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Specialists in the Brain Stimulation Program in Psychiatry at Brigham and Women’s Hospital are studying and offering numerous techniques to treat a broad range of refractory psychiatric conditions, including depression, obsessive compulsive disorder, schizophrenia, apathy, and other conditions.

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Using an innovative collaborative care model, Brigham and Women’s Hospital psychiatrists are working with primary care physicians, pharmacists, social workers, and health counselors to treat patients with opioid dependence in the primary care setting.

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Psychiatrists at Brigham and Women’s Hospital and Brigham and Women’s Faulkner Hospital work closely with obstetricians, gynecologists, maternal-fetal medicine specialists, and neonatal intensive care specialists to deliver personalized care for women with depression throughout all stages of pregnancy.

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Together with infectious disease specialists, Brigham and Women’s Hospital psychiatrists are focusing on high levels of psychiatric illness, poor adherence to medication, and cognitive changes among patients with HIV/AIDS.
Brain Stimulation Benefits Patients with Intractable Psychiatric Disorders

In the Department of Psychiatry’s Brain Stimulation Program, Brigham and Women’s Hospital (BWH) psychiatrists, neurosurgeons, neuropsychologists, psychologists, and other specialists collaborate to provide advanced brain stimulation approaches, including deep brain stimulation, for patients with refractory psychiatric disorders.

Led by Arielle D. Stanford, MD, the Brain Stimulation Program within the Department of Psychiatry at Brigham and Women’s Hospital studies and offers numerous techniques to treat a broad range of refractory psychiatric disorders, including depression, obsessive compulsive disorder (OCD), schizophrenia, apathy, and other conditions.

“We are striving to improve function and long-term outcomes among patients with difficult-to-treat psychiatric disorders,” said Dr. Stanford.

Brain stimulation techniques offered by Program specialists involve varying levels of invasiveness and include:

- **Transcranial magnetic stimulation (TMS)** – This treatment applies magnetic pulses to targeted areas of the brain. It can feel like a mild tapping or cause tingling sensations. TMS does not require sedation or anesthesia and does not cause confusion or memory loss. TMS is being offered for the treatment of depression, schizophrenia, and apathy, and is being evaluated for other conditions as well. Specialists in the Program are identifying new TMS treatment targets and are using imaging to guide the localization of TMS. In addition, a new clinical trial evaluating this therapy for use in patients with apathy related to Alzheimer’s disease will open at BWH in early 2013;

- **Vagus nerve stimulation (VNS)** – Originally approved for the treatment of epilepsy, VNS has been shown to offer benefits in patients with depressive symptoms. A pulse generator delivers electrical pulses to the vagus nerve via a lead wire. Program specialists also are collaborating with other BWH researchers to study the physiological effects of VNS to treat other morbidities associated with depression;

- **Electroconvulsive therapy (ECT)** – Advances in ECT, which uses electrical current to induce a controlled therapeutic seizure, have helped to reduce side effects for this highly effective treatment for severe depression, bipolar disorder, and schizophrenia. Common side effects of ECT treatment, performed under general anesthesia, include headache, gastrointestinal upset, and muscle aches. Some patients also experience memory loss, which can be minimized with the use of unilateral ECT and changes in the dosing schedule;

- **Deep brain stimulation** – BWH is among few sites nationwide to offer deep brain stimulation (DBS) for psychiatric disorders, including severe depression, intractable OCD, and other conditions. Psychiatrists, neurologists, functional neurosurgeons, neuropsychologists, psychologists, and other specialists with expertise in DBS collaborate to evaluate patients with refractory psychiatric conditions and determine whether DBS is appropriate. Travis S. Tierney, MD, PhD, a BWH neurosurgeon who is fellowship trained in functional neurosurgery, performs DBS using detailed magnetic resonance images to coordinate targets. Microelectrode mapping and tracking of electrical cellular activity guide placement of probes, and testing of the system in the OR ensures that probe placement is not creating adverse effects.

