

MINDSCAPES

MGH DEPARTMENT OF PSYCHIATRY NEWSLETTER FOR FRIENDS AND SUPPORTERS • FALL 2010

The Right Treatment for the Right Person *MGH Psychiatry Researchers Advance Personalized Medicine*

In psychiatry today, the best a clinician can do for a patient is to prescribe a treatment that has worked in research studies and clinical practice, closely monitor the results and switch to another treatment if the first one fails. Using this trial-and-error approach, doctors and their patients may wait weeks – even months – before they find an effective treatment.

“Personalized medicine” promises a better way to treat psychiatric illness. In this emerging medical discipline, doctors look for indicators in the human body, called “biomarkers,” to help them predict which individuals will respond to which treatment.

Personalized medicine is already transforming other areas of clinical care. For example, researchers at the MGH Cancer Center have discovered that instead of treating cancer based on where in the body it originates, e.g., the colon or breast, they can match a “smart drug” to a tumor’s specific genetic mutation, offering patients targeted treatments that can result in better outcomes with fewer side effects.

In the MGH Department of Psychiatry, Roy Perlis, MD, MSc, A. Eden Evins, MD, MPH, and Joshua Roffman, MD, MMSc, are among the many clinician-researchers whose work is paving the way for personalized medicine in psychiatry.

GENES THAT PREDICT LITHIUM RESPONSE IN BIPOLAR PATIENTS

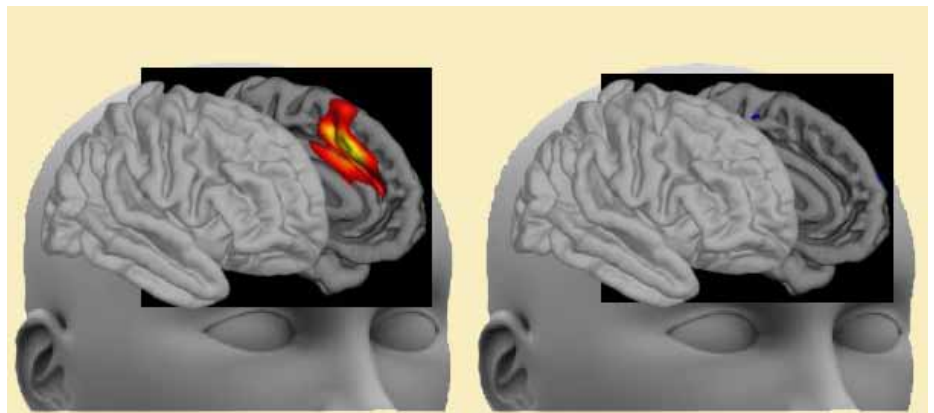
In the MGH Bipolar Clinic and Research Program, **Dr. Roy Perlis** and colleagues are studying genes that may help predict which patients with bipolar disorder will respond best to lithium. Although lithium is the gold standard for treatment of this disorder, it is not universally effective, and it carries the risk of serious side effects.

Prior research had suggested that an individual will respond well to lithium if a family member with bipolar disorder benefited from lithium. But Dr. Perlis wanted to find a more

reliable way to predict which patients should be given lithium. He and fellow researchers at Mass General and the Eli and Edythe L. Broad Institute of Harvard and MIT began to analyze genetic material from several thousand patients to see whether specific genes might be associated with a person’s response to lithium.

“Personalized medicine – finding the right treatment for the right person – is one of the ‘holy grails’ of the exciting, emerging field of psychiatric neuroscience.”

– Jerrold F. Rosenbaum, MD, MGH Chief of Psychiatry



Composite brain scans from 56 volunteers show how people who have a genetic deficit associated with schizophrenia (*right*) fail to respond to making errors, compared to people who have the normal version of the gene (*left*). MGH researchers are using neuroimaging to develop a treatment for this defect, linked to symptoms of apathy and lack of motivation.

In 2009, Dr. Perlis and colleagues reported in *The American Journal of Psychiatry* the results of the first study to look ‘across the genome’ at genes that influence lithium response. Dr. Perlis hopes the team’s findings of promising gene variants will lay the groundwork for a blood test to help psychiatrists determine which patients will benefit from lithium. “Clinical trials that use genetics to guide lithium prescription may be only a few years away,” predicts Dr. Perlis.

(Continued on Page 6)

From the Chief

You may have heard me say it before, that the burden and suffering associated with psychiatric disorders are so prevalent that everyone is affected. In the words of our Leadership Council mantra, "No family goes untouched."

