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MINDS CAPES

MGH DEPARTMENT OF PSYCHIATRY NEWSLETTER FOR FRIENDS AND SUPPORTERS • SUMMER 2016

Mass General Researchers Explore Promising Therapies for Treatment-resistant Depression

EVERY YEAR, nearly 16 million American adults experience an episode of major depressive disorder. Cardinal symptoms are persistent sadness or indifference to familiar pleasures and interests. Anxiety, or a sense of emptiness, hopelessness or worthlessness may surface. Snowballing problems with sleep, concentration and decision-making can make even simple tasks seem overwhelming, and thoughts of death or suicide may start intruding with increasing frequency.

Fortunately, many people find that depression eases with medication, psychotherapy and time, often in combination. Yet research shows that only a third of those treated with medication respond to the first antidepressant prescribed, while another third gain relief with the second.

But what happens if depression refuses to abate? Treatment-resistant depression (TRD) – that is, depression that fails to recede despite several approved treatments – crushes quality of life and can even be life-threatening. Almost one in five people struggling with TRD report attempting suicide, sometimes repeatedly.

Responding to the urgent need to expand the toolbox of well-tolerated, effective therapies for depression, the MGH Depression Clinical and Research Program is investigating many innovative treatments. Ketamine and near-infrared light, two promising approaches currently being explored through research, will soon be more widely available to Mass General patients.

Mass General researchers are testing other novel treatments, including therapies that target brain circuitry, such as transcranial magnetic stimulation, and natural substances, such as omega 3 supplements.

“For more than 5 decades, all approved antidepressants, including the current SSRIs and SNRIs, have been based on mechanisms involving the neurotransmitters serotonin, norepinephrine and dopamine. Given that a significant number of our patients do not

respond or respond only partially or temporarily to these standard antidepressants, we must be unrelenting in our quest to develop safe and effective treatment alternatives that engage other mechanisms so that we can help every patient find relief and stay well,” says Jonathan E. Alpert, MD, PhD, director of the Depression Program.

KETAMINE: AN IMMEDIATE RESPONSE

Ketamine is a medication that has been used for decades in anesthesia, particularly in emergencies and during surgery. Years ago, researchers serendipitously discovered that a single intravenous infusion had remarkably quick, mood-lifting effects in some people with depression.

Cristina Cusin, MD, a staff psychiatrist at the MGH Depression Program who has helped lead research on ketamine, has seen this firsthand. “Within one day, the severity of symptoms may be cut in half,” she says. “People say, ‘I don’t feel the weight of the world on my shoulders. I don’t feel like killing myself anymore.’ Their thought processes shift, they’re not in pain, and they’re better able to cope.”

A preliminary study at Mass General, published in May in the *Journal of Clinical Psychiatry*, enrolled 14 people with treatment-resistant depression who had been wrestling with suicidal thoughts for at least three months – a unique population because most studies exclude those who are suicidal. A series of six intravenous



Jonathan E. Alpert, MD, PhD; Cristina Cusin, MD; Paolo Cassano, MD, PhD

Ketamine and near-infrared light, two promising approaches currently being explored, will soon be more widely available to Mass General patients.

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From the Chief

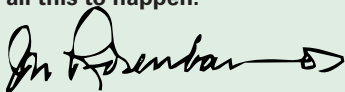
In early June, I sat down with our 16 new psychiatry residents as they exuberantly began to get to know each other, eager and anxious to begin the journey of transformation from medical student to psychiatrist, from potential to actualization. And a few days later we graduated a like number of now competent, committed and passionate graduating residents, set to make their mark on the world.



This process of becoming a modern psychiatrist – of adding to and renewing the team of educators, caregivers and researchers – is not static. With renewal hopefully comes advancement and growth, not only of the trainee but of the field. We do so well for so many, only to fall short for too many. Thus we must struggle, innovate, plod on, reconsider, study and test. We owe it to you and to millions of others. We are on the job, and we will continue to deliver on that promise.

