Hopkins Brain Wise
THE NEWSLETTER OF THE JOHNS HOPKINS DEPARTMENT OF PSYCHIATRY AND BEHAVIORAL SCIENCES
JOHNS HOPKINS MEDICINE
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Mood Disorders Precision Medicine Center Elevates Research and Personalized Care

Johns Hopkins psychiatrists and colleagues mine genetic clues and lab results, and use digital assessments to evaluate patients and provide individualized treatments.

"Our goal is to find causal or etiologic clues that will ultimately lead to new, urgently needed, targeted drugs."
—FERNANDO GOES

Mood disorders are far more prevalent than one might imagine, says psychiatrist **Fernando Goes**, a faculty member of the Johns Hopkins Department of Psychiatry and Behavioral Sciences. Regardless of socioeconomic status, 21.4% of adults in the U.S. experience a mood disorder at some point in their lives, according to The National Alliance on Mental Illness. The most common are depression and bipolar disorder.

Goes and psychiatric epidemiologist **Peter Zandi** aim to change the status quo by advancing research and care at the recently established Johns Hopkins Mood Disorders Precision Medicine Center. Working alongside colleagues, Goes and Zandi probe genetic clues, lab results and digital phenotyping — using smart devices that track markers of depression and anxiety — to assess patients.

Then, based on their findings, they choose targeted medications and provide psychiatric counseling. With this model, Zandi and Goes believe they're better positioned to ascertain which treatments are most likely to be effective for each patient. They envision a time when discoveries based on a person's risk for mood disorder will lead to treatments as targeted as immunotherapies are for patients with cancer.

"There is a clear need for a comprehensive, interdisciplinary approach to the study and treatment of mood disorders, and we are leveraging the strengths of our current programs in the Department of Psychiatry to do so," says Goes.

Clinicians and researchers at the Mood Disorder Center work to advance those efforts. The workup begins with giving patients a basic questionnaire lasting no longer than a few minutes. Once completed, the results are collected at regular clinical visits and made available to providers as part of the clinical record. "In a subset of patients, we also pilot more intensive digital assessment technologies, including mobile mood measurements, basic actigraphy (body movement) and sleep measurements," Zandi says.

Psychiatry researchers at the center then tap into interdisciplinary expertise available throughout Johns Hopkins Medicine, such as that in geriatric psychiatry. "We integrate research with clinical care in a dynamic manner, central to a learning health care system that will yield novel scientific insights," says Goes. "This approach makes us fully competitive for NIH research funding, while providing high-quality, evidence-based care to the local and referral community."

With these efforts, Zandi and Goes say they're inching closer to identifying a person's risk for mood disorders. "Our goal," says Goes, "is to find causal clues that will ultimately lead to new, urgently needed, targeted drugs."

The team also envisions the creation of a biobank with human tissue and blood specimens that will form part of "an integrated research mission and that will ultimately become available to all researchers in the Johns Hopkins community," says Zandi. "As part of the biobank, we will establish a clinical workflow to approach all patients during routine care and seek consent to collect a biological sample for biomarker discovery."

Perhaps the most compelling aspect of this approach, says Goes, is that a more targeted treatment of mood disorders will not only provide relief for patients suffering with symptoms, but might also significantly reduce the risk of suicide. ■

Learn more at hopkinsmedicine.org/psychiatry/specialty_areas/moods. To request an appointment, call 410-955-5212.

A Four-Pronged Approach to Treating Mood Disorders

1. Enhance digital assessment (phenotyping) of mood and related disorders.
2. Create an active "learning" biobank available to the broader research community.
3. Integrate and strengthen collaborative ties across the broad research and clinical community at Johns Hopkins.
4. Provide opportunities for trainees to become involved in mood disorders research.

FROM THE DIRECTOR

Jimmy Potash, M.D., M.P.H.

Greetings and Happy New Year!

