

# Brain SCAN

McGOVERN INSTITUTE

FOR BRAIN RESEARCH AT MIT

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## From the director

**People facing mental illness urgently need new and better treatment options. I am more hopeful now than ever before in my career that real progress is truly on the horizon.**

From my years at National Institute of Mental Health, I know too well the enormous toll that mental illness takes on people, their families, and society at large. Mental illness is a major source of human misery around the world, and it exacerbates

many other ills, including poverty, substance abuse and violence. But we haven't made progress in treating it because we know too little about its underlying causes.

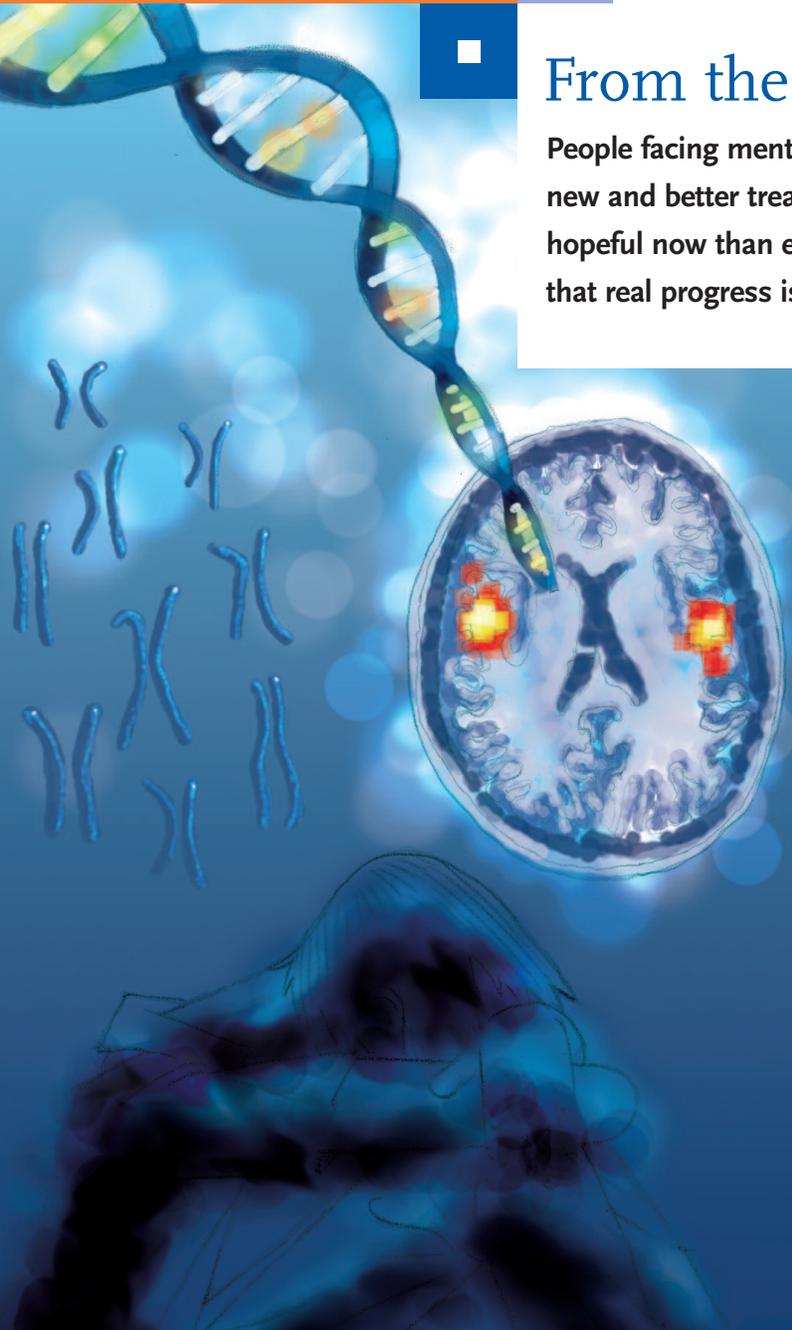
Our mission at the McGovern Institute is not just to understand the brain, but also to use that understanding to alleviate human suffering caused by brain disorders. I'm therefore very happy to announce the Institute's new Poitras Center for Affective Disorders Research, which will support a concerted effort to apply our neuroscience expertise to the study of mental illness. We are extremely grateful to Jim and Pat Poitras, members of our Leadership Board, for making the generous donation that is enabling us to establish this center.

