A determined man with a warm smile, Jack Gorgone enlisted in the U.S. Navy at 17. Later, he trained as a registered nurse, landing a demanding job at Boston Children’s Hospital, where he worked for more than three decades. A serious car accident left him with injuries requiring repeated surgeries, which sparked chronic pain and depression.

Psychotherapy and medication helped. But last fall, after successfully tapering off of opioid pain relievers through a program based on mindfulness meditation, he found that nothing lightened his deep depression. Unhappy thoughts circled constantly. His pain spiked again, and he was irritable and withdrawn.

“You put yourself in a cave,” Mr. Gorgone says. “You don’t answer the phone. You don’t want to go out. It was difficult all around – not only for me, but for everyone around me.” His therapist recommended a new treatment called repetitive transcranial magnetic stimulation (rTMS). It made a world of difference.

Rebalancing brain circuits

Every year an estimated 16 million American adults struggle with major depression. At worst, depression is life-threatening, prompting suicidal thoughts and actions. More common symptoms include trouble sleeping; loss of appetite, sex drive, and interests; irritability; and distorted, negative thoughts. Feelings of helplessness, hopelessness, and worthlessness can make even simple tasks hard to accomplish.

Depression also leaves a distinct imprint on the complex neural networks of the brain. “Areas of the brain in charge of thinking tend to be underactive, triggering mental sluggishness and depressed mood,” explains Darin D. Dougherty, MD, director of the MGH Division of Neurotherapeutics. “Other areas tend to be overactive in depression, cranking up anxiety and interfering with sleep and appetite. With treatment, the brain goes back into balance.”

Psychotherapy and medications help many people regain this balance over time. However, some people need a fast-acting treatment to prevent self-harm. Others need, or want, to avoid medications. And some don’t respond to psychotherapy or medications even when many different treatments are tried, a problem called treatment-resistant depression.

“Often, the next step is neurotherapeutics: devices that use electricity, magnets, or implants to activate neural networks across the whole brain, or in targeted regions,” says Dr. Dougherty. The MGH Department of Psychiatry offers several types of neurotherapeutics. Among them are two nonsurgical options approved by the U.S. Food and Drug Administration for treatment-resistant depression: electroconvulsive therapy (ECT), which has been used since 1938, and the newer technology, repetitive transcranial magnetic stimulation.

“[In depression,] areas of the brain in charge of thinking tend to be underactive, triggering mental sluggishness and depressed mood. Other areas tend to be overactive in depression, cranking up anxiety and interfering with sleep and appetite. With treatment, the brain goes back into balance.”

— Darin D. Dougherty, MD

(Continued on page 7)
Message from the Chief

However it arrives at a state of dysregulation – of circuits out of balance – the brain is ultimately a system of connections between nodes. Components and functions of the brain must work in harmony for us humans to think, feel and behave the way we need to – to solve problems, to regulate emotions, to maintain and nourish attachments, to manage drives and to achieve goals.

Trillions of neurons in our brains are organized into systems of circuits, with each circuit distributed over connections across the brain. These circuits are “wired” by genes and experience. Glitches in our genes, experience or both leave us vulnerable to the vicissitudes of life and the dysfunctions of suffering we call psychiatric disorders.

Our department’s neuroimaging team, headed by Randy Buckner, PhD, was the first to categorize this complexity into approximately 17 discrete functional circuits.

Our neurotherapeutics group, profiled in this issue, is pioneering new methods of targeting those circuits directly to restore balance, and to restore optimal function of feeling, thinking and behavior. From longstanding tools like electroconvulsive therapy, to an array of more modern devices that gently and safely target points in the brain’s circuits, we are helping to create a future where implantable devices may keep the sickest well.

Finally, our genetics group, headed by Jordan W. Smoller, MD, ScD, in partnership with the Broad Institute’s Stanley Center, is paving the way to personalized medicine. It is hoped that analysis of patients’ DNA, early in the course of illness, will help clinicians predict which medication, device and/or therapy will produce the best response. We are grateful for the support of an iconic leader in psychiatric genetics, Dr. Edward Scolnick, and of Mrs. Barbara B. Scolnick, to create a fellowship (pp. 4-5) that will strengthen the partnership of MGH and the Stanley Center at the Broad Institute and hasten the arrival of this new era.