The 2021–2022 academic year got off to a good start when we learned that, for the second consecutive year, we were ranked the nation's #1 hospital for psychiatry by *U.S. News & World Report*. The recent email below in praise of our Women's Reproductive Mental Health fellow helps to explain why that distinction is merited:

I have been a patient of Dr. ***Julia Riddle****'s for the past two years. I'm writing to commend her care, expertise, brilliance and commitment to her patients … When I first met her, I was at a very low point in my life — anxious, depressed and lost. With no "road map" to follow, I reached out … and got connected to Dr. Riddle. Little did I know that two years later, I would feel this bond and amazing care I had never experienced within the psychiatric world ... I can't begin to tell you the difference I have felt being under her care. I know I can always reach out to her, and even with her ridiculously busy schedule, I will receive a response within 24 hours … She has shown me steps to take in my mental wellness and made me realize attributes I never thought I had. I have come so far and know I have, with her guidance, a future of finding the "best me"… With sun on my back and a bright future ahead, I'm thanking Dr. Riddle for making this possible.*

Dr. Riddle practices what we preach: a deep commitment to our patients — a defining feature of Johns Hopkins psychiatrists. Also central to our mission is creating next-generation approaches to care. In that vein, we were thrilled to learn recently that Dr. **Matt Johnson** was awarded a National Institutes of Health (NIH) grant to test psilocybin as a treatment for smoking addiction — remarkable for its being the first NIH grant for a treatment study of a classic psychedelic in more than 50 years! This constitutes a real sea change, and is an important stamp of approval for the scientific legitimacy of this program of investigation.

Jimmy Potash, M.D., M.P.H.
Henry Phipps Professor of Psychiatry and Behavioral Sciences

Department Director and Psychiatrist-in-Chief, Johns Hopkins Medicine

RESEARCH

Nicola Cascella and colleagues explore the benefits of deep brain stimulation for patients with treatment-resistant schizophrenia.

Deep Brain Stimulation Used for Parkinson's Tremors May Also Quell Hallucinations for Patients with Schizophrenia

As many as one-fifth to one-half of patients with schizophrenia have symptoms that are resistant to treatment, says psychiatrist **Nicola Cascella**. A decade ago, Cascella began looking into the use of deep brain stimulation (DBS) for neuropsychiatric conditions other than Parkinson's disease, treatment-resistant depression or obsessive-compulsive disorder. Now, he and his colleagues have what they've deemed promising results from the first patient with schizophrenia they have treated in this manner.

In a letter to the editor of *Biological Psychiatry*, Dr. Cascella and colleagues described what is believed to be the first use of DBS in a patient with treatment-resistant schizophrenia in the United States. DBS involves the implantation of a pacemaker-like device into the chest, connected to electrodes placed in specific parts of the brain. When activated, the device emits electric current to modulate communication among brain cells. For patients with schizophrenia, the team determined that the best approach is to target the substantia nigra pars reticulata (SNr) — an area in the basal ganglia in the midbrain that serves as an important processing center of information from cortical areas.

The patient implanted with the DBS device is a 35-year-old woman with treatment-resistant schizophrenia and obsessive-compulsive disorder. She experienced persistent auditory and visual hallucinations, thought broadcasting (a belief that others can hear one's thoughts), and delusions of being persecuted, which had emerged when she was 19. Antipsychotic medications, including clozapine, failed to significantly reduce her symptoms.

Activating the two DBS leads placed in the SNr produced quick resolution of the hallucinations. However, unbeknownst to the patient, the team turned the system off during the initial activation visit to see what would happen. At that point, the patient reported that the voices were coming back.

"We did some video recording during that session, and it was quite amazing to see how the patient responded to this stimulation," Cascella says.

DBS allowed the team to adjust the patient's medication regimen, including decreasing the dose of the antipsychotic drug haloperidol from 30 milligrams to 10 milligrams and discontinuing the anticonvulsant drug oxcarbazepine. After 24 weeks of stimulation, the patient's score on the Brief Psychiatric Rating Scale decreased from a total of 42 at baseline to 20. Ratings for hallucinations decreased from 7 (extremely severe) to 1 (not present), while ratings for unusual thought content and suspiciousness each decreased from 6 (severe) to 1. After a year and half from the onset of stimulation, the patient remains stable, without hallucinations or delusions.