The Poitras Center will support collaborations between MIT neuroscientists and our neighbors at the Broad Institute to understand the role of genes in mental illness, and with Boston-area hospitals for translating those findings to patients. A generation ago, when researchers launched a similarly multi-pronged war on cancer, they did not have the enabling technologies of genomics and imaging technologies that we can now apply to the study of complex psychiatric disorders. I'm optimistic that in this new drive to understand mental illness we are starting from a position of strength, and that the time is ripe for bridging the gap from molecules to mind, in health and disease.

I'm also pleased to be part of another effort that will bridge the gap between neuroscience and society, the new Law and Neuroscience Project funded by The John D. and Catherine T. MacArthur Foundation. I hope you'll enjoy reading about these new initiatives and other recent news from the McGovern Institute, in this issue of *Brain Scan*.

**Bob Desimone, Director**

Artwork: Julian Wong



## POITRAS CENTER TO SUPPORT MENTAL ILLNESS RESEARCH

Mental illness devastates the lives of millions, and it costs the nation billions of dollars. Yet scientists understand little about the causes of mental illness, and that lack of knowledge obstructs the search for treatments, cures, and prevention. That's beginning to change as new methods for studying mental illness come on line, and the McGovern Institute's new Poitras Center for Affective Disorders is part of that change.

When Patrick J. and Lore Harp McGovern founded the McGovern Institute in 2000, their mission was to advance human welfare through brain research, and mental illness ranked high among their concerns. Now, the institute has established a new center to focus specifically on psychiatric disease, thanks to a \$20 million commitment from James and Patricia Poitras of Narcoossee, FL. Their gift establishes the James W. and Patricia T. Poitras Center for Affective Disorders Research. The Poitras Center will support research on bipolar disorder, major depression, schizophrenia, and other serious psychiatric diseases. The Center will also collaborate with the neighboring genetic powerhouse, the Broad Institute of MIT and Harvard, and with local clinical research institutions such as Massachusetts General Hospital and McLean Hospital.

**Mental or behavioral disorders:**  
450 million worldwide, 57 million in US

**Depression:**  
~154 million worldwide;  
21 million in US



**Schizophrenia:**  
~25 million worldwide;  
2.5 million in US



**Suicide:**  
~1 million yearly worldwide;  
33,000 in US



Sources: World Health Organization (2003), US National Institute of Mental Health (2007)

“We are indebted to Jim and Pat for their generosity and are pleased that the Poitras Center will be part of the McGovern Institute,” say Patrick and Lore McGovern, the cofounders of the McGovern Institute. “We are deeply gratified that others share this vision for a better future.”

### Depressing Facts

Affective disorders represent the most common class of psychiatric disease. In the US alone, the National Institute of Mental Health estimates that depression affects 9.5% of the population, almost 21 million people, in any given year. All together, mental illness ranks above heart disease, diabetes, and cancer in prevalence.

Given its frequency, most people know first or second hand the terrible personal cost of mental illness. Tragically, that toll too often begins just as young people embark on higher education, promising careers, or parenthood. In fact, the National Alliance of Mental Illness cites major depression as the leading cause of disability in the U.S. and Canada between ages 15 and 44.

Mental illness also comes with a high economic price tag. According to a 2007 report by the Milken Institute, loss of productivity from mental illness runs \$171 billion in the US alone, with another \$46 billion in treatment costs, for a total economic loss of \$217 billion per year. These estimates are for 2003, and the report projects that the number of cases will increase 54% over the next twenty years.

Despite this heavy disease burden, scientists understand very little about the underlying causes of mental illnesses or how antidepressant and anti-psychotic drugs work. But cancer and heart disease provide encouraging examples of how science-driven discovery can make headway against very complex diseases and produce life-prolonging new treatments such as targeted chemotherapies and cholesterol-lowering statins. Now, a similar concerted effort is directed towards mental illness.