Jerrold F. Rosenbaum, MD
Psychiatrist-in-Chief
Massachusetts General Hospital
Stanley Cobb Professor of Psychiatry
Harvard Medical School

Department of Psychiatry Honors Michael S. Jellinek, MD

Michael S. Jellinek, MD, MGH chief of Child Psychiatry for 32 years (1979 to 2012), was honored on Sept. 11, 2014, at the Inaugural Michael S. Jellinek, MD, Endowed Grand Rounds Lecture in the Ether Dome. Dr. Jellinek was joined by his wife Barbara, son David, and daughter-in-law, Sarah.

The inaugural lecture, titled “Environments, Genes, Brains and Behavior: Why child psychiatry should be directing rational health care reform,” was presented by James J. Hudziak, MD, founder and director of the Vermont Center for Children, Youth and Families, professor of Child Psychiatry and chief of the Division of Child and Adolescent Psychiatry at the University of Vermont Medical School.

Dr. Hudziak presented an innovative clinical model, the Vermont Family Based Approach. Designed by Dr. Hudziak and his team, the model is based on research from scholars around the world, including Mass General, demonstrating that all health emerges from emotional-behavioral health.

Based on his longstanding research on the reciprocal influence of genes and the environment, Dr. Hudziak called on the field of psychiatry to take a family- and community-based approach to mental health, offering people tools to engage in brain healthy behavioral change, much the same way that the field of cardiology has given people the tools to engage in heart healthy behavioral change.

“Mike Jellinek has created an extraordinary legacy in child psychiatry.”

— Jerrold F. Rosenbaum, MD

Dr. Jellinek and Dr. Hudziak are long-time collaborators. “Both are giants in the field of psychiatry,” notes MGH Chief-of-Psychiatry Jerrold F. Rosenbaum, MD. “Mike Jellinek has created an extraordinary legacy in child psychiatry,” he continues, “through his extensive body of research, his thought leadership in the field, and his development - with J. Michael Murphy, EdD - of the Pediatric Symptom Checklist, a brief screening instrument used worldwide to help pediatricians identify children with emotional problems.”

Thanks to the generosity of 64 philanthropic donors, the endowed Grand Rounds lectureship will ensure that each year the department can engage a leading clinician or scientist from around the world to speak to MGH Psychiatry residents and faculty about cutting-edge issues in child psychiatry.
Conversation with Dr. Suzanne Bird, Director of the Acute Psychiatry Service

The twin shortfalls of inpatient psychiatric beds and trained mental health professionals are causing a nationwide mental health crisis. According to the Agency for Healthcare Research and Quality, the number of public psychiatric hospital beds in the U.S. dropped from 207 to 21 beds per 100,000 people between 1970 and 2000. The American Hospital Association reports that 55 percent of U.S. counties have no practicing psychiatrists, psychologists or social workers.

Despite recent initiatives to achieve mental health parity in public and private insurance programs, mental health care is often reimbursed poorly or not at all. Because of these and other potent economic forces, people who need psychiatric care often can't get the treatment they need. As a result, they may become more acutely distressed and, with nowhere else to turn, end up in hospital emergency rooms.

At Mass General, the Acute Psychiatry Service (APS) – one of only two hospital-based psychiatry emergency services in the city of Boston – offers assessment and consultation for adults and children in acute psychiatric distress who visit the Sumner Redstone Emergency Department (ED). The APS occupies a small, dedicated area within the ED in the Lunder Building, and provides care for an average of 18 patients each day and 6,000 patients annually. The main goal of the APS team is to stabilize patients in crisis, and refer them to appropriate mental health treatment within Mass General or elsewhere.

A recent conversation with APS Director, Suzanne A. Bird, MD, revealed significant efforts being made at Mass General to improve emergency mental health services, and reduce the need for such care.