However, despite the abundance of need and the size of the population affected, the actual individual story of anyone we treat is unique; unique in terms of age of

onset, symptoms, course, severity, co-existence with other conditions and response to treatments. Our challenges of unlocking the neurobiological underpinnings of these conditions are mirrored by the need to understand the unique vulnerabilities and resiliencies of each individual.

So we proceed simultaneously to address the best approach to care for affected and vulnerable populations who suffer while engineering optimal

interventions for individual patients. Several examples of this effort are revealed in this issue of our newsletter, including stories about our intensified focus on the most needy and vulnerable in society, our efforts to "personalize" care, and our initiative to offer a unique set of services for children and adults on the autism spectrum.

When I stand back and survey the 45 sub-specialized clinical and research programs and units in this department, the rallying cry of the Ghostbusters keeps intruding on my thoughts: "Who you gonna call?" With the inspiration from this extraordinary institution and its compassionate and visionary leadership, 21st century psychiatry has taken root and flourished, a place where world class experts who focus on every issue, however rare or complicated, are gathered to help in a way where few others can.

As always, much of what we have accomplished, continue to do, and strive yet to achieve is the product of your care, concern, support and generosity. Thank you again.



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

Psychiatry Faculty News

Jeffrey O. Bostic, MD, EdD, director of the MGH School Psychiatry Program, was awarded the 2010 Sidney Berman Award from the American Academy of Child and Adolescent Psychiatry for his contributions to the study and treatment of learning disabilities and mental health. The award recognizes Dr. Bostic's leadership in creating www.schoolpsychiatry.org, a web site that addresses the mental health needs of children and adolescents.

Lori R. Eisner, PhD, post-doctoral fellow in psychology in the MGH Bipolar Clinic and Research Program, was awarded the Kaplen Fellowship on Depression (2010-2011) and a Livingston Award (2010-2011) to study a new group treatment for bipolar disorder that focuses on emotional regulation skills. The Kaplen Fellowship supports training in research on depression and related affective disorders. The Livingston Award provides support for beginning investigators in psychiatry.

John A. Fromson, MD, associate director of MGH Psychiatry Postgraduate Medical Education, was elected Class A (nonalcoholic) Trustee of the General Service Board of Alcoholics Anonymous, Inc. (AA). Founded in 1935, AA is a fellowship of more than 2,000,000 recovered alcoholics in the United States, Canada and other countries who meet in 115,000 local groups for self-help.

Donald C. Goff, MD, director of the MGH Schizophrenia Clinical and Research Program, was designated a 2009 NARSAD Sidney R. Baer, Jr. Foundation Investigator for his research combining a drug called D-cycloserine with cognitive remediation (computerized exercises for the brain) to facilitate healing of the brain and improved thinking in individuals with schizophrenia.

Mohammed R. Milad, PhD, director of the MGH Behavioral Neuroscience Laboratory and Britta Holzel, PhD, research fellow in the MGH Division of Psychiatric Neuroscience, received the Templeton Foundation's Positive Neuroscience Award to examine the effects of meditation on the structure and function of brain regions involved in fear extinction.

Paula K. Rauch, MD, director of the Marjorie E. Korff PACT Program (Parenting at a Challenging Time), and director of the family component of the Red Sox Foundation and Mass General Hospital Home Base Program, was instrumental in development of the PBS Arthur Family Activity booklet, "When Someone You Know Has Cancer," which recently was awarded the National Health Information Gold Award.

Jerrold F. Rosenbaum, MD, MGH chief of Psychiatry, was elected president of the Anxiety Disorders Association of America (ADAA). Mark H. Pollack, MD, director of the MGH Center for Anxiety and Traumatic Stress Disorders, was elected to the Board of Directors. The ADAA is the only national nonprofit organization solely dedicated to the prevention, treatment and cure of anxiety disorders.

Jedidiah Siev, PhD, clinical fellow in Psychology in the OCD and Related Disorders Program, received a grant from the International OCD Foundation to study scrupulosity, a type of obsessive compulsive disorder characterized by religious or moral obsessional fears.

Psychiatric Care for the Most Vulnerable Members of Our Community

A Conversation with Dr. Derri Shtasel

Q: Last year, the MGH Department of Psychiatry established the Division of Public and Community Psychiatry and recruited you to serve as its director. Why was this division formed?