### Obstacles to Treatment

Currently, three major obstacles stand in the way of better therapies for mental illness. First, the biological mechanisms that underlie psychiatric disease are still poorly understood, which greatly limits scientists' ability to design better drugs to target the disease process. The major classes of drugs currently used to treat psychiatric illness were discovered by serendipity rather than through a scientific understanding of the underlying disease pathology. Scientists subsequently gathered clues about how the first-generation anti-depressant and anti-psychotic drugs may work, and then developed additional drugs based on these clues in the hope of producing a new generation of drugs with greater efficacy or fewer side effects. But the results have often been disappointing. For example, a major study funded by the National Institute of Mental Health recently concluded that the newer antipsychotic drugs are not clear superior to the first generation drugs.

Second, researchers do not yet have realistic animal models that replicate fundamental features of psychiatric diseases. Animal models are central to the drug discovery process, but without a clear scientific understanding of the disease process it is very difficult to develop such models.

Finally, scientists also have not yet identified reliable markers of the disease state. In sharp contrast to most diseases, there is no

physical measurement that can be used to diagnose psychiatric disease or to measure its severity. Instead, diagnosis of psychiatric disease is based entirely on patients' behavioral symptoms and subjective reports. The lack of objectively measurable markers greatly limits the ability to measure the effectiveness of current drugs or to test new drug candidates in clinical trials.

### Genes and Environment Share Responsibility

Researchers have long known that many psychiatric diseases have a strong genetic, or heritable, component, but they have only recently developed the tools needed to search for those genes. For example, if one identical twin has schizophrenia, the other twin, who shares all the same genes, has about a 50% risk of developing the disease. A non-identical sibling, who shares only half of the genes, has a lower risk, around 5 to 10%.

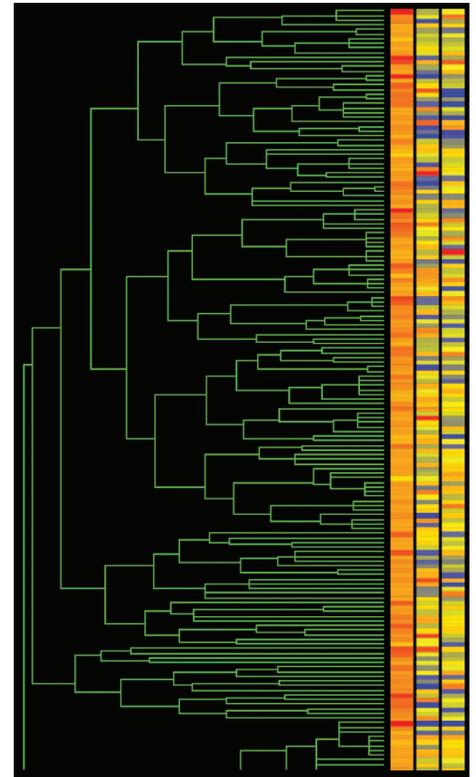
Rather than being caused by a single defective gene, researchers believe that psychiatric diseases are caused by multiple genes, each of which contributes only slightly to the risk of disease, but whose effect is cumulative—in other words, the more such risk genes a person inherits, the greater their risk of disease. Such genes are difficult to identify, but thanks to recent advances in genomic technology, researchers can now begin to search systematically for those risk genes, using a technique called genome-wide association. This technique allows researchers to scan the genomes of thousands of individuals to identify genes that increase the risk of disease. At the Broad Institute, the Stanley Center for Psychiatric Research is working to identify genes implicated in major psychiatric disorders such as bipolar disorder and schizophrenia. Finding these genes will prove invaluable for neuroscience research at the new Poitras Center.

Yet genes alone cannot fully explain the occurrence of psychiatric diseases; witness the 50% of identical twins who do not develop schizophrenia like their affected twin. Scientists believe the difference has to do with environmental triggers, ranging from prenatal events to a stressful personal life. In tandem with their search for risk genes, scientists are seeking to understand how these environmental factors interact with genes to increase the risk of mental illness.