Which patients coming into the APS are hardest to find appropriate referrals for?

Dr. Bird: Unfortunately, we’re seeing more children and adolescents getting stuck in the APS, sometimes for several days, because they aren’t stable enough to be discharged but there is no appropriate place to refer them. We are also seeing more people with alcohol and opiate addictions, often in combination with other psychiatric disorders. It’s particularly hard to find the right services for these patients. Mass General is now rolling out a major new substance use disorder strategy [see Mindscapes, Summer 2014], which we hope will help patients find better treatment solutions.

How is Mass General helping people get the care they need on an outpatient basis so they don’t end up in the Emergency Department?

Dr. Bird: Two new hospital-wide initiatives have been launched. The first, called D-Care, or Depression-Care, provides psychiatric consultation to primary care physicians who treat patients with depression. The second, called IMPACT, embeds behavioral health navigators in primary care practices to help patients get the mental health care they need. With these rapid response systems in place, we aim to provide appropriate treatment before patients’ symptoms become so distressing that they require emergency care.

What is Mass General doing to address the lack of inpatient beds?

Dr. Bird: Fortunately, about half of our APS patients can be stabilized without being hospitalized. For patients who don’t need hospitalization, but don’t have their own outpatient treatment in place, we can offer appointments in our urgent care clinic. Recognizing the need for more intensive inpatient services, Mass General is hoping to create new inpatient beds for adults and children on the North Shore.

What is your vision for where you want to take the APS in the future?

Dr. Bird: I’d like to focus on training more residents to specialize in emergency psychiatry. I’ve spent 17 years practicing emergency psychiatry, and I hope to model it as a desirable professional future for our talented young psychiatry residents. I want residents to have a view of the emergency service not just as a defined point in their residency, but as a crucial part of a continuum of care.

Dr. Bird has directed the APS since 2013. She formerly directed the Psychiatry Emergency Service at the Cambridge Health Alliance for 16 years. Dr. Bird trained at Dartmouth Medical School and the Tufts Adult Psychiatry Residency program where she was chief resident of Emergency Psychiatry.
When Francis Crick and James Watson first described the molecular structure of DNA in the scientific journal *Nature* in 1953, they may only have imagined that their findings would someday unlock the secrets of the human mind and mental illness.

Now more than six decades after the discovery of the double helix, teams of scientists and researchers in Boston and beyond have embarked on a quest to identify the genetic code of disorders as complex and elusive as schizophrenia, bipolar disorder and depression.

As part of this multinational collaborative effort, researchers from the Broad Institute of Harvard and MIT, Mass General, McLean Hospital and other institutions from around the world have identified more than 100 locations in the human genome associated with the risk of developing schizophrenia. And that’s just the start.

In the forefront of the emerging field of molecular psychiatry is Edward M. Scolnick, MD. A Harvard-schooled physician-researcher who trained at Mass General in the mid-1960s, Dr. Scolnick began his career at the National Heart Institute, where he worked for three years under the tutelage of Dr. Marshall Nirenberg, a Nobel Prize winner who helped unravel the genetic code. Later, at the National Cancer Institute, Dr. Scolnick demonstrated the cellular origin of sarcoma virus oncogenes in mammals and defined specific genes that cause human cancer.

During this time, he also developed a deep personal interest in the subject of mental illness. “I saw the effects of severe mental illness on families and realized how primitive the scientific basis for treatment was. I wanted to do something about it,” he explains.

Originally recruited by Merck Research Laboratories in 1982 to revitalize and modernize its virus and cell biology department, Dr. Scolnick was promoted to senior vice president for basic research in 1984 and to president in 1985. He later served as executive vice president for all science and technology at Merck & Co., Inc. During his tenure, Merck developed, among many others, the first drugs to lower cholesterol, halt osteoporosis and treat HIV/AIDS, and the first vaccine against the human papilloma virus which causes cervical cancer.

Moving the Science Forward

“Late in my career at Merck I realized that the field of psychiatry was hopeless unless we could understand the genetics, because you can’t do biochemistry, biopsies or blood work on a living brain,” he
collaborators worldwide, the Broad Institute proved the ideal setting to fuel Dr. Scolnick’s passion for research and personal interest in the biological underpinnings of severe and persistent mental illness.