We truly believe there is no other place as well positioned to make this promise as Mass General, the number one rated hospital in the country. Within the nation's largest hospital-based biomedical research program, we have a unique set of assets: the depth of subspecialty expertise, quality of those who come to training here and array of best-in-class technologies – from genetics to neuroimaging, stem cells to big data, software engineering to treatment development – examples of which are reported in each issue of *Mindscapes*.

What a gift! What a privilege and duty. Thank you all for your part and for energizing and enabling all this to happen.



Jerrold F. Rosenbaum, MD
Psychiatrist-in-Chief

Wilens Honored with Endowed Chair in Addiction Medicine

Timothy E. Wilens, MD, chief of the Division of Child and Adolescent Psychiatry, was honored as the inaugural incumbent of the MGH Trustees Endowed Chair in Addiction Medicine at a celebration on April 4, 2016, at the Paul S. Russell, MD Museum of Medical History and Innovation. The chair was made possible through the generosity of an anonymous donor.

The Trustees Chair will help expand efforts to address substance use disorders that affect patients and families at Mass General and in surrounding communities. Addressing addiction is one of the hospital's top strategic priorities. "Substance use is one of the most significant public health issues our country is facing today, a public health threat that affects our patients and their families, our communities, and the care we give here at the hospital," said Peter L. Slavin, MD, president of Mass General. "I'm proud of the substance use disorder initiative that's in place here at the hospital. We're hopeful and excited that this chair will further the work needed in addiction medicine."



Peter L. Slavin, MD; Timothy E. Wilens, MD; Jerrold F. Rosenbaum, MD

Wilens is also the co-director of the Center for Addiction Medicine at Mass General, and a leading expert in substance use disorders, addiction medicine, attention-deficit hyperactivity disorder and pediatric and adult psychiatry. He has published more than 300 peer-reviewed articles and four books on these topics.

Half of substance use disorders in young people begin before age 18, and more than three-quarters begin before age 24. In light of these figures, the chair is a validation of working in the field of substance use disorders, Wilens says. "Now our third endowed chair in addiction medicine, this sends a signal to how important it is to understand the roots, mechanisms and treatments of substance use disorders."

"I am deeply moved by being named the inaugural recipient of this chair," said Wilens. "This honor will be taken very seriously, and in the spirit of Mass General, with devotion to clinical care, research and education."

Article adapted from *Mass General Hospital for Children Totline*, April 26

Faculty News

Maurizio Fava, MD, executive vice chair, Department of Psychiatry, and director of Clinical Research, Massachusetts General Hospital, was elected Councilor of the Association of American Physicians. He also received the Award for Clinical Excellence for High Scientific Contribution in the Psychopharmacological Treatment of Depressive Disorders at the 20th Annual Congress of the Italian Society of Psychopathology in Milan, Italy.

The **Louis V. Gerstner III Research Scholar Awards** for 2016-2018 have been awarded to **Franziska Plessow, PhD**, of the Neuroendocrine Unit, and **Mai Uchida, MD**, in the Pediatric Psychopharmacology and Adult ADHD Program.

Dawn F. Ionescu, MD, was selected for the 2016 Career Development Leadership Program of the Anxiety and Depression Association of America, and received the 2016 Society of Biological Psychiatry Travel Award.

Christopher J. McDougle, MD, director of the Lurie Center for Autism, edited the *Primer on Autism Spectrum Disorder*, published by Oxford University Press, 2016.

Dennis K. Norman, EdD, faculty chair of the Harvard University Native American Program and senior psychologist at Mass General, received the Harold Amos Faculty Diversity Award from Harvard Medical School.

Cultural Sensitivity in Child and Adolescent Mental Health, published by the MGH Psychiatry Academy, 2015, was edited by **Ranna Parekh, MD** and **David H. Rubin, MD**. A number of MGH faculty and staff also contributed to the book, including **Tara Kenworthy, Stephanie Furtak, Mai Uchida, MD, Justin A. Chen, MD, MPH**, and **Ginette Sims**.

Yakeel Quiroz, PhD, director of MUNDOS (MGH Multicultural Neuropsychology Program), has been selected as a recipient of an MGH 2015 Service Excellence Team Award.