## Systems Neuroscience A Key Component

Identifying risk genes will be a major advance, but scientists then need to understand how genes and environmental factors affect the brain to produce the disease state. The key to bridging this gap is systems neuroscience—a core interest of the McGovern Institute. Systems neuroscience refers to studying the brain in terms of neurons and their connections, with the ultimate goal of understanding

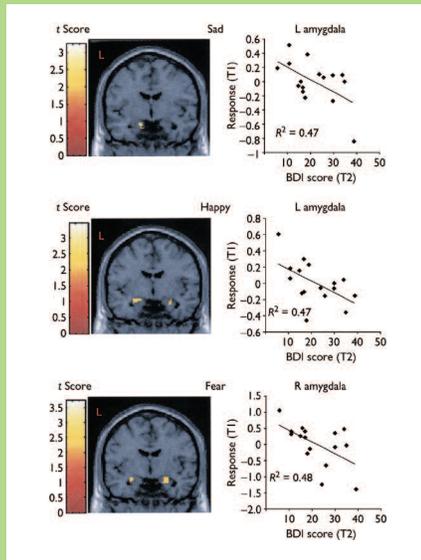
*continued, page 4*



### Studying Fear and Anxiety

*This graphic shows how chronic stress affects gene expression in three different parts of the rat brain. The three columns correspond to three brain regions: the amygdala, the hippocampus and the prefrontal cortex. The columns are composed of colored bars that correspond to individual genes: the color signifies how expression of that gene is altered by stress, with orange representing an increase, blue a decrease and yellow signifying no change. Note the predominance of orange bars in the first column, representing stress-induced increases in the expression of many genes in the amygdala, a brain region that is involved in fear and anxiety. The green lines to the left indicate genes with similar patterns of response to stress across the different brain regions.*

*Image: Ki Ann Goosens*



*Brain scans showing amygdala activation in depressed patients who are shown faces with sad, happy or fearful expressions. This 2005 study by John Gabrieli and colleagues demonstrated that patients with greater brain responses to emotional expressions showed greater improvement in their symptoms after 8 months. The ability to predict clinical outcomes through brain scans might help to guide treatment decisions in the future.*

*Images: John Gabrieli*

how a network of some hundred billion neurons gives rise to the human mind and human behavior.

McGovern Institute investigators are enthusiastic about applying their discoveries to psychiatric disease, and as the Institute continues to grow to its eventual size of 16 faculty members, it is expected that at least two of the new hires will be in the field of mental illness and disease-related research. The Poitras Center will also involve neuroscience researchers from other parts of MIT, including the Department of Brain and Cognitive Sciences (BCS) and the Picower Institute for Learning and Memory.

Among the first projects to be funded by the new center will be several brain imaging studies to be led by John Gabrieli, in collaboration with clinical psychiatrists at MGH and McLean Hospital. Gabrieli, who directs the Martinos Brain Imaging Center at the McGovern Institute, will bring his wide-ranging expertise in neuroimaging and cognitive science to the study of brain disease. Since joining MIT in 2005, he has already established numerous collaborations with clinical researchers investigating depression, bipolar disorder, schizophrenia, and other conditions. Some of these collaborations combine brain imaging and genetics, and as new risk genes are identified, Gabrieli plans to use human neuroimaging methods to study their effects on brain function. He also hopes to use neuroimaging to understand in greater depth how genes

and environmental influences interact within the brain, and to identify 'fingerprints' of disease within the brain that may be useful for clinical diagnosis and for the design of future drug trials.

Another project already underway is a pilot study by Tomaso Poggio in collaboration with Debora Levy at McLean Hospital, in which schizophrenic subjects are tested for possible deficits in rapid processing of visual information, using tests based on Poggio's computational models of visual perception. The Poitras Center will also support a range of other projects, ranging from basic studies on the neural circuits that go awry in mental illnesses to new technologies and brain stimulation devices that can be used to manipulate those circuits. Researchers will also be working to develop more realistic animal models of psychiatric diseases, based on newly discovered insights from human patients.

