McGOVERN INSTITUTE
FOR BRAIN RESEARCH AT MIT

Brain SCAN

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The Learning Brain

By unraveling the neuroscience behind learning disabilities, McGovern researchers hope to improve education interventions in the classroom.

FROM THE **DIRECTOR**

We often emphasize biomedical insights from neuroscience, but brain research could also impact education. As we develop personalized medicines, shouldn't education also be personalized, with specific interventions tailored to children's individual needs? John Gabrieli has long been interested in using neural markers to better target learning and reading disability interventions for children. His work, alongside approaches being taken by teachers, is discussed in this issue.

In other news, the pace of awards recognizing McGovern faculty was brisk this spring, including two prestigious awards for groundbreaking work on brain organization. Ann Graybiel won the 2018 Gruber Prize in Neuroscience for her work on the basal ganglia and their role in brain functions ranging from movement to cognition, in health and disease. Nancy Kanwisher won the 2018 Heineken Prize, the premier scientific prize of the Netherlands, for her work on cortical organization of functions ranging from face recognition to music perception. We all celebrate such well-deserved, international recognition for our colleagues.

Bob Desimone, Director
Doris and Don Berkey Professor
of Neuroscience

On the cover: Learning to read is a foundational skill for academic success. In this issue, we explore research from John Gabrieli's lab and look at how some teachers are trying to increase the success of interventions for learning and reading disabilities.
Image: sturti/iStock

Photo: Justin Knight

"There's a slogan in education," says McGovern Investigator John Gabrieli. "The first three years are learning to read, and after that you read to learn."

For John Gabrieli, learning to read represents one of the most important milestones in a child's life. Except, that is, when a child can't. Children who cannot learn to read adequately by the first grade have a 90 percent chance of still reading poorly in the fourth grade, and 75 percent odds of struggling in high school. For the estimated 10 percent of schoolchildren with a reading disability, that struggle often comes with a host of other social and emotional challenges: anxiety, damaged self-esteem, increased risk for poverty and eventually, encounters with the criminal justice system.

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Most reading interventions focus on classical dyslexia, which is essentially a coding problem—trouble moving letters into sound patterns in the brain. But other factors, such as inadequate vocabulary and lack of practice opportunities, hinder reading too. The diagnosis can be subjective, and for those who are diagnosed, the standard treatments help only some students. "Every teacher knows half to two-thirds have a good response, the other third don't," Gabrieli says. "It's a mystery. And amazingly there's been almost no progress on that."

For the last two decades, Gabrieli has sought to unravel the neuroscience behind learning and reading disabilities and, ultimately, convert that understanding into new and better education interventions—a sort of translational medicine for the classroom.

The Home Effect

In 2011, when Julia Leonard was a research assistant in Gabrieli's lab, she planned to go into pediatrics. But she became drawn to the lab's education projects and decided to join the lab as a graduate student to learn more. By 2015, she helped coauthor a landmark study with postdoc Allyson Mackey, that sought neural markers for the academic "achievement gap," which separates higher socioeconomic status (SES) children from their disadvantaged peers. It was the first study to make a connection between SES-linked differences in brain structure and educational markers. Specifically, they found children from wealthier backgrounds had thicker cortical brain regions, which correlated with better academic achievement.

"Being a doctor is a really awesome and powerful career," she says. "But I was more curious about the research that could cause bigger changes in children's lives."

Leonard collaborated with Rachel Romeo, another graduate student in the Gabrieli lab who wanted to understand the powerful effect of SES on the developing brain. Romeo had a distinctive background in speech pathology and literacy, where she'd observed wealthier students progressing more quickly compared to their disadvantaged peers.

Their research is revealing a fascinating picture. In a 2017 study, Romeo compared how reading-disabled children from low and high SES backgrounds fared after an intensive summer reading intervention. Low SES children in the intervention improved most in their reading, and MRI scans revealed their brains also underwent greater structural changes in response to the intervention. Higher SES children did not appear to change much, either in skill or brain structure.

Image: Julia Leonard

Strong reasoning skills are correlated with greater cortical thickness in the prefrontal cortex (red) in lower-SES children, which supports Boston public school teacher Colleen Labbe's (above, left) theory that the brain of a struggling child can change in response to the right interventions.

Julia Leonard and Rachel Romeo, former graduate students in John Gabrieli's lab, collaborate on studies exploring the relationship between the developing brain, a child's home environment, and learning ability.

