



**At the Broadway Center for Addiction, Kenneth Stoller, left, sees patients and mentors newly minted addictions psychiatrists Ann Ruble and Vinay Parekh.**

## A Medical Model to Treat Opioid Addiction—and Link Care

**A**t a time when some 2.2 million people in the United States are addicted to heroin or prescription painkillers and overdoses claim tens of thousands of lives every year, **Kenneth Stoller** feels the urgency.

As director of the Johns Hopkins Broadway Center for Addiction, he champions a structured yet compassionate approach to opioid use disorder—one that destigmatizes medication-assisted treatment. Last year, the center was cited by the U.S. Office of National Drug Control Policy for its successes. Now Stoller aims to fill in the gaps and help cement patients' gains nationwide.

Focusing on coordination with community physicians trained to provide buprenorphine in-office, Stoller wants to increase access to the comprehensive, tailored help offered by opioid treatment programs (OTPs) like the Broadway Center.

For two decades, as one of the nation's 1,400 OTPs, the center has offered adults with opioid use disorder methadone, buprenorphine or naltrexone maintenance therapy. But as The Johns Hopkins Hospital's ambulatory addiction treatment program, the center focuses more attention on provision of other services, like counseling and housing.

Notably, the center requires addictions counseling and participation in group classes. Only a few sessions may be necessary for stable patients, but more for those struggling with ongoing use. Instilling self-understanding and a hopeful attitude are key to helping clients.

To be sure, Stoller expects many to falter. But he favors a focus on learning opportunities over criti-

cism. "Once people understand what led them to veer off," he says, "they're more likely to choose a better track." He remembers one woman, greatly distraught about her relapse: "I told her she'd had an amazing self-discovery—a 'good' relapse. The message was that we believe she can succeed."

The center's adherence to counseling tops 60 percent. For most other centers offering psychosocial support, Stoller notes, literature reports around 25 percent adherence.

Still, a major problem surfaces as people seek care—a basic shortage of maintenance therapy. It troubles Stoller that many community physicians licensed to provide buprenorphine choose not to. A Maryland survey, for example, found that only 50 percent of 545 waived physicians prescribed it. Barriers to treating these patients are well-known. They include poor compliance with care and limited attendance at counseling.

Subtler things are also troubling; it can be hard for doctors not to take patients' dishonesty personally. "I try to help them understand that it's a symptom of substance use disorder—just as chest pain is a symptom of heart disease," he says.

Stoller believes there is great opportunity for OTPs to encourage buprenorphine prescribing by offering physicians support and improving the chance of a positive experience. "We can work through struggles together," he says. To streamline that help, he's created a collaborative model he calls Co-OP (Collaborative Opioid Prescribing), which makes OTP expertise available. Patients are concur-

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### Keeping Things Real

Robert Alston catapulted to success in the 1990s as a self-employed fashion designer. His high-profile clients included Patti LaBelle and Boyz II Men. But under the pressure to produce, Alston turned to cocaine and alcohol.

"Using" wasn't new. At 14, he'd smoked marijuana "to escape the reality of being molested and taking on more responsibility." Arrested in 1986, Alston struggled with drug dependence before hitting rock bottom in 1996. "I was completely broken," he says.

Determined to be drug-free by his 35th birthday, Alston sought help at what is now the Johns Hopkins Broadway Center for Addiction. Despite setbacks, he completed the program in 1997. He's been drug-free ever since.

At first active in the center's alumni recovery group, Alston then worked some 15 years as an HIV counselor for Baltimore's health department. For the past two years, he's been a peer recovery advocate at the very site that helped him reclaim his life. He coaches some 60 clients a year about services like housing and job readiness.

More important, Alston's considerable skills help clients stay focused and see a future without drugs. "They love me," he says, "because I'm honest with myself and keep things real. They know I've been in recovery a long time. I tell them: 'My hopes are with you, but you have to go through growing pains to heal. My strength—my hope—is that if I can overcome drugs, you can overcome them.'"



**Robert Alston says he sees himself in every person coming through the clinic. "The key," he says, "is to guide them through short-term goals."**

# Treating Adolescent Stress: Timing Matters

It's no surprise that adolescence, a critical period of neural development, coupled with exposure to chronic stress, can leave a lasting impact on mental health. Finding optimal ways to intervene to prevent long-term depression or other disorders has been the goal of psychiatry researcher **Minae Niwa**, a junior faculty member in the Johns Hopkins Schizophrenia Center.