Dr. Shtasel: A pillar of Mass General's mission is commitment to the health of the community. The MGH Department of Psychiatry embraces this critical responsibility, and established the division to help meet the needs of patients in our community suffering from severe and persistent mental illness, substance abuse, poverty, immigration challenges, homelessness and multiple traumas.

Q: What are the division's goals?

Dr. Shtasel: The division has several overarching goals: to improve clinical services and systems for underserved, vulnerable populations, to improve our training in this area, to collaborate with community partners in order to advance mental health research that benefits underserved populations, and to create a pipeline for a new generation of psychiatrists committed to public sector patients and social justice.

- Adults with serious mental illness treated in public systems die on average 25 years earlier than Americans overall—at age 51, compared with age 76.
- Among people who are homeless, 66 percent report substance use and/or mental health problems
- More than 90 percent of sheltered and low-income mothers have experienced physical and sexual assault over their lifespan.
- By age 12, 83 percent of homeless children have been exposed to at least one serious violent event, and 25 percent have witnessed acts of violence within their families.

Q: What's your approach to accomplish some of these goals?

Dr. Shtasel: In this past year we've created a structure to allow the division to work most effectively toward our goals. Building relationships is at the core of this process. Our approach is to listen to our community partners – we need to understand their challenges and priorities – and then work with them to establish shared objectives and initiate specific projects. As we're able to extend and deepen our collaboration with our shared community of providers, we'll get better at working together and solving problems.

Q: Can you provide an example of a project this division has been working on?

Dr. Shtasel: Sure – we're very excited about a fundamental change we're making in our psychiatry residency training program. We met with representatives from the Massachusetts Department of Mental Health and other local entities including

Boston Health Care for the Homeless, North Suffolk Mental Health Association and the MGH Addiction Research Program, to design a required six-week rotation emphasizing system integration and patient advocacy. In July, our residents began working with an outpatient population of homeless patients suffering from severe and persistent mental illness, addictions and chronic medical disorders. Through this collaboration, we will bring primary care, substance abuse treatment and psychiatric care to the patients, and our residents will become part of a new model of service delivery.

Aidan Parkinson



Derri Shtasel, MD, MPH

Q: How do the MGH Health Centers fit in?

Dr. Shtasel: We've been working very closely with the behavioral health directors of MGH Chelsea, Charlestown and Revere Community Health Centers. They have been concerned about systematic access to child psychiatry and child psychiatrists, and identified this as a priority. We've been able to develop a better referral process for consultation and treatment for kids in the community and here at the hospital; we've also re-invigorated a program through which Massachusetts pediatricians can, in real time, speak to a child psychiatrist for consultation. This is just the beginning, and I have confidence we'll find many areas of shared need and interest.

Q: In the current economic climate, care options for people affected by chronic psychiatric illness and poverty have diminished. How do you avoid getting discouraged?

Dr. Shtasel: I've spent my career working with very sick and disenfranchised populations, doing what I can, in whatever small ways, to improve their care. If anything, the work has stimulated me, not discouraged me: the patient population I've been describing is remarkable for their resilience, and this is both humbling and inspiring. The hospital's and MGH Department of Psychiatry's commitment to serving all members of the community means we can bring our greatest asset – incredible human capital – to those most in need. This is energizing and exhilarating. It is a privilege to be able to do this work, and I am grateful for this opportunity.

Derri Shtasel, MD, MPH, is director of the MGH Department of Psychiatry's new Division of Public and Community Psychiatry. A long-term advocate of the need for improved care for patients with severe and persistent mental illness, Dr. Shtasel is also director of Adult Ambulatory Psychiatry at Mass General and associate professor of Psychiatry at Harvard Medical School.

Massachusetts Couple Makes Autism a Priority

Bresslers' Gift Launches Clinic and Research Program

ALAN AND LORRAINE BRESSLER have always been committed to giving back to the Boston-area community where they have lived for more than half a century and raised three daughters. Lorraine is a long-time overseer of the Museum of Fine Arts, where the couple created a named gallery, and Alan is a trustee of the Boston Symphony Orchestra. In addition to art and music, they

support education through the Boston Latin School Association and other Boston education projects.

During the last decade, the Bresslers became aware of another pressing community need, one that was brought home to them when their grandson, now 12, was diagnosed with Asperger's Syndrome. People with Asperger's, also known as "high-functioning autism," have normal intelligence and language development, but have difficulty with social interaction and communication. They often have difficulties with behavioral and emotional control as a result of co-occurring psychiatric conditions. "After our grandson's diagnosis, we became aware that many people we know have grandchildren with similar problems, and that it's common for these

children to have psychiatric conditions as well," says Lorraine Bressler. "Having a child or grandchild with autism and emotional problems can rip a family apart."