Advancing Research in Brain Stimulation

Research in the Brain Stimulation Program is ongoing to identify additional brain circuits associated with psychiatric conditions, including those mentioned above. “Since not every patient responds to the same treatment dose, new paradigms, including treatment targets, need to be developed in order to improve treatment response and reduce dysfunction,” said Dr. Stanford.
Case Study: DBS for Intractable Depression

Background:
A 47-year-old female patient with a history of anxiety and severe treatment-resistant depression was referred for deep brain stimulation (DBS) treatment. The patient’s symptoms began in her late teens/early 20s primarily as anxiety and agitation and progressed to thoughts of suicide, accompanied by severely depressed mood and a low energy state. She was ultimately hospitalized after having a minimal response to tricyclic antidepressants and benzodiazepines. Following initial successful electroconvulsive therapy (ECT), her depression remitted and she was released from the hospital. She continued to battle with anxiety, however, and her depression eventually relapsed. She was hospitalized multiple times with decreasing depression-free intervals after ECT and has been trialed on many different classes of antidepressants, mood stabilizers and anxiolytics.

Approach:
The patient has been followed for many years by Brigham and Women’s Hospital psychiatrist and Medical Director of the Center for Medical Depression, Jane L. Erb, MD, whose primary concern was the failing of all forms of standard therapy. Dr. Erb referred the patient for evaluation for DBS of the subcingulate gyrus.

Although this experimental procedure is not covered under Medicare, BWH approved bilateral DBS as a novel therapy compassionate care exemption. The patient underwent the procedure during the summer of 2012.

Note: Deep brain stimulation of the subcingulate cortex was developed as a novel therapy for treatment-resistant depression. Approximately 40 patients have undergone the procedure worldwide. The initial response rate is approximately 60 percent with the time-to-response occurring over several weeks.

Follow up:
The patient made an uneventful recovery from surgery. The stimulators were activated two weeks after surgery. No adverse stimulation effects were noted. Over the course of the first three postoperative months, the patient’s Hamilton Depression Index has improved, from 26 to 15. Although she still has some elements of anxiety, her mood and energy levels have improved as well as her daily function. She was recently able to return to work full time after being on disability leave for depression.
Addressing Opioid Dependence in the Primary Care Setting

Brigham and Women’s Hospital (BWH) psychiatrists collaborate with primary care physicians, pharmacists, social workers, and health counselors to treat patients with opioid dependence in the primary care setting.

Using an innovative collaborative care model, BWH psychiatrist Joji Suzuki, MD, is addressing opioid dependence in the primary care setting. His initiative, which is funded through the Harvard Medical School Center for Primary Care, is one of few of its kind in the nation and incorporates a primary care physician, psychiatrist, pharmacist, social worker, and health counselors to treat opioid dependence.

“The vast majority of patients who could benefit from treatment for opioid addiction are simply not receiving the care that they need. This issue is compounded by a dramatic increase in the incidence of prescription opioid dependence over the past 15 years,” said Dr. Suzuki. “Our model improves access to care, is much less stigmatizing for patients than addiction clinics, and strengthens the relationship between patients and their medical providers.”

Within the past year, the integrated team led by Dr. Suzuki has treated 25 patients with opioid dependence in the Phyllis Jen Center for Primary Care at BWH. The team uses buprenorphine, a high affinity partial opioid agonist. The drug is an effective alternative to methadone, which carries cardiac toxicities, has a high overdose risk, and must be administered in a designated addiction clinic. Similar models to address opioid addiction are embedded within the BWH Center for Fetal Medicine and Prenatal Genetics (see Page 5 for more information) and the BWH HIV Program (see Page 6 for more information).

While buprenorphine became available approximately 10 years ago, it is not widely prescribed by physicians today due to lack of training and experience with the medication and with substance abuse in general. Dr. Suzuki leads training for physicians in the use of buprenorphine, a requirement to be able to prescribe the medication. This will improve access for patients.

“As patients with opioid dependence frequently utilize health care services, including hospital emergency rooms, and account for a high percentage of cases of unintended drug overdose, the need to address this dependence is becoming more widely recognized,” said Dr. Suzuki. “An integrated care model within a primary care setting offers an effective way to treat these patients, improve longer-term outcomes, and reduce costs.”