"In the few studies that have looked at SES effects on treatment outcomes," Romeo says, "the research suggests that higher SES kids would show the most improvement. We were surprised to find that this wasn't true." She suspects that the midsummer timing of the intervention may account for this. Lower SES kids' performance often suffer most during a "summer slump," and would therefore have the greatest potential to improve from interventions at this time.

However, in another study this year, Leonard uncovered unique brain differences in lower-SES children. Only among lower-SES children was better reasoning ability associated with thicker cortex in a key part of the brain. Same behavior, different neural signatures.

"So this becomes a really interesting basic science question," Leonard says. "Does the brain support cognition the same way across everyone, or does it differ based on how you grow up?"

Not a One-Size-Fits-All

Critics of such "educational neuroscience" have highlighted the lack of useful interventions produced by this research. Gabrieli agrees that so far, little has emerged.

"The painful thing is the slowness of this work. It's mind-boggling," Gabrieli admits. Every intervention requires all the usual human research requirements, plus coordinating with schools, parents, teachers, and so on. "It's a huge process to do even the smallest intervention," he explains. Partly because of that, the field is still relatively new.

But he disagrees with the idea that nothing will come from this research. Gabrieli's lab previously identified neural markers in children who will go on to develop reading disabilities. These markers could even predict who would or would not respond to standard treatments that focus on phonetic letter-sound coding.

Romeo and Leonard's work suggests that varied etiologies underlie reading disabilities, which may be the key. "For so long people have thought that reading disorders were just a unitary construct: kids are bad at reading, so let's fix that with a one-size-fits-all treatment," Romeo says.

Such findings may ultimately help resource-strapped schools target existing phonetic training rather than enrolling all struggling readers in the same program, to see some still fail.

Think Spaces

At the Oliver Hazard Perry School, a public K-8 school located on the South Boston waterfront, teachers like Colleen Labbe have begun to independently navigate similar problems as they try to reach their own struggling students.

"A lot of times we look at assessments and put students in intervention groups like phonics," Labbe says. "But it's important to also ask what is happening for these students on their way to school and at home."

For Labbe and Perry Principal Geoffrey Rose, brain science has proven transformative. They've embraced literature on neuroplasticity—the idea that brains can change if teachers find the right combination of intervention and circumstances, like the low-SES students who benefited in Romeo and Leonard's study.

"A big myth is that the brain can't grow and change, and if you can't reach that student, you pass them off," Labbe says.

The science has also been empowering to her students, validating their own powers of self-change. "I tell the kids, we're going to build the goop!" she says, referring to the brain's ability to make new connections.

"All kids can learn," Rose agrees. "But the flip of that is, can all kids do school?" His job, he says, is to make sure they can.

"Think Spaces" at Perry K-8 School in South Boston are designed to boost mindfulness and reduce stress.

Postdoc Clemens Bauer (left) and John Gabrieli (right) are exploring whether mindfulness training can reduce stress and improve attention in schoolchildren.

The classrooms at Perry are a mix of students from different cultures and socioeconomic backgrounds, so he and Labbe have focused on helping teachers find ways to connect with these children and help them manage their stresses and thus be ready to learn. Teachers here are armed with "scaffolds"—digestible neuro- and cognitive science aids culled from Rose's postdoctoral studies at Boston College's Professional School Administrator Program for school leaders. These encourage teachers to be more aware of cultural differences and tendencies in themselves and their students, to better connect.

There are also "Think Spaces" tucked into classroom corners. "Take a deep breath and be calm," read posters at these soothing stations, which are equipped with de-stressing tools, like squeezable balls, play-dough, and meditation-inspiring sparkle wands. It sounds trivial, yet studies have shown that poverty-linked stressors like food and home insecurity take a toll on emotion and memory-linked brain areas like the amygdala and hippocampus.

In fact, a new study by Clemens Bauer, a postdoc in Gabrieli's lab, argues that mindfulness training can help calm amygdala hyperactivity, help lower self-perceived stress, and boost attention. His study was conducted with children enrolled in a Boston charter school.

Taking these combined approaches, Labbe says, she's seen one of her students rise from struggling at the lowest levels of instruction, to thriving by year end. Labbe's focus on understanding the girl's stressors, her family environment, and what social and emotional support she really needed was key. "Now she knows she can do it," Labbe says.