TREATMENT OF CO-OCCURRING PSYCHIATRIC CONDITIONS

The Bresslers learned that Joseph Biederman, MD and his colleagues in the Clinical and Research Program in Pediatric Psychopharmacology and Adult ADHD at Mass General were studying how treatment of co-occurring psychiatric conditions can enable individuals with high-functioning autism to reach their potential and lead fulfilling lives. The Biederman team's research was prompted by their observation that about 15 percent of the children they were treating for ADHD, depression, anxiety and bipolar disorder had this form of autism.

"Dr. Biederman and his group were developing a system of coordinated care to provide practical solutions for families dealing with these challenges," says



MGH Photo Lab

ALAN AND LORRAINE BRESSLER

Alan Bressler. "That approach made sense to us, so we began a discussion of how we could support his efforts." The couple's overture soon led to the creation of the Alan and Lorraine Bressler Clinical and Research Program for Autism Spectrum Disorders at Mass General. The program opened to patients in October 2007. It is one of only a few in the country to provide comprehensive psychiatric evaluation of children and adults with high-functioning autism, and to focus on treating their psychiatric conditions.

"In many cases, young people can learn to manage and live with the symptoms of high-functioning autism," says Dr. Biederman. "But if such a child is inattentive because of ADHD, or agitated, aggressive or violent because of bipolar disorder, teachers cannot reach the child, and he or she is likely to fail in school and function poorly in work, social and family life."

SUPPORT INTO ADULTHOOD

Dr. Biederman and colleagues have found that with proper psychiatric treatment, their patients with autism can take fuller advantage of educational, vocational and social skills programs. The team is also developing driving and work simulation programs to provide older patients with strategies for acquiring these essential life skills; about one in five patients treated in the Bressler Program is 18 or older.

"With children and grandchildren ourselves, we've come to understand that it's up to us (...) to support the research and clinical care that will help kids with these disorders lead productive and rewarding lives. We can't sit back and wait for others to do the job."

— Lorraine Bressler

Patients come from all over the country to seek evaluation and treatment. "Before the Bressler Program existed, many parents of children with high-functioning autism were at their wits' end, diagnostically confused and unable to find programs that offered effective treatment," says Gagan Joshi, MD, scientific director. "The Bressler Program offers them a 'home,' where their child is fully understood and can receive treatment and support well into adulthood."

"We knew that supporting this renowned group of psychiatrists and psychologists would yield benefits far beyond what anyone could have imagined, and this has already begun to happen," says Alan Bressler. The Bresslers hope that the program will become a national model. Since the number of referrals exceeds current clinical capacity, they also hope that other families will step forward to support the program so that the team can help more families and conduct further research. "With children and grandchildren ourselves, we've come to understand that it's up to us, families who are affected by autism and co-occurring psychiatric conditions, to support the research and clinical care that will help kids with these disorders lead productive and rewarding lives," says Lorraine Bressler. "We can't sit back and wait for others to do the job."



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For information about ways to support the clinical care, research, teaching and community health activities of the MGH Department of Psychiatry, please contact Carol Taylor at (617) 724-8799/ cwtaylor@partners.org or Frank Soldo at (617) 724-0186/ fsoldo@partners.org.

The right treatment for the right person

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BRAIN IMAGING TO UNDERSTAND CRAVING AND RISK OF RELAPSE IN ADDICTION

The many forms of addiction – whether they involve alcohol, opiates, gambling or food – have in common the phenomenon of craving: the powerful and unrelenting urge to consume or engage in an unhealthy behavior. Craving leads to persistent use, despite efforts to stop, and to relapse, often after years of abstinence. **Dr. Eden Evins** and colleagues in the MGH Center for Addiction Medicine are using brain imaging to understand the underlying biological mechanism of the craving response.

The initial focus of their efforts is smoking. In the United States, more than 40 percent of people with a psychiatric disorder smoke cigarettes, about twice the rate of the general



Using brain imaging, Dr. Evins and colleagues measured the brain activity of smokers responding to visual smoking cues such as the image above. They discovered that people whose brains were highly reactive to these stimuli before quitting were more likely to relapse after nicotine replacement therapy.

population. Of those smokers with a psychiatric disorder who successfully quit smoking, as many as three out of four relapse within two weeks of discontinuing smoking cessation treatment.