“They had the reputation, the technologies and the network of collaborators, including many at MGH, needed to move the science forward,” he recalls.

When the Broad Institute formed the Stanley Center for Psychiatric Research in 2007 – thanks to Dr. Scolnick and his team’s vision and the philanthropic generosity of Ted Stanley and his late wife Vada – Dr. Scolnick was named senior associate member and founding director of the Stanley Center and director of the Broad Institute’s Psychiatric Disease Program. Named a core member of the Broad Institute in 2010, he currently serves as the Stanley Center’s chief scientist.

LONG-TIME CONNECTION WITH MASS GENERAL
From the time Dr. Scolnick trained at Mass General in the 1960s, his admiration for the hospital never waned. “I’ve always felt the medical training at MGH was superb, the intellectual abilities outstanding, and the medical care the highest quality of any I’ve encountered. MGH is just a fabulous hospital indescribably devoted to first-rate patient care.”

These passions and interests have led Dr. and Mrs. Scolnick to make a planned gift to the MGH Department of Psychiatry. Through a bequest, they will establish an endowed fellowship in molecular psychiatry at Mass General, to be carried out collaboratively between the hospital and the Broad Institute.

“The worst feeling for a patient or family suffering from severe mental illness is to have no hope. Through the advances that are being made and that will be made, there’s much more hope now.”
— Edward M. Scolnick, MD

Uniting the clinical research and patient care strengths of MGH Psychiatry with the Broad’s expertise in pure research produces an extremely powerful collaboration,” Dr. Scolnick notes.

The annual fellowship award is to be applied to investigating the molecular and biochemical basis of schizophrenia and bipolar disorder based on genetic risk factors. The goal of the research is to further the discovery of novel therapies for severe and persistent mental illness.

Dr. Scolnick has also made gifts to sponsor an MGH Psychiatry Academy patient and family education program, and to support primary care training at Mass General.

ENCOURAGING HOPE
“The field of psychiatry hasn’t attracted enough top-level PhDs and post-doctoral students to work on the underlying molecular mechanisms and genetics of these diseases – precisely because the biochemistry and genetics haven’t been known,” Dr. Scolnick explains. “Now, through the work of researchers at the Broad Institute, MGH and many other institutions, clear and genuine findings of the underlying genetics have emerged, along with lots to work on to unravel the abnormal biochemistry.

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Faculty News

Eight MGH Psychiatry researchers were included in Thompson Reuters’ 2014 list of The World’s Most Influential Scientific Minds: Joseph Biederman, MD; Randy L. Buckner, PhD; Stephen V. Faraone, PhD; Maurizio Fava, MD; John D. E. Gabrieli, PhD; Nikolaos Makris, MD, PhD; Andrew A. Nierenberg, MD; Gary S. Sachs, MD; and Larry J. Seidman, PhD. The list includes researchers whose publications between 2002 and 2012 were the most highly cited in the world (top 1 percent) for their field and year of publication.

Antoine Besnard, PhD, a postdoctoral fellow in the Laboratory of Neural Stem Cells, Circuits and Brain Function, was awarded a 2014 NARSAD Young Investigator Grant from the Brain and Behavior Research Foundation.

Hannah E. Brown, MD, assistant in Psychiatry in the Schizophrenia Clinical and Research Program, received a 2013 NARSAD Young Investigator Grant and the 2014 American Psychiatric Foundation’s Early Academic Career Award in Schizophrenia Research.

Christine A. Darsney, PhD, program manager for the Juvenile Court Consultation Program, received the Richard W. Barnum, MD, Distinguished Service Award from the Massachusetts Department of Mental Health, Juvenile Forensic Services in conjunction with the Trial Court of Massachusetts, Juvenile Court Division.

David C. Henderson, MD, director of the Schizophrenia Clinical and Research Program, was named by the National Alliance on Mental Illness as an Exemplary Psychiatrist for his inspirational work to improve the lives of individuals living with mental illness.