Jerrold F. Rosenbaum, MD, Psychiatrist-in-Chief, was awarded the 2016 Joseph B. Martin Dean's Leadership Award for the Advancement of Women Faculty from the Joint Committee on the Status of Women at Harvard Medical School and Harvard School of Dental Medicine.

Ronald Schouten, MD, JD, has been named the first Visiting Scholar at St. Elizabeth's Hospital in the Department of Behavioral Health in Washington, DC.

Lara N. Traeger, PhD, a psychologist in the Mass General Cancer Center and the Behavioral Medicine Service, has received a 2016 MGH American Cancer Society Institutional Research Grant Award.

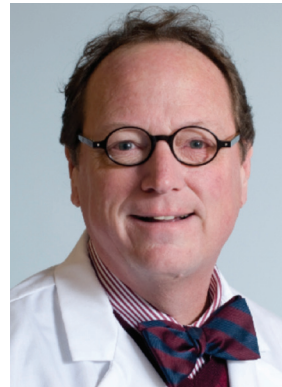
Alexander C. Tsai, MD, PhD, staff psychiatrist in the Chester M. Pierce, MD, Division of Global Psychiatry, received the 2015-2016 Young Mentor Award from Harvard Medical School.



Maurizio Fava, MD



Dawn F. Ionescu, MD



Christopher J. McDougle, MD



Ranna Parekh, MD



Franziska Plessow, PhD



David H. Rubin, MD



Ronald Schouten, MD, JD



Mai Uchida, MD

Ammon-Pinizzotto Gift Names Center for Women's Mental Health



Carol A. Ammon; MGH President, Peter L. Slavin, MD; and Marie E. Pinizzotto, MD, at the October 22 celebration of the Ammon-Pinizzotto Center for Women's Mental Health

“Psychiatry, at best, breaks even. Research grants hardly cover the cost, and training is a net loss. The department has managed, nonetheless, to launch and sustain some of the nation’s best programs through the glorious support of people like Carol Ammon and Marie Pinizzotto.”

—Jerrold F. Rosenbaum, MD

MATCH two successful women in the life sciences field with a world-renowned program in women's mental health and you have a recipe for innovative research and quality clinical care for women.

With an education in biology and business, Carol A. Ammon began work in the pharmaceutical industry as an associate scientist, rising to become president of DuPont Merck's Pharmaceutical Division. In 1997, she led a management team to purchase 37 pharmaceutical products. The group became known as Endo Pharmaceuticals. Dr. Marie E. Pinizzotto earned her medical degree from Jefferson Medical College in Philadelphia and completed her residency in obstetrics and gynecology at the Medical Center of Delaware. Following a decade in private practice, Dr. Pinizzotto became Endo's senior director of Global Safety and Pharmacovigilance.

Eventually, the two women turned their considerable energy toward the philanthropic goals of the Carol A. Ammon Foundation where Dr. Pinizzotto serves as president. The Ammon Foundation focuses on education and health care.

MEMBERSHIP IN THE LEADERSHIP COUNCIL

Both women learned about the incredible life-altering care that women were receiving at Massachusetts General Hospital through their participation in the MGH Leadership Council for Psychiatry, which they joined in 2008. Through the Leadership Council, they became aware of the work of the then-Center for Women's Mental Health, founded by Lee Cohen, MD.

Ms. Ammon was impressed with the center's work to better understand and report on the safety aspects of medications for pregnant women. From her ten years as a practicing physician,

Dr. Pinizzotto appreciated the center's attention to the mental health needs of women over the course of the reproductive cycle, especially during and after pregnancy. "Busy doctors and nurses are hard pressed to treat women with signs of postpartum depression, or other psychiatric conditions while tending to the physical needs of their patients. Even finding someone to refer the women to is difficult," Dr. Pinizzotto noted.

Dr. Pinizzotto and Ms. Ammon felt that supporting Dr. Cohen's work was not only a perfect fit but also absolutely imperative.