Rose and Labbe only wish they could better bridge the gap between educators like themselves and brain scientists like Gabrieli. To help forge these connections, Rose recently visited Gabrieli's lab and looks forward to future collaborations. Brain research will provide critical insights into teaching strategy, he says, but the gap is still wide.

From Lab to Classroom

"I'm hugely impressed by principals and teachers who are passionately interested in understanding the brain," Gabrieli says. Fortunately, new efforts are bridging educators and scientists.

This March, Gabrieli and the MIT Integrated Learning Initiative—MITili, which he also directs—announced a $30 million-dollar grant from the Chan Zuckerberg Initiative for a collaboration between MIT, the Harvard Graduate School of Education, and Florida State University.

The grant aims to translate some of Gabrieli's work into more classrooms. Specifically, he hopes to produce better diagnostics that can identify children at risk for dyslexia and other learning disabilities before they even learn to read.

He hopes to also provide rudimentary diagnostics that identify the source of struggle, be it classic dyslexia, lack of home support, stress, or maybe a combination of factors. That in turn, could guide treatment—standard phonetic care for some children, versus alternatives: social support akin to Labbe's efforts, reading practice, or maybe just vocabulary-boosting conversation time with adults.

"We want to get every kid to be an adequate reader by the end of the third grade," Gabrieli says. "That's the ultimate goal for me: to help all children become learners." ■

Boston Public School Principal Geoffrey Rose distributes "Shark Bites" to children at the Perry K-8 School to encourage positive behavior.

McGovern Scientists Named Howard Hughes Medical Institute Investigators

Ed Boyden and Feng Zhang are among 19 top scientists who were named Howard Hughes Medical Institute (HHMI) Investigators this May. Both researchers have been instrumental in recognizing, developing, and sharing robust tools with broad utility that have revolutionized the life sciences.

HHMI selects new investigators to join its flagship program through periodic competitions that focus on identifying "people, not projects" that are trail blazers in the biomedical sciences. This new group of investigators, selected from a pool of 675 eligible applicants, is the first to be appointed to a seven-year term (previous terms lasted five years). The organization provides support for an unusual length of time, seven years, with a renewal process at the end of that period, giving selected scientists the time and freedom to tackle difficult and important biological questions.

Boyden's work initiated optogenetics, along with Karl Deisseroth and Feng Zhang, and subsequently extended it into a multicolor, high-speed, and noninvasive toolbox. Boyden and his team continue to expand the neurobiology toolkit. Their recent developments include expansion microscopy, a system that overcomes the limits of light microscopy, as well as a directed evolution system that can robotically screen hundreds of thousands of mutated proteins for properties, used to develop a high-performance voltage indicator.

Zhang's achievements include the landmark deployment of the microbial CRISPR-Cas9 system for genome engineering in eukaryotic cells. The ease and specificity of the system has led to its widespread adoption. He continues to mine bacterial CRISPR systems for additional enzymes with useful properties. This search led to the discovery of Cas13, which targets RNA, rather than DNA, as well as the use of Cas13 in a molecular detection system, termed SHERLOCK, which can sense trace amounts of genetic material such as viruses. ■

Caltech Neurobiologist Wins 2018 Scolnick Prize

David J. Anderson of Caltech is the winner of the 2018 Edward M. Scolnick Prize in Neuroscience.

We are delighted to announce that David J. Anderson of Caltech is the winner of the 2018 Edward M. Scolnick Prize in Neuroscience. The prize is awarded annually by the McGovern Institute to recognize outstanding advances in the field of neuroscience.

Anderson was awarded the prize for his contributions to the isolation and characterization of neural stem cells and for his research on neural circuits that control emotional behaviors in animal models.

Anderson is the Seymour Benzer Professor of Biology at Caltech and is currently the director of the Tianqiao and Chrissy Chen Institute for Neuroscience. He is also an investigator of the Howard Hughes Medical Institute.