Michael S. Jellinek, MD, former chief of Child Psychiatry, won the Massachusetts School of Professional Psychology Humanitarian Award. He also won the Agnes Purcell McGavin Award from the American Psychiatric Association for his work with J. Michael Murphy, EdD, to create and validate the Pediatric Symptom Checklist.

Dara S. Manoach, PhD, director of the Laboratory for Multimodal Neuroimaging of Cognitive Function in Neuropsychiatric Disorders, was awarded a 2013-2014 Simons Center for the Social Brain Seed Award.

Olivia I. Okereke, MD, MS, clinical affiliate in the Department of Psychiatry, won the 2014 Columbia University Psychiatric-Neurological Epidemiology Early Career Award.

Derri L. Shtasel, MD, MPH, director of Public and Community Psychiatry, received the Dr. Jim O’Connell Award from Boston Health Care for the Homeless in recognition of her work to improve the lives of the most vulnerable members of society.

Lara N. Traeger, PhD, clinical assistant in Psychology in the Psychiatric Oncology and Behavioral Medicine Programs, won a five-year Mentored Research Scholar Grant from the American Cancer Society.

SAVE THE DATES

Psychiatry Academy Patient and Family Education Series

February 21, 2015
Obsessive Compulsive Disorder
Sabine Wilhelm, PhD,
Lee Baer, PhD, and colleagues
Sponsored by The Chirag Foundation

May 9, 2015
Bipolar Disorder and Genetics
Andrew A. Nierenberg, MD,
and colleagues
Sponsored by Dr. Edward M. Scolnick
and Barbara B. Scolnick

June 13, 2015
Eating Disorders
Kamryn T. Eddy, PhD,
Jennifer J. Thomas, PhD,
and colleagues
Sponsored by the Lawrence J. and Anne Rubenstein Charitable Foundation

October 3, 2015
Depression and Neurotherapeutics
Darin D. Dougherty, MD,
and colleagues
Sponsored by Elissa Freud and Steve Willis

November 7, 2015
Schizophrenia Education Day
David C. Henderson, MD,
and colleagues
Sponsored by an Anonymous Donor Family
with Gratitude to
Oliver Freudenreich, MD, and
Corrine Cather, PhD

Information
www.mghpatientfamily.org
or 866.644.7792
Neurotherapeutics (Continued from page 1)

ECT: THE GOLD STANDARD FOR TREATMENT-RESISTANT DEPRESSION

“Usually, ECT is reserved for people with severe forms of unipolar or bipolar depression who haven’t found other treatments effective; those who are really stuck,” says Michael E. Henry, MD, director of the ECT service and medical director of the Bipolar Clinic and Research Program. Because it’s comparatively fast-acting, ECT works well for individuals with severe suicidal thoughts or behaviors.

“The ECT service at MGH takes care of people who cannot be treated elsewhere because of their co-occurring medical illnesses,” says Dr. Henry, “for example, individuals with severe illnesses such as heart or pulmonary disease or different types of cancers that increase their risks when receiving anesthesia.”

After a patient receives general anesthesia and a muscle relaxant, brief electrical pulses are sent through electrodes on the scalp to painlessly induce a controlled seizure, which causes neurons throughout the brain to fire. Typically, ECT is given three times a week for two to three weeks, then sessions are tapered off. Maintenance treatments may be used to prevent relapse.

Although ECT suffers from a negative image popularized decades ago, modern treatment techniques are vastly improved and remission rates are strikingly high: 65 to 85 percent. “ECT is very different from the way it has been portrayed in movies. It is a medical procedure with many precautions to ensure safety and consent of the patient,” says Cristina Cusin, MD, a clinician-researcher in the MGH Depression Clinical and Research Program. “People tend to forget that depression, especially when severe, can be a lethal disorder.”

As with any medication or procedure, side effects can occur. Transient confusion following ECT is common, but usually resolves quickly. A small percentage of patients experience memory difficulties related to forgetting episodes from the past. In most cases, however, ECT reverses the negative effects of depression on memory and thinking.