A GLOBAL LEADER IN WOMEN'S MENTAL HEALTH

The center, founded in 1989 by Dr. Cohen, the Edmund and Carroll Carpenter Professor of Psychiatry at Harvard Medical School, is a global leader in women's mental health research and clinical care. It is part of the world-renowned Department of Psychiatry at Mass General which has been named the number one psychiatry department in 17 of the past 20 years by *U.S. News and World Report*.

The center began as a clinical service for women seeking information about using psychiatric medications during pregnancy. Under the guidance of Dr. Cohen and colleagues, it has evolved to conduct research into psychiatric disorders often linked to female reproductive biology including postpartum depression, premenstrual syndrome, infertility, mood disturbances and issues relating to infertility, menopause and other women's mental health conditions.

"As clinicians taking care of both younger and older women, we are keenly aware of so many important areas where better answers are needed," says Dr. Cohen, who is known as one of the founders of the field of perinatal and reproductive psychiatry. The research published by the center informs mental health treatment for women around the globe.

Among the research projects and programs to be supported by Ms. Ammon and Dr. Pinizzotto are a long-term study of children whose mothers used psychiatric medications during pregnancy, a study to identify genes that influence postpartum psychosis and a study of women veterans with post-traumatic stress syndrome. "The ability to support this work will set new standards for the care of women," Ms. Ammon says.

PHILANTHROPY FOCUSED ON HEALTH AND EDUCATION

Both Ms. Ammon and Dr. Pinizzotto now make philanthropy a priority. Ms. Ammon serves on the Board of Trustees at the University of Delaware where a foundation grant contributed to the construction of the new College of Health Sciences Complex. She also served as a trustee and chairman of the board of Christiana Care Health System and is a member of the Harvard Business School Healthcare Advisory Board.

In addition to her role as president of the Carol A. Ammon Foundation, Dr. Pinizzotto is a member of the board of Eisenhower Medical Center in Rancho Mirage, Calif., and a trustee of Christiana Care Health System where endowed chairs are named in her honor. She is on the board of the Multiple Myeloma Research Foundation and sits on the President's Leadership Council of the University of Delaware and the President's Leadership Council at Jefferson Medical College. She is a member of the Visiting Committee for Hematologic Oncology at Dana-Farber Cancer Institute.

Philanthropy, as exemplified by Dr. Pinizzotto and Ms. Ammon, plays a critical role in funding psychiatric care and research at Mass General, said Psychiatrist-in-Chief Jerrold F. Rosenbaum, MD, at the Oct. 22, 2015 naming celebration of the Ammon-Pinizzotto Center for Women's Mental Health. "Psychiatry, at best, breaks even. Research grants hardly cover the cost, and training is a net loss," he says. "The department has managed, nonetheless, to launch and sustain some of the nation's best programs through the glorious support of people like Carol Ammon and Marie Pinizzotto." He also praised Dr. Cohen as "a pioneering clinical researcher, committed teacher and mentor who has fostered the growth of the next generation of clinician experts and clinical researchers in this area."



MINDSCAPES

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CHIEF OF PSYCHIATRY
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WAYS TO GIVE

Bequests have provided vital support throughout Mass General's history. You too can remember the hospital in your estate plan and create a legacy to advance medicine. Call the Office of Planned Giving at (617) 726-2200 for more information on how to include Mass General in your will.

(Continued from page 1)

infusions were used (the first three at a lower dose; the second three at a higher dose). After receiving the biweekly infusions over three weeks, seven out of 12 patients who had all six infusions improved on depression scales. All but one experienced fewer, or no, suicidal thoughts. A more rigorous follow-up trial at Mass General will randomize patients to receive ketamine or a placebo.

On average, the anti-depressant effects of ketamine last no longer than 3 to 7 days after an infusion, Dr. Cusin reports. Short-term side effects, such as dizziness, nausea or disembodied feelings, disappear quickly. However, ketamine can be addictive for some patients, and long-term effects are not yet known. The infusions are not covered by insurance and require costly, skilled administration and observation.