Anderson will deliver the Scolnick Prize lecture at the McGovern Institute on Monday, September 17 at 4:00pm in MIT Bldg 46-3002 (Singleton Auditorium). The event is free, open to the public, and followed by a reception. ■

RESEARCH NEWS

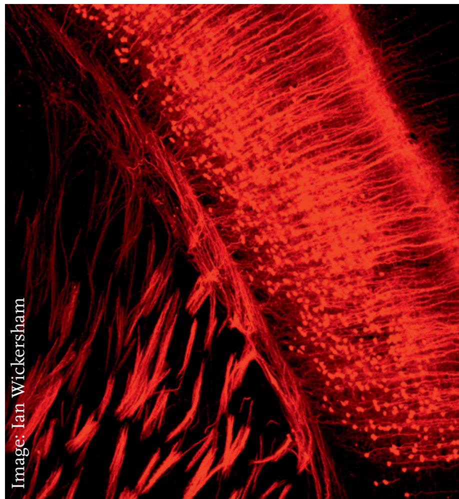
The **Jasanoff** lab has developed a new MRI sensor that monitors neural activity deep within the brain by tracking calcium ions. Because calcium ions are directly linked to neuronal firing—unlike the changes in blood flow detected by other types of MRI—this new sensor will allow researchers to link specific brain functions to neural activity, and help determine how distant brain regions communicate during particular tasks.

Humans use an ability known as Theory of Mind (ToM) whenever they infer someone else's mental state. Children begin succeeding at a key behavioral measure of this ability around age 4. A new fMRI study out of the **Saxe** lab has found that the relevant ToM brain network forms earlier than previously expected, in children as young as 3.

Catching a bouncing ball or hitting a ball with a racket requires estimating when the ball will arrive. Neuroscientists have long thought that the brain does this by calculating the speed of the moving object. However, a new study by **Mehrdad Jazayeri** shows that the brain's approach is more complex, tracking speed and integrating this with additional temporal information that reflects the pattern of an object's movement (for example, how the ball moves around a bounce, or even the timing of an object's movement before and after traveling behind an opaque obstacle). In a separate study, Jazayeri applied a mathematical framework, known as dynamical systems analysis, to model and identify a strategy that the brain uses to rapidly select and flexibly perform different mental operations.

For the past decade, neuroscientists have been using a modified rabies virus to label neurons and trace the connections between them. Although this technique has proven very useful, it is toxic to cells and can't be used for longer-term studies. McGovern principal research scientist **Ian Wickersham** has developed a version of this virus that stops replicating once it infects a cell, allowing it to deliver its genetic cargo without harming the cell, enabling longer-term studies of neural functions and connections.

Studies of amyotrophic lateral sclerosis (ALS) patients have shown that an abnormally expanded region of DNA in a specific region of a specific gene accounts for up to 40 percent of all familial cases of ALS. The **Horvitz** lab used the microscopic worm *Caenorhabditis elegans* to examine the function of this gene, discovering that it plays a key role in helping cells remove waste products via structures known as lysosomes. When the gene is mutated, these unwanted substances build up inside cells. If this also happens in neurons of human ALS patients, it could account for some of their symptoms. ■



Mouse neurons visualized using nontoxic rabies viral vectors.

AWARDS & HONORS

Ed Boyden has been named a recipient of the 2018 Canada Gairdner International Award—Canada's most prestigious scientific prize—for his role in the discovery of light-gated ion channels and optogenetics, a technology to control brain activity with light.

McGovern investigators (from left to right) Ed Boyden, Ann Graybiel, Nancy Kanwisher, and Feng Zhang.

Ann Graybiel has won the 2018 Gruber Prize in Neuroscience for her work on the complexity and function of the basal ganglia.

Nancy Kanwisher has been named a recipient of the 2018 Heineken Prize — the Netherlands' most prestigious scientific prize — for her work on the functional organization of the human brain.

Feng Zhang has been elected to the American Academy of Arts and Sciences and the National Academy of Sciences for his work developing molecular biology tools, including the CRISPR-Cas9 system. ■

Members of the MIT neuroscience community pose for a group photo at the annual retreat in Newport, Rhode Island.

MIT Neuroscience Retreat

Members of the McGovern Institute, Picower Institute and Department of Brain and Cognitive Sciences gathered for a joint scientific retreat in Newport, Rhode Island on June 4-5. ■

WBUR reporter Carey Goldberg interviews McGovern investigator Feng Zhang at CRISPRcon 2018.

Feng Zhang Headlines CRISPRcon 2018

On June 4-5, the McGovern Institute and Broad Institute co-hosted CRISPRcon 2018, a conference featuring a dynamic and diverse lineup of panels, keynotes and interactive discussions about science, society, and the future of gene editing. Videos from the event will be posted to our website. ■

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 Lore Harp McGovern and the late Patrick J. 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

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