RTMS: A TARGETED THERAPY

While ECT affects the whole brain, repetitive transcranial magnetic stimulation focuses on a specific brain region. No anesthesia is necessary, and no confusion or memory loss occurs.

Using anatomical calculations or available brain imaging, a magnetic coil precisely positioned on the scalp directs magnetic pulses to a portion of the brain involved in mood regulation. “RTMS allows us to direct treatment to the brain networks we want to target,” says Joan Camprodon, MD, PhD, MPH, director of the MGH RTMS clinical service and the Laboratory for Neuropsychiatry and Neuromodulation. RTMS may also relieve physical pain, he notes, because the brain circuits for depression and pain overlap.

“RTMS allows us to direct treatment to the brain networks we want to target.”
— Joan Camprodon, MD, PhD, MPH

Typically, RTMS requires 40-minute sessions, five days a week for four to six weeks, then is tapered to two sessions a week for three more weeks. The dose and device position are individualized for each patient. Side effects may include headaches and scalp tingling or discomfort.

This treatment approach continues to evolve. “We now understand more about the required dose,” says Dr. Camprodon, who is leading research on RTMS. Recent studies show remission in 30 to 37 percent of patients, many of whom were simultaneously taking antidepressants without gaining sufficient relief.

Several weeks into his RTMS treatment, Jack Gorgone’s depression began to lift. His irritability and sad thoughts declined. Surprisingly, so did much of his physical pain, scaling down from a self-rated nine out of ten (with ten being the worst) to a five, a number he says he can handle.

Neurotherapeutics: Beyond ECT and TMS

Neurotherapeutic devices use electricity, magnets, or implants to rebalance complex neural networks in the brain affected by depression, anxiety, obsessive-compulsive disorder, Parkinson's disease and other illnesses. Some devices require surgery; others like ECT and TMS do not. Most focus on specific areas of the brain.

At Mass General, researchers are actively investigating and refining many neurotherapeutic approaches, including epidural cortical stimulation, transcranial direct current stimulation, vagus nerve stimulation and deep brain stimulation. “The hope with all of these treatments is that they wind up normalizing the entire brain network,” says Dr. Dougherty. “Essentially, they’re different paths leading to the same place.”

An acknowledged leader in this exciting field, Mass General received a five-year, $30 million dollar grant from the Defense Advanced Research Projects Agency (DARPA) earlier this year to help develop a tiny, sophisticated brain implant able to recognize and treat episodes of post-traumatic stress disorder and other mental health problems in military personnel.
Dr. Eden Evins named first incumbent of the William Cox Family Professorship

Substance use disorders are the nation’s number one public health problem. More than 20 million people in the U.S. have an addiction to drugs or alcohol. Anne Eden Evins, MD, MPH, founding director of the MGH Center for Addiction Medicine, recently was recognized for her exceptional work in this area as the first incumbent of the William Cox Family Professorship in Psychiatry in the Field of Addiction Medicine.

The establishment of this professorship and the appointment of its first incumbent were celebrated July 30, 2014 during a ceremony at Harvard Medical School (HMS). Named in honor of the late William Cox, the professorship was established through a gift from the Cox family, as well as other donor contributions. Nancy Tarbell, MD, HMS dean for Academic and Clinical Affairs, hosted the event, which featured remarks by Peter L. Slavin, MD, MGH president; and Jerrold F. Rosenbaum, MD, chief of the MGH Department of Psychiatry; Heidi Cox; and Dr. Evins.

“At the MGH, we are determined to take the lead in preventing, identifying, treating and managing substance use disorders and we will rely heavily on Eden’s leadership and inspiration,” said Dr. Slavin.

“I am deeply grateful for the inspirational gifts of the Cox family and the many generous others that have made this opportunity possible,” said Dr. Evins. “There are pivotal questions around the biological underpinnings of addiction that the critical support of this professorship will help us address. These discoveries will help us better counsel families and develop more targeted and effective treatments.”

Article adapted from MGH Hotline, August 22, 2014