Another method of administering ketamine is via nasal spray. While the dose of the drug in this form is less potent, it is a much simpler and less costly treatment alternative for the clinical setting. After the dose is carefully tailored for effectiveness, patients are monitored by experienced clinicians for the first few administrations and then continue the treatments at home.

Questions abound. Exactly how does ketamine work? What's the best dose? Can its antidepressant effect be predicted or extended?

New information will continue to be explored at Mass General. An important multicenter trial led by Mass General and sponsored by the National Institute of Mental Health will compare four different doses of ketamine with placebo. And results from an ongoing Mass General study using neuroimaging before and after treatment may shed light on how ketamine affects brain circuitry.



Two small devices positioned on either side of the forehead are used for a session of near-infrared light therapy (NIR), which is one of several new therapies being tested for treatment-resistant depression at Mass General.

NEAR-INFRARED LIGHT: VISIBLE EFFECTS

Light, whether through the longer days of summer or the rays emitted by phototherapy boxes, has long been associated with an improvement in mood. Another line of research in depression treatment at Mass General involves the study of near-infrared (NIR) light, one of several new therapies aimed at stimulating the brain.

“Major depressive disorder is associated with an abnormal energy state and lowered activity in the brain,” explains Paolo Cassano, MD, PhD, a staff psychiatrist at the MGH Depression

Program. For example, the amygdala, a deep brain repository for memories stamped by strong emotions like fear and anger, tends to be overactive when these emotions are triggered. Additionally, the amygdala tends to disconnect and communicate less with the prefrontal cortex, which is responsible for high-level thought and attention.

“Within one day, the severity of symptoms may be cut in half. People say, ‘I don’t feel the weight of the world on my shoulders. I don’t feel like killing myself anymore.’ Their thought processes shift, they’re not in pain, and they’re better able to cope.”

– Cristina Cusin, MD

Many treatments for depression are believed to help rebalance brain circuitry, partly by controlling overactivity in deeper regions. Yet widely used treatments like antidepressants can have significant side effects. Early research suggests that in some people NIR may help ease depression, tamp down anxiety, and strip away mental fogginess with minimal side effects.

A small double-blinded study led by Dr. Cassano, and recently presented at the 2016 meeting of the Society of Biological Psychiatry in Atlanta, compared the use of NIR light therapy with a mock or “sham” technique that mimicked it. Treatments were given biweekly for eight weeks. During 20-30 minute sessions, a device about the size of a cell phone was placed on either side of a patient’s forehead at spots that correspond to two areas in the prefrontal cortex. Although near-infrared light is invisible, patients wore goggles to protect against any possible eye damage.

Side effects, such as insomnia or irritability, were minor and transient. Long-term side effects are unknown. Patients reported feeling calmer, more focused, energetic and optimistic, Dr. Cassano says. Two-thirds of the group receiving NIR, versus one-third of the group receiving sham treatment, improved on depression scores. Among those who responded to NIR, half reported improved moods within two weeks, and all experienced improvement within six weeks. The study did not show how long effects would last.

A two-site study at Mass General and Mount Sinai Hospital in New York will compare two different types of NIR to determine whether continuous light or pulsed light is more effective in relieving depression. Animal models suggest that pulsed light works better.

Ketamine in nasal form is used clinically at Mass General, and NIR will be available on a limited basis with the opening of a photobiomodulation clinic in the fall of 2016. But before any novel treatment for depression becomes mainstream, rigorous research must be conducted to prove that it is safe and effective. Studies to help predict who might respond, and whether to use these therapies alone or combined with other treatments, are needed, too. At Mass General, this essential work is already underway.