Joji Suzuki, MD
Psychiatrist

Lori Wiviott Tishler, MD
Medical Director, Phyllis Jen Center for Primary Care

Compared with heroin and cocaine, prescription opioids are the largest contributor to the increase in drug-induced deaths.
Personalized Care for Depression and Anxiety during Pregnancy: From preconception through the postpartum period

Psychiatrists at Brigham and Women’s Hospital (BWH) work with obstetricians, gynecologists, maternal-fetal medicine specialists, and neonatal intensive care specialists to deliver personalized care for women with depression throughout all stages of pregnancy.

The Women’s Mental Health Division, part of the BWH Department of Psychiatry, delivers personalized services for women with depression and anxiety who are pregnant, postpartum, or planning a pregnancy. Psychiatrists in this Division, led by Laura Miller, MD, provide specialized support for one of the largest women and newborn programs in the country.

“With extensive expertise and close interdisciplinary collaboration with mental health providers, OB/GYNs, neonatal intensive care specialists, and other specialists, we employ an innovative and balanced approach for optimal health and safety for the mother, the newborn, and other family members,” said Dr. Miller.

The Women’s Mental Health Division incorporates a wide range of preconception and perinatal mental health programs through its Women’s Mental Health Service, Infertility Mental Health Clinic, Reproductive Psychiatry Consultation Service, and services at ambulatory care locations. Together, these programs offer diagnostic evaluation, preconception planning, inpatient consultation and stabilization, and psychopharmacologic and psychotherapeutic treatment for women throughout pregnancy and the postpartum period, as well as women undergoing infertility treatment.

Preconception Planning
Women with a history of mental illness and a desire to prevent exacerbation of depression, panic disorder, bipolar disorder, obsessive compulsive disorder, and other psychiatric conditions during or after pregnancy participate in preconception planning sessions with a women’s mental health psychiatrist at BWH.

Psychiatrists work with these patients to identify physical and psychological risk factors, such as vulnerability to hormonal fluctuations, nutritional deficiencies, lack of physical exercise, pain, sleep interference, cognitive styles, and maladaptive interpersonal patterns, that may contribute to risk of developing perinatal depression and other psychiatric disorders (Psychiatric Clinics of North America 34:53-65, 2011). A treatment plan is then developed based on the modifiable risk factors and may include specific psychotherapies, medications, and lifestyle modifications. (Expert Rev Obstet Gynecol 5(4):421-35, 2010).

Weighing the Risks and Benefits of Antidepressants during Pregnancy
Psychiatrists in the Women’s Mental Health Service also work with the patient and the patient’s OB/GYN to address depression and anxiety and weigh the risks and benefits of treatment during pregnancy using an evidence-based approach. They consult the latest findings from prospective controlled studies on the use of antidepressants during pregnancy and studies regarding the risks of untreated severe depression and anxiety to help patients make informed decisions regarding treatment.

Screening for Bipolar Disorders during Pregnancy
Researchers in the Reproductive Psychiatry Consultation Service have initiated a pilot study to screen women for bipolar disorder during pregnancy in order to more accurately identify patients with this disorder and appropriately treat them.

“Because the treatments for depression and bipolar disorder are vastly different, it is important to distinguish between patients exhibiting depressive symptoms related to unipolar depression and those related to bipolar disorder,” said Leena P. Mittal, MD, Director of the Reproductive Psychiatry Consultation Service. “In addition, patients with bipolar disorder are at very high risk of developing severe mood disorders, including psychosis, during the postpartum period. It is critical that these severe and emergent conditions are addressed before a patient is discharged home with a newborn.”

Analysis of data from the surveys will help researchers determine whether all women who are pregnant should be screened for bipolar disorder, or only those who screen positively for depression.

Addressing Substance Abuse during Pregnancy
Psychiatrists in the Service also work to treat pregnant women with addiction within the patient’s prenatal care setting. A new pilot program is designed to engage pregnant women with opioid addiction in treatment. Buprenorphine, a newer agent, is provided, along with additional services to address co-existing issues related to poor lifestyle habits and other behaviors that can be detrimental to the health of the mother and the fetus.

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Improving Medication Adherence, Managing Substance Abuse, and Evaluating Long-term CNS Effects in HIV/AIDS

Together with infectious disease specialists, psychiatrists at Brigham and Women’s Hospital (BWH) are focusing on high levels of psychiatric illness, poor adherence to medication, and cognitive changes among patients with HIV/AIDS.