### Translating Basic Research to Clinical Benefit

The ultimate goal of the Poitras Center is to make research discoveries that will lead to better treatments for psychiatric disease. An important aspect of this work will be clinical studies on psychiatric patients, which will be conducted in collaboration with local clinical research institutions such as Massachusetts General Hospital and McLean Hospital. In addition to basic questions about the biological causes of mental illness, research at the Poitras Center will also address issues of diagnosis and prognosis in human patients. For example, it may be

possible, by combining genetics with neuroimaging or behavioral studies, to predict the future course of disease and to identify which treatments will be most effective for a particular individual patient.

Equally important, the Poitras Center expects to benefit from MIT's long-standing ties to industry, and from its track record of transferring basic research into practical applications through partnerships with the private sector. The Center intends to explore a wide range of approaches to therapeutic development, including the identification of new drug targets as well as device-based therapies such as electrical stimulation of the brain, which has recently been shown to alleviate treatment-resistant depression. Bringing new therapeutic concepts from the laboratory to the clinic is a major challenge that cannot be undertaken by academia alone. The cost of developing new therapies is high, but the commercial incentive for companies undertaking this challenge is also very strong, given the size of the psychiatric drug market. The Poitras Center expects to work closely with the MIT technology licensing office and with industry partners, as basic research begins to bear fruit and to suggest new commercial opportunities.

### A Brighter Future

Robert Desimone, Director of the McGovern Institute, envisions that the Poitras Center may eventually evolve to become part of a larger center encompassing not only psychiatric disease, but also other brain disorders including developmental and neurodegenerative diseases. Many of the technologies and strategies that the center will apply to psychiatric disease are also applicable to other disorders, including movement disorders arising from Parkinson's disease and stroke, developmental disorders like autism or dyslexia, neurological diseases such as Alzheimer's and Huntington's disease, traumatic brain injury, epilepsy, substance abuse, and normal cognitive decline with age. The cumulative cost to society of brain disorders is enormous (over \$1 trillion per year by some counts), and by leveraging the McGovern Institute's resources and expertise, Desimone hopes to have a far reaching impact on some of the most challenging health problems of our time. ■

## A \$20M Gift for Psychiatric Disease Research

Jim and Pat Poitras decided to make their generous gift to establish the Poitras Center for Affective Disorders Research, very shortly after hearing Robert Desimone address a meeting of the McGovern Institute’s Leadership Board in November 2006. There, Desimone described a long-range plan for the future of the Institute and the creation of a new initiative for brain disease and mental illness.

“We were pleased with this newly stated purpose to bring basic research into practice. We had decided many years ago that our philanthropic efforts would be directed towards this psychiatric research. We could not have imagined then that this perfect synergy between research at MIT’s McGovern Institute and our own philanthropic goals would develop,” recalls Jim Poitras, a 1963 MIT alumnus with a degree in electrical engineering.

“After hearing Bob, we talked with Pat and Lore McGovern over dinner,” continues Pat, “and realized we could help make this happen faster than even they had hoped. We are very hopeful for the future.” The Poitras’s have committed \$20 million to support research on major depression,

bipolar disorder, schizophrenia and other psychiatric disorders at the center.

When friends ask why they are contributing to MIT rather than to a new research facility near their Orlando home, Jim tells them: “The best bang for the buck is at MIT, right here, right now.”

After graduating from MIT, Jim worked in research, computer programming, and administration at Massachusetts General Hospital until 1979. For 22 years, he headed the family’s medical products manufacturing business, Highland Laboratories, Inc., based in Ashland, MA. Jim retired in 2006 as President and CEO of the company, and he continues to manage other family investments.