MGH Psychiatry Out and About

THE INAUGURAL SUSAN N. SWEENEY PSYCHIATRY GRAND ROUNDS LECTURE



Jerrold F. Rosenbaum, MD; Stacy Sweeney, EdD; Carlos A. Zarate, Jr., MD

THE INAUGURAL GEORGE J. ROSENBAUM, MD PSYCHIATRY GRAND ROUNDS LECTURE



Arlene Neiditz; Lidia Rosenbaum; Eleanor Caplan; Donna B. Greenberg, MD; Daniel Neiditz; Linda Busch; Jerrold F. Rosenbaum, MD; Peter L. Slavin, MD

PEDIATRIC PSYCHOPHARMACOLOGY COUNCIL MEETING



Gagan Joshi, MD and Joseph Biederman, MD



Deborah Robinson and son Truman Mitchell

LEADERSHIP COUNCIL FOR PSYCHIATRY LUNCHEON, NEW YORK CITY



Lee S. Cohen, MD and Jeanne Andlinger



Ellen B. Braaten, PhD; Jerrold F. Rosenbaum, MD; Valerie Post

ENDOWMENT FOR THE ADVANCEMENT OF PSYCHOTHERAPY 2016 LEADERSHIP IN MENTAL HEALTH AWARD



Kathleen H. Ulman, MD and Leonard Campanello, Chief of Police, Gloucester, Massachusetts

DINNER IN HONOR OF DANIEL A. GELLER, MD HOSTED BY MICHELE AND DAVID MITTELMAN



David R. Mittelman; Michele H. Mittelman; Daniel A. Geller, MD; Maurizio Fava, MD; Sabine Wilhelm, PhD; Jerrold F. Rosenbaum, MD



SAVE THE DATES

Psychiatry Academy Patient and Family Education Series

September 24, 2016:

Child and Adolescent Psychiatry

Directed by Timothy Wilens, MD

*Sponsored by the
Joan and Leonard Engle
Family Foundation*

October 8, 2016:

Substance Use Disorders and Addiction

Directed by Eden Evins, MD, MPH

*Sponsored by Elissa Freud and
Steven Willis*

November 5, 2016:

Schizophrenia Education Day

Directed by Oliver Freudenreich, MD

*Sponsored by an Anonymous Donor
in honor of Cori Cather, PhD, and
Oliver Freudenreich, MD*

All sessions are held at the Starr Center,
Richard Simches Building, 185 Cambridge Street,
Charles River Plaza, Boston

Faculty Books

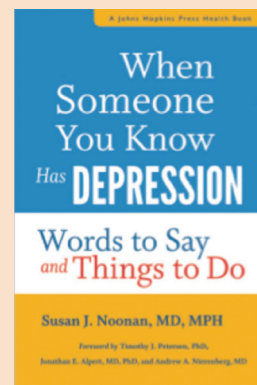
WHEN SOMEONE YOU KNOW HAS DEPRESSION: WORDS TO SAY AND THINGS TO DO

by Susan J. Noonan

with forewords by Timothy J. Petersen, PhD; Jonathan
E. Alpert, MD, PhD; and Andrew A. Nierenberg, MD

Johns Hopkins Press, 2016

In *When Someone You Know Has Depression*, Dr. Susan J. Noonan draws on first-hand experience of the illness and evidence-based medical information. As a physician she has treated, supported, and educated those living with – and those caring for – a person who has a mood disorder. She also has lived through the depths of her own mood disorder. Here, she has written a concise and practical guide to caring for someone who has depression or bipolar disorder. This compassionate book offers specific suggestions for what to say, how to encourage, and how to act around a loved one – as well as when to back off.



THE BIPOLAR II DISORDER WORKBOOK: MANAGING RECURRING DEPRESSION, HYPOMANIA, AND ANXIETY

by Stephanie McMurrich Roberts, PhD;

Louisa Grandin Sylvia, PhD;

Noreen A. Reilly-Harrington, PhD

Newharbingerpublications, Inc., 2014

Bipolar disorder II differs from bipolar disorder I in that sufferers may never experience a full manic episode, although they may experience periods of high energy and impulsiveness (hypomania), as well as depression and anxiety. Written by an accomplished team of bipolar experts, the guide is designed to help people manage the recurring depression, hypomania, and anxiety that can arise as a result of bipolar II. The accessible and engaging workbook format combines evidence-based cognitive behavioral therapy (CBT), dialectical behavioral therapy (DBT), and other mindfulness-based exercises to help people manage their emotions, track progress, and ultimately live happier and more productive lives.