Using functional magnetic resonance imaging (fMRI), the team has developed a way to predict which patients will respond to standard nicotine replacement

therapy, and which ones will need additional treatment. In a study reported in *Biological Psychiatry*, the investigators measured how smokers' brains reacted to smoking-related cues before they attempted to quit smoking. The team found that smokers whose brains were more reactive at baseline (before quitting) were prone to relapse despite treatment with nicotine replacement therapy. In contrast, smokers with less brain reactivity at baseline were likely to quit smoking successfully with standard treatment. Using brain imaging and other study data, the researchers were able to predict with a remarkable 79 percent accuracy who would succeed at quitting with standard nicotine replacement therapy.

“We can now identify relapse-vulnerable smokers *before* they attempt to quit,” says Dr. Evins, “and test supplementary treatments with these smokers to increase their odds of success.” One such treatment is neurofeedback, a non-invasive procedure that displays a smoker's brain waves through fMRI, while training the smoker to change the way his or her brain responds to smoking cues. A second treatment involves D-cycloserine, a drug

used to desensitize trauma victims, together with gradual exposure to cigarettes, under a therapist's supervision.

“We're optimistic about this area of translational addiction treatment research,” says Dr. Evins. “It has profound implications for patient care and public health, and for effective and lasting treatments for all addictions.”

TREATING GENETIC DEFICIT LINKED TO NEGATIVE SYMPTOMS IN SCHIZOPHRENIA

In the MGH Schizophrenia Clinical and Research Program, **Dr. Joshua Roffman** and other faculty are examining patients' genes to help predict who might benefit from a nutritional supplement that improves so-called “*negative symptoms*” of schizophrenia. These subtle and largely untreatable symptoms – apathy, flat affect, weak social skills, lack of motivation and lack of engagement in life – often impair people with schizophrenia more than the treatable symptoms of hallucinations or hearing voices.

In 2004, the team discovered a correlation between *negative symptoms* of schizophrenia and low blood levels of folate. Folate, a B-vitamin commonly found in our diets, is crucial for healthy brain development and functioning. Dr. Roffman and colleagues hypothesized that there was a connection between *negative symptoms* and a particular form of a gene that affects the way our bodies metabolize folate. The gene is called MTHFR, and people with schizophrenia are more likely to have a low-functioning variant of this gene.

The team's research, reported in *Biological Psychiatry* and the *Proceedings of the National Academy of Sciences*, found that when individuals with schizophrenia have the low-functioning variant of MTHFR, they are likely to have more severe *negative symptoms* along with certain brain changes that can be seen in a brain scan. The team is now studying whether folate supplements can reduce *negative symptoms* and associated brain changes. Dr. Roffman notes that this encouraging work “not only gives us a basis for using folate to treat patients with the low-functioning MTHFR gene variant, but also a model for creating new treatments that address other genetic deficits.”

Other department researchers are making discoveries about biomarkers such as genes and brain activity that will one day allow doctors to prescribe highly individualized treatments for depression, post traumatic stress disorder and obsessive compulsive disorder. “Personalized medicine – finding the right treatment for the right person – is one of the ‘holy grails’ of the exciting, emerging field of psychiatric neuroscience,” says MGH Chief of Psychiatry, Jerrold Rosenbaum, MD.

A. Eden Evins, MD, MPH, is director of the Center for Addiction Medicine

Roy Perlis, MD, MSc, is director of Pharmacogenomics Research and director of the Bipolar Clinical Program

Joshua Roffman, MD, MMSc, is director of the Brain Genomics Laboratory

MGH Psychiatry Out and About



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1. Kelan and Mark Thomas with Joseph Biederman, MD, (*center*) at a dinner in their home for families and friends of the MGH Pediatric Psychopharmacology Program



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2. Nancy Harris, receiving the American Academy of Child and Adolescent Psychiatry's 2009 Catcher in the Rye Humanitarian of the Year Award for her leadership in improving the lives of individuals with eating disorders



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3. Britain W. Nicholson, MD, (*left*), chief medical officer of Mass General, with Mary O'Neill Herman and John B. Herman, MD, associate chief of Psychiatry, at the launch of the MGH Campaign for the Third Century of MGH Medicine