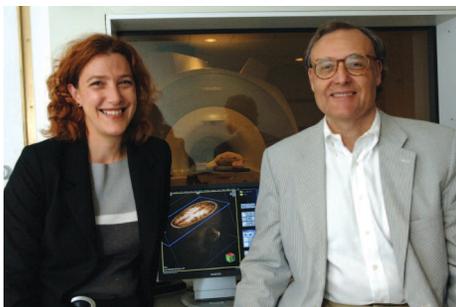
Pat’s career was in social work, and she is president of the Poitras Charitable Foundation. Both are members of the McGovern Institute leadership board. They are longstanding donors to MIT and have previously endowed the James W. and Patricia T. Poitras Professorship Fund in the Department of Brain and Cognitive Sciences in the field of psychiatric research. In addition to their gifts to MIT, Pat and Jim fund community outreach programs for the mentally ill.



James and Patricia Poitras of Narcoossee, FL  
Photo: Chris Casler

Jim recalls that his father, Edward J. Poitras (MEE 1928), credited his success to what MIT gave him—a full scholarship, including train fare for his daily commute. “He reciprocated generously throughout his life and encouraged me to give back to MIT, too. But our philanthropic focus was psychiatry and MIT wasn’t doing much psychiatric research. Now, with the McGovern Institute, that problem is resolved.” ■

## IN THE NEWS



Noa Ofen and Professor John Gabrieli sit by a monitor displaying an image of a 9-year old child’s brain taken using the MRI scanning machine in the Martinos Center at the McGovern Institute.

The *Boston Globe* ran a story about the Poitras Center for Affective Disorders on October 22, 2007, entitled “MIT to study genes’ role in mental illness.”

The *Financial Times* wrote about Patrick McGovern and his support for the McGovern Institute in a September 21, 2007 article, “Cogitating on what happens in our heads.”

The August 11, 2007 *Economist* magazine’s article “Blossoming Brains” covered work by John Gabrieli and postdoctoral researcher Noa Ofen comparing memory formation in children, teenagers, and adults. ■

## Robert Desimone participates in \$10 million MacArthur Foundation Project



In the 1990s, the courts grappled with how to handle DNA evidence. Today, they are considering what bearing neuroscience can or should have on the law, and McGovern Institute Director Robert Desimone will be helping to address this complex issue as part of a new Law and Neuroscience Project. Funded by John D. and Catherine T. MacArthur Foundation, the project brings together scientists, legal scholars, jurists, and philosophers to help integrate new developments in neuroscience into the legal system.

The Project is the first systematic effort to bridge these two fields and consider how courts should deal with new findings in brain research. Desimone will co-chair a working group on addiction. Other groups will address topics of brain abnormalities and decision making as they relate to issues such as criminal responsibility. Each working group will be directed by a neuroscientist and a legal expert and will include up to 15 neuroscientists, legal scholars, philosophers, and practitioners involved in the legal system, including a judge. These groups will address the

difficult legal and ethical questions that will arise as neuroscience progresses in its ability to explain and predict behavior.

In its first three years, the Law and Neuroscience Project hopes to fund neuroscience research relevant to law, including the formulation and testing of neuroscience research hypotheses designed to directly address gaps in legal/policy issues and understanding. When appropriate, the working groups will develop recommendations for judicial guidelines in handling neuroscientific evidence, ethical guidelines concerning proposed treatments, and law and policy regarding addiction and related criminal behavior, treatment of psychopaths or criminally insane persons, and determination of competency or culpability.

The project will also prepare a primer on neuroscience for judges and practicing lawyers that provides the necessary neuroscientific and technical background for cases that they must consider. It will likely include such issues as: functional neuroanatomy; the uses and limits of brain scans; experimental designs and what they can and cannot reveal; and how the basic laws of responsibility and evidence may relate to the neuroscience of addiction, psychopathy, impulsivity, lies, prejudice,

*Graphics: MacArthur Law and Neuroscience Project*

and memory. This primer will be accessible to the general public. The project will also prepare course materials on law and neuroscience and will sponsor three major conferences, the first of which will be held in Spring 2008.

