing over 17,000 pounds. In creating the work, the artist first produced a wood model in her studio using 4x4-inch cedar beams milled for the construction industry. Using circular saws and a range of cutting tools, she sliced, marked, and shaped the wood elements, then stacked them to create layers that were glued and screwed into place. The full-scale wood model was then transported to Polich Tallix Fine Art Foundry (founded by Richard Polich SM '65), where the majority of the sculpture was sand-cast in bronze while the delicate filigree sections were cast using the lost-wax technique. Von Rydingsvard created the surface patina by hand with chemicals and a blow torch.

"This powerful sculpture will inspire many and will be one of the signature pieces in our collection," says List Visual Arts Center Director Paul C. Ha. "We're grateful for Ms. McGovern's thoughtfulness and generosity in helping us acquire this magnificent piece for MIT." ■

Pourian Family Gift to Support Basic Neuroscience Research

Reza "Rae" Pourian has a document framed on the wall of his Northern California home: his daughter's acceptance letter to MIT. Jessica Pourian '13 earned a degree from MIT's Department of Brain and Cognitive Sciences, working in the labs of Ann Graybiel, who studies the basis of neurodegenerative and developmental brain disorders, and Nancy Kanwisher, whose group uses neuroimaging to understand the organization and development of the human brain.

These days, Jessica is attending medical school, pursuing an interest in pediatrics and autism that was sparked by her undergraduate research experience. Meanwhile, work in the Graybiel and Kanwisher labs is moving forward, bolstered by a gift from the Pourian family. The Pourians have also provided support to the Koch Institute for Integrative Cancer Research, whose mission is to confront cancer through the convergence of life sciences and engineering.

According to Rae Pourian, the family's gifts to MIT are aimed at supporting scientific discoveries that benefit the health of future generations—"we are the beneficiaries of a lot of pure research done by generations before us," he says—and also to enhance the education of the current generation of MIT students. He witnessed this firsthand as an MIT parent: "What MIT offers is a culture of cooperation, opening their hearts and labs to undergraduate students so they can learn cutting-edge research." ■

Photo: McGovern Institute

Jessica Pourian '13, center, with mentor Nune Lemaire Martiros '08, PhD '16, left, and Professor Ann Graybiel PhD '71.

RESEARCH NEWS

A team led by **Ann Graybiel** and **Ed Boyden** has discovered connections deep within the brain that appear to form a communication pathway between areas that control emotion, decision-making, and movement. The researchers suspect that these connections, which they call striosome-dendron bouquets, may be involved in controlling how the brain makes decisions that are influenced by emotion or anxiety.

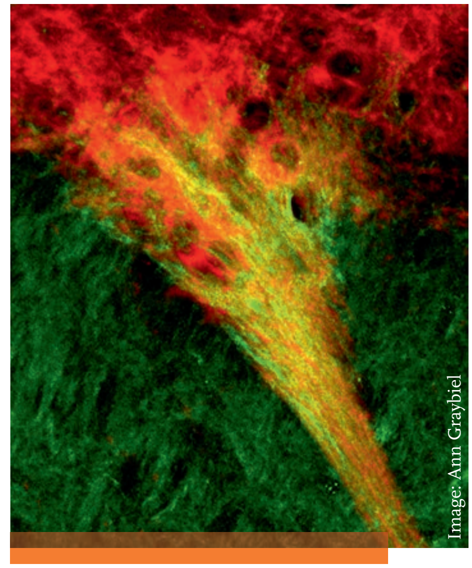
A team led by **Nancy Kanwisher** and **John Gabrieli** has studied a part of the brain known as the visual word form area (VWFA), which is thought to be specialized for reading. In 5-year-olds who have not yet learned to read, the VWFA does not respond to written words, but the researchers found that they could predict its future location (in the same children, three years later) based on its connections to other language areas of the brain.

In a separate study, **Nancy Kanwisher** and her colleagues collaborated with Joshua Tenenbaum at MIT to identify a network of human brain regions involved in physical intuition. These regions are activated when subjects watch simulations of bouncing objects or make judgments about the stability of piles of objects, and may underlie our ability to understand intuitively the physical properties of the world around us.

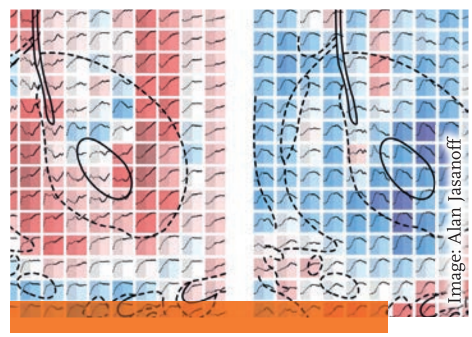
Serotonin is a neurotransmitter that is involved in mood regulation in humans, and many antidepressants work by blocking the removal of serotonin, thereby increasing its concentration and prolonging its effects on the brain. Now researchers in **Alan Jasanoff**'s lab have developed an imaging technique that, for the first time, enables three-dimensional mapping of serotonin as it is reabsorbed into neurons. This technique gives an unprecedented view of serotonin dynamics in the living brain, and could be a powerful tool for the development of new antidepressants.

Yingxi Lin and colleagues have developed a genetic method for labeling active neurons, enabling researchers to visualize the detailed patterns of brain activity that are triggered by specific stimuli or tasks.

Guoping Feng and collaborators at MIT and in Singapore have discovered that brain cells called astrocytes play a critical role in controlling appetite and feeding behavior. In a study of mice, the researchers found that activating these cells within the hypothalamus stimulates overeating, and that when the cells are suppressed, appetite is also suppressed. The findings could offer scientists a new target for developing drugs against obesity and other appetite-related disorders. ■



Connections between dopamine-producing cells of the substantia nigra (red) and neurons in the striatum (green) may play a role in the brain's decision-making processes.



Molecular fMRI data showing signal changes from serotonin sensors in the absence (left) and presence (right) of the antidepressant Prozac.

AWARDS & HONORS

Nancy Kanwisher has received an NIH Director's Pioneer Award for her work studying the functional organization of the developing human brain. The Pioneer Award "challenges investigators at all career levels to pursue new research directions and develop groundbreaking, high-impact approaches to a broad area of biomedical or behavioral science." Kanwisher is one of twelve researchers nationwide to be selected for the 2016 Pioneer Award. ■

NIH Pioneer Award recipient Nancy Kanwisher.

EVENTS

Feng Zhang (second from left), pictured with his family at the 2016 Gairdner Award Ceremony in Toronto.

Feng Zhang was presented with a Canada Gairdner International Award at a formal dinner in Toronto on October 27. Zhang, who shared the prize with four other CRISPR researchers, received the award "for development of CRISPR-CAS as a genome editing tool for eukaryotic cells." ■

Gloria Choi (right) with her lab manager Natalie Soares (dressed as Emperor Kuzco) at the annual McGovern Halloween party.

On Halloween, the McGovern Institute headquarters hosted a costume party for the neuroscience community at MIT. Guests enjoyed spooky treats and voted on the most creative costumes. Visit our website for a photo gallery from the party. ■

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, with the goal of 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

Brain SCAN
Quarterly Newsletter of the McGovern Institute

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