> The hope is that the next generation of DBS devices can recognize electrical markers in the brain associated with hallucinations and activate before anything happens.

The team's members plan to study the treatment in two additional patients to complete this first pilot. They're also applying for a grant from the National Institute of Mental Health to trial a different DBS device that both delivers current and records the electrophysiological field of the neurons being stimulated. Ideally, this could help identify a biological marker to know whether or not patients are experiencing hallucinations, Cascella says.

The hope is that the next generation of DBS devices can recognize electrical markers in the brain associated with hallucinations and activate before anything happens. "That would be the ultimate goal," Cascella says. ■

Support for Young Adults Grappling with Mental Health Struggles

Young adulthood presents a time of rapid change, with many transitioning to and from college, entering the workforce and navigating interpersonal relationships. It's also a period when mental health conditions such as major depressive disorder or bipolar disorder are likely to arise, says psychiatrist **Jennifer Coughlin**, who, two years ago, assumed leadership of a consultation clinic that psychiatrist **Elizabeth Kastelic** started a decade ago for 18- to 35-year-olds at crossroads.

"It's not uncommon for young adults who are off at college, apart from their parents, to be struck with depressive episodes, and managing them with their psychiatrist is often helpful," Coughlin says. "But when it's a hard-to-treat mood episode, having the ability to consult with an expert and get a second opinion on the diagnosis and next steps in treatment can have a major impact in getting them efficiently and effectively back on their trajectory."

Through the clinic, Coughlin and psychiatric nurse practitioner **Ana Soule**, who joined the service this year, review records and conduct thorough evaluations to provide recommendations for patients and their families to take back to their psychiatrists. With their expertise in working with young adults, Coughlin and Soule not only can address questions about next steps in therapy or medication, but also guide them in navigating conversations with academic offices or employers.

"It's also very important in this age group to provide education, because it often is the case that these diagnoses are new to them," Coughlin says. "It's key to explain that these conditions are often very treatable. Even if they haven't responded to treatment early on in their course, we can provide expert guidance as to how to get to a more optimal response."

"We see a lot of young adults who are kind of bouncing around and trying various medications and treatments, and meanwhile, their life is stalled," adds Soule. "Identifying an accurate diagnosis and optimal treatment plan is really critical for getting them back on track and setting them up for a stable, successful adulthood."

Coughlin also directs the Young Adult Mood Disorders Inpatient Unit at The Johns Hopkins Hospital — a specialty service where patients receive care from attending physicians with expertise treating young adults with these conditions. A social worker dedicated to the unit is skilled in interfacing with colleges and universities, when a patient cannot attend classes. Clinicians also have experience in educating patients and their families about what it means to have a mood disorder, what to expect in a treatment plan, and how to effectively support the young adult patient.

The addition of Soule positions the clinic to offer more appointments, and to move toward adding other services in development. Through expanding the clinic, Coughlin and Soule aim to fill a gap in specialized services available to this young adult population, toward getting patients successfully back to health.

"Right now, mental health is in the spotlight," Soule says. "Being able to expand the number of appointments that we offer and the number of young adults that we're able to help is exciting, and we're happy to be spreading the word about our consultation program." ■

For more information or to refer a patient, email youngadultconsult@jhmi.edu.

A Comprehensive Approach to Treating Postpartum Depression

At The Johns Hopkins Hospital, certain patients with postpartum depression receive infusions of brexanolone, and are treated and monitored in the inpatient psychiatry unit.

If it were up to psychiatrist **Lauren Osborne**, postpartum anxiety would be as well known as postpartum depression (PPD). That's because postpartum depression symptoms, which may affect 1 in 7 new mothers, are "complicated to define, and, in fact, anxiety is just as prevalent but less well studied," says Osborne, director of the Johns Hopkins Center for Women's Reproductive Mental Health. The postpartum state can intensify both types of symptoms, leading to debilitating effects. "Irritability and lack of sleep exacerbate symptoms," she notes. "And, younger mothers appear to be more vulnerable to PPD than older ones."