The Law and Neuroscience Project is supported by an initial, three-year \$10 million MacArthur Foundation grant and is centered at the University of California, Santa Barbara (UCSB). It involves scientists and legal scholars from more than two dozen universities nationwide. Former Supreme Court Justice Sandra Day O'Connor serves as honorary chair. ■

*Additional information is available at [www.lawandneuroscienceproject.org](http://www.lawandneuroscienceproject.org).*

**Nancy Kanwisher** is now the proud owner of a Golden Brain, bestowed upon her by the Minerva Foundation, based in Berkeley, CA. Each year, the foundation awards a Golden Brain to a researcher who has made fundamental contributions to our knowledge of vision and the brain. Kanwisher received the award for her seminal work on the human visual system. She joins a distinguished roster of previous recipients, including McGovern Institute Director Robert Desimone, who won the award in 1994.



*Nancy Kanwisher receives Golden Brain award from the Minerva Foundation*



*Ed Boyden*



*Alan Jasanoff*

**Ed Boyden** was one of three recipients for the newly established “Research Award for Innovation in Neuroscience” from the 38,000-member Society for Neuroscience. The award consists of \$25,000 in unrestricted funds and was established to honor imaginative research that will advance novel ideas and potentially lead to significant breakthroughs in the understanding of the brain and nervous system and related diseases.

**Alan Jasanoff** and **Ed Boyden** received New Innovator Awards from the National Institutes of Health. “The conceptual and technological breakthroughs that are likely to emerge from their highly innovative approaches to major research challenges could speed progress toward important medical advances,” said NIH Director Elias A. Zerhouni of the 11 nationwide recipients. Zerhouni praised Jasanoff for

devising genetically controlled, noninvasive methods for measuring brain activity in animals. He also lauded Boyden for developing new methods of controlling the neural circuits that malfunction in neurological and psychiatric disorders. They will each receive \$1.5 million to support their research. ■

EVENTS

Visit by President of Tsinghua University

Professor Binglin Gu, the president of Tsinghua University in Beijing, visited the McGovern Institute on October 11, 2007. Professor Gu was accompanied by Professor Yi Zhang, Director of the Office of International Cooperation & Exchange, and by Peter Little of the university’s overseas liaison office. The McGovern Institute is developing a new scientific with Tsinghua and other institutions in China, supported by a grant from Hugo Shong, Executive Vice President of International Data Group and founding General Partner of IDGVC Partners. ■



Celebrating Tom Pyle

On October 20, 2007, friends and family joined Regina Pyle and the McGovern Institute in celebrating the life of Thomas O. Pyle, who died on July 18, 2007 after a 15-month battle with pancreatic cancer. Tom and Regina (shown here on their honeymoon in 1962) were founding chairs of the Friends of the Institute. ■



*Top: Tsinghua University President Binglin Gu (center) and Yi Zhang (left) with Charles Jennings (right), Director of the McGovern Institute Neurotechnology (MINT) Program. Bottom: Tom and Regina Pyle on their honeymoon in 1962.*



## Rebecca Schwarzlose Receives Razin Graduate Fellowship

Rebecca Schwarzlose, a graduate student in Nancy Kanwisher's lab, received the 2007–2008 Razin Fellowship to support her studies on areas of the human visual system that specialize in processing different object categories. A recurring theme in neuroscience is that perceptual representations often have a meaningful layout, or map, in the cortex. Visual areas that selectively recognize faces, bodies, scenes, and shapes also have a relatively consistent layout across individuals. Schwarzlose wants to find out if this layout is determined by the type of computations they perform, or the properties of the objects they respond to.

"I'm particularly intrigued that these areas come in pairs," Schwarzlose says. "For each object category, one region is located on the ventral temporal surface of the brain while the other on the lateral occipital surface. I want to find out why there are two sets of regions and what do they do differently."

In addition to improving the understanding of the visual system, Schwarzlose expects her research to have clinical relevance for mental illness. For postdoctoral studies, she plans to investigate the cognitive and genetic bases of schizophrenia and bipolar disorder. "Knowing how areas involved in face processing typically function, we can tease out how perception and cognition go wrong for people with these illnesses and use them as markers to help discover new genes that contribute to these disorders."

The Razin Fellowship program is supported by a gift from McGovern Institute Leadership Board Member Shelly Razin '59 (described in the Fall 2006 *Brain Scan*). ■



Leadership Board Member Shelly Razin '59 and graduate student Rebecca Schwarzlose.

■ *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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