4. *Left to right*: David Henderson, MD, director of the MGH Chester M. Pierce Division of Global Psychiatry, and Julia Carney, Pierce Division administrator, with Crown Prince of Perak, Malaysia, Raja Nazrin Shah, PhD, and psychiatrist Tan Sri Mahadevan, MD, sponsor of the Mahadevan Fellowship at MGH

5. David Herzog, MD, founder of the MGH Harris Center for Education and Advocacy in Eating Disorders (*left*); Natalia Vodianova, model; Michael Kors, designer; and Anna Wintour, Vogue editor-in-chief, at the center's 13th annual public forum in March 2010 at Harvard Business School

Fred Seligman, MD



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Roger Farrington

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Aidan Parkinson

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6. *From left*: Janet Wozniak, MD, director of the MGH Pediatric Bipolar Program, with Pediatric Psychopharmacology Council members Chris and Bessie Wolfington at the sixth annual Seminar in Boston in September 2010

7. *From left*: Mark Pollack, MD, of Mass General and Ross Zafonte, MD, of Spaulding Rehabilitation Hospital, with Cheryl Zafonte and Patricia Normand, MD, at the launch of the Campaign for the Third Century of MGH Medicine in October 2010. Dr. Pollack and Dr. Zafonte direct clinical programs of Home Base, the Red Sox Foundation/MGH initiative for returning soldiers and their families



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8. Also at the Pediatric Psychopharmacology Seminar, Norma Fine (*left*) with Gagan Joshi, MD, scientific director of the Bressler Program for Autism Spectrum Disorders (*See pp. 4-5*) and incumbent of the Norma Fine Fellowship

9. *From left*: Edward P. Lawrence, Esq., immediate past chair of the MGH Board of Trustees; Jerrold F. Rosenbaum, MD, MGH chief of Psychiatry; and J. Stuart Ablon, PhD, director of Think:Kids, at an event hosted by Kate and Scott Murray in May 2010



Aidan Parkinson

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Roger Farrington

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Development Office

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MGH and Harvard Celebrate Fourth and Fifth Psychiatry Chairs

WITH RECENT celebrations at Harvard Medical School, the Department formally gained two professorships, or chairs, for the Depression Clinical and Research Program (DCRP). The combined initial value of the endowment principal of the two new chairs exceeds \$6.0 million. Income will be distributed annually and in perpetuity to support the work of DCRP psychiatrists with the rank of associate professor or professor.

On May 21, 2010, Dean Jeffrey Flier, MD of Harvard Medical School and others paid tribute to the family of Shirley Slater and the late Alvin Slater for creating the Slater Family Professorship in Psychiatry, and honored the first incumbent, Maurizio Fava, MD. Dr. Fava is executive vice chair of Psychiatry and founding director of the DCRP.



From left: Jerrold F. Rosenbaum, MD; Kenneth Z. Slater; Dean Jeffrey S. Flier, MD; Shirley Slater; Maurizio Fava, MD; Maxine Chrein; MGH President Peter L. Slavin, MD; Ellen Slater; Jackie Slater; Richard Slater and Sam Slater

Speaking on behalf of the Slater family, Kenneth Slater said, “Both my mother and father believed in the funding of people as opposed to bricks and mortar. Now, they were in real estate so they obviously liked bricks and mortar. But the idea of funding something that has an indefinite life and that can evolve with the learning and the pursuit of knowledge was important to them.”

Harvard Medical School and MGH leaders gathered again on September 15, 2010 with friends and colleagues of Richard Tedlow and the late Dr. Joyce Root Tedlow to inaugurate the Joyce Root Tedlow Professorship in Psychiatry. Dr. Joyce Tedlow was a beloved member of the DCRP faculty until her death in 2003. In a moving tribute, Richard Tedlow, professor emeritus at Harvard Business School, recounted Dr. Tedlow’s transition from a private therapist to a gifted psychiatry researcher.



Prof. Richard S. Tedlow (left) with Jenny Moriarty and Dr. Rowland Moriarty

Citing her relationship with the chair’s first incumbent, Jonathan Alpert, MD, PhD, Tedlow said, “Joyce once cared for some of Jonathan’s patients. She came away from that experience extraordinarily impressed by the care he provided them and by their devotion to him. I remember her saying, ‘this is the kind of psychiatry the world needs, and Jonathan is the kind of psychiatrist who provides it.’” Dr. Alpert is associate chief of Psychiatry and director of Clinical Services for the department.

In addition to major donations by the Slater family and Prof. Tedlow, a total of 72 other donors helped fund the two endowed chairs.