BWH psychiatrist John Grimaldi, MD, is working with infectious disease specialists at BWH to manage psychiatric illness and improve outcomes in patients with HIV/AIDS.

“Patients with HIV and AIDS have a much higher prevalence of psychiatric illness, including depression, anxiety disorders, post traumatic stress disorder (PTSD), dysthymia, and substance abuse, compared with the general population,” said Dr. Grimaldi. “By managing mental health issues within the BWH HIV Program, we are hoping to improve care for these patients.”

Antiretroviral Medication Adherence

Dr. Grimaldi collaborated with BWH psychiatrist Joji Suzuki, MD, BWH fellow Siu Ping Chin Feman, MD, and BWH medical social worker Susan Larrabee, LICSW, to develop a brief training program in motivational interviewing skills and techniques for BWH infectious disease specialists. Through this program, the infectious disease specialists are learning to enhance patients’ motivation to engage in health-promoting behaviors, such as taking antiretroviral and antidepressant medications as prescribed and reducing alcohol and substance use.

“Optimal health and outcomes for patients with HIV/AIDS, as well as prevention of the spread of HIV infection, are dependent on patients’ compliance with antiretroviral medications,” said Dr. Grimaldi. “In the United States, only about 28 percent of all patients with HIV/AIDS are adequately adhering to their medications, so we are investigating ways to change patient behaviors in this area.”

Following the training with the specialists, monthly meetings are held to sharpen skills learned in the program. In early 2013, the psychiatrists will begin to look at the effectiveness of the training based on the number of infectious disease specialists implementing the techniques. Ultimately, they will review outcomes based on patient adherence to prescribed medications.

Substance Abuse Treatment Integration

Brigham and Women’s Hospital is among few sites to co-locate and integrate a substance abuse program within an HIV clinic. BWH psychiatrists and infectious disease specialists are trained in the use of buprenorphine and naloxone for the treatment of opioid dependence in patients with HIV/AIDS. Substance abuse counselors in the BWH HIV Program clinic offer individual and group sessions for alcohol and other drug addictions as well.

“Patients with HIV/AIDS are already burdened by the disease, so providing treatment for mental health conditions and substance abuse within the patients’ primary treatment setting eliminates obstacles to care,” said Dr. Grimaldi.

Understanding the Effect of HIV on the Central Nervous System

BWH psychiatrists are looking at early clues of cognitive changes in patients with HIV/AIDS. Low-grade neuroinflam-
matory response initiated by HIV is often amplified and sustained by co-factors, such as aging, Hepatitis C (a common co-infection among patients with HIV), substance use, and cerebrovascular disease. This response can result in neurocognitive and functional impairment and, in some cases, shortened survival.

“While incidence of dementia has declined since the introduction of combination antiretroviral medications, prevalence of milder forms of cognitive impairment has remained constant or even expanded,” said Dr. Grimaldi. “It’s important to recognize early cognitive changes and to address these conditions early in the course of illness.”

Personalized Care for Depression and Anxiety during Pregnancy: From preconception through the postpartum period . . . continued from page 5

Neonatal Intensive Care Unit Collaboration
The Reproductive Psychiatry Consultation Service offers specialized care for new mothers with critically-ill babies, a population at particularly high risk for depression and post traumatic stress disorder, through a collaborative relationship with neonatal intensive care specialists, nurses, and social workers. The Service is implementing a new screening program for depression and acute stress disorder to identify mothers with depression and anxiety.

Research in Fetal Programming
Jill M. Goldstein, PhD, Director of Research for Women’s Mental Health and Gender Neurobiology in the Department of Psychiatry is leading the investigation of fetal programming of sex differences in the incidence of psychiatric disorders and numerous comorbidities.

The team has identified prenatal factors and conditions that are associated with risk for major depressive disorder and psychoses and contribute to explaining sex differences in these disorders in adulthood. Clinical, epidemiologic, and basic science researchers are collaborating in a wide range of studies in this area.

“By looking closely at pregnancy and fetal development, we are gaining a better understanding of sex differences in the etiology of major depressive disorder and the likelihood of offspring to develop this condition,” said Dr. Goldstein. “Ultimately, through these discoveries, we will be able to contribute to developing novel clinical treatments for women and men with depression, and eventually create sex-specific strategies for depression prevention.”