There's reason for concern: 10% to 15% of all new birth mothers suffer with PPD symptoms annually, "and some women also have depression in pregnancy," says Osborne. Depression is the leading complication of childbirth. Left untreated, it can lead to severe consequences for both mother and child, including suicide and developmental problems for children. In addition to classic symptoms of depression, PPD can include severe anxiety, obsessions, guilt, self-blame and feeling overwhelmed. "For many women, giving birth during the pandemic has amplified those feelings," says Osborne.

At the Center for Women's Reproductive Mental Health, Osborne leads a team that conducts research into the causes of PPD — and provides the latest state-of-the-art treatment for the disorder. In research, she works closely with colleagues **Zachary Kaminsky** and **Jennifer Payne**, who together study epigenetic patterns — marks on DNA — that affect how genes act in psychiatric disorders, and have identified certain epigenetic patterns that predict risk for PPD. The team also works on allopregnanolone, a hormone that is a

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A Comprehensive Approach to Treating Postpartum Depression

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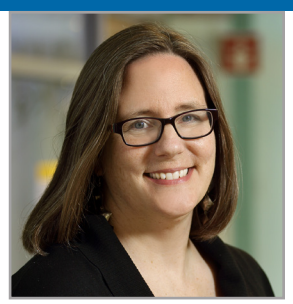
breakdown product of progesterone; Osborne's team has shown that low levels of this hormone early in pregnancy predict who will go on to develop PPD.

This last line of research is particularly pertinent to a new treatment the center is offering on Johns Hopkins inpatient units. The treatment uses the first drug ever approved by the FDA for PPD: brexanolone — a synthetic version of the hormone Osborne's team studies. Brexanolone, an intravenous infusion, works quickly to modulate brain excitability. The drug had a 70% response rate in initial clinical trials, says Osborne, though it also had a high placebo response rate. At Johns Hopkins, "many of the women we've treated with the drug have responded well," she notes.



Lauren Osborne

To Osborne's knowledge, the program has the added benefit of being the only one of its kind in the U.S. that offers the drug on a psychiatry unit, instead of a medical unit, so that patients are able to receive routine inpatient psychiatric care as well. Osborne hopes to collect patient outcomes data from this new program, and eventually incorporate biomarker research to help predict markers of response.

"PPD can be a major problem during the first year after birth," says Osborne. Women with multiples (twins or triplets) tend to suffer higher rates of depression, she adds. "It's incredibly important to connect with these patients, especially because PPD affects the partner and children as well."

While only a minority of women will be diagnosed with PPD, exhaustion following the birth of a baby remains a universal struggle (and can be linked to the development of PPD). In many other countries, says Osborne, care for the mother and extended family after a baby arrives is a priority: "The Australians have it down. They have family centers, where parents who have newborns are given the space to sleep. We have a long way to go to reach that point." But, Osborne is quick to add, staying attuned to — and ahead of — signs of PPD can prove transformative and lifesaving. ■

Learn more about The Johns Hopkins Center for Women's Reproductive Mental Health at ***wmdcbaltimore.org****.*

Watch epigenetic researcher Zachary Kaminsky in his lab describe his work to help predict PPD, suicide and other mental illnesses: ***bit.ly/PPDcare***

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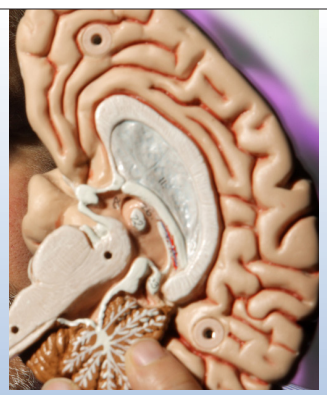

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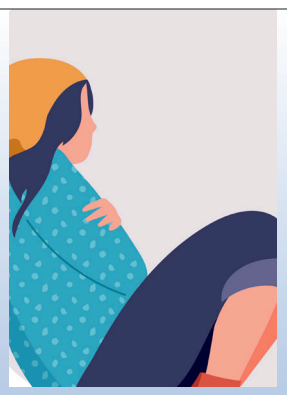

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