In a paper in *Science*, published in 2013, Niwa and colleagues demonstrated that adolescent stress in mice bred with a genetic risk for psychiatric disorders led to biochemical, behavioral and epigenetic changes that lasted well into adulthood. These changes turned genes on and off by adding chemicals—methyl groups—to the DNA for the gene tyrosine hydroxylase (Th), which is the rate-limiting enzyme in the synthesis of dopamine, a neurotransmitter implicated in cognition and mood that goes awry in depression and other psychiatric disorders.

The epigenetic changes also resulted in excess production of glucocorticoids, hormones that are released in response to stress exposure. Treating the animals with the nonselective glucocorticoid receptor antagonist RU486 during stress, the researchers found, could ameliorate these pathological changes.

While exciting, the research left two crucial unanswered questions: Is Th the only target of epigenetic modifications mediated by the glucocorticoids? And what is the precise time period during which medication could have the most impact?

To address these questions, Niwa, psychiatry researcher **Richard Lee** and colleagues conducted a follow-up study in the genetically susceptible mice, which were placed in separate cages during the three-week stress regimen. The results were published in the journal *Human Molecular Genetics*.

The investigators examined several genes along the animals' hypothalamic-pituitary-adrenal axis,

the brain's key stress pathway. Findings showed significant epigenetic changes—not only in Th, but also in brain-derived neurotrophic factor (BDNF), which helps regulate connections important for learning and memory, and in FK506 binding protein 5 (Fkbp5), which plays a role in stress response and immune function. Treatment with RU486 during the three-week stress period (5 to 8 weeks of age in the adolescent mice) prevented epigenetic changes in the Th, BDNF and Fkbp5 genes.

To identify the precise period when RU486 could offer the most benefit, the researchers divided the treatment periods into three windows: the first week of the stress regimen, the first two weeks of the stress regimen and the two weeks after the stress regimen.

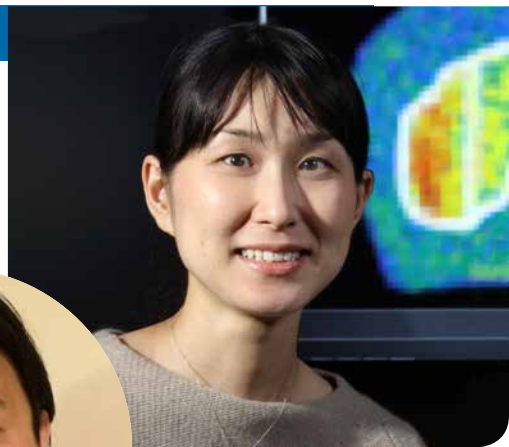
"What we found was that treatment during the first week seems to have the most effect in terms of blocking the epigenetic, behavioral and biochemical deficits initially observed," Lee says. This suggests, he explains, that early adolescence may be a specific period of maturation and function of dopaminergic neurons and their sensitivity to glucocorticoids. Treatment during the first two weeks was also helpful; however, "treating these adolescent mice after the stressor doesn't reverse any of the effect, because the stress hormone has already done its damage."

Niwa and Lee are now looking to study the impact of adolescent stress in typical mice that do not carry the genetic risk and to examine epigenetic changes genomewide using a platform Lee developed. They also plan to test a newer, more selective compound that blocks only the glucocorticoid receptor.

The work has relevance for neural development in adolescence, says Lee. In particular, he notes, this past January, President Obama announced a ban on solitary confinement for jailed juveniles. "I think



In her lab, **Minae Niwa** continually looks for optimal ways to intervene to prevent long-term depression.



**"I think [people are realizing] what social isolation does to your mental health, especially around the time when your brain is still developing in terms of maturation and reorganization."**

—RICHARD LEE

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Therapeutic strategies that can amend the debilitating consequences of stress are highly desirable, adds Niwa. "We need to develop a new compound that can reverse these changes, even after their establishment," she says, as well as identify a biomarker for the maturation of dopaminergic neurons. "If we can find such a biomarker, we could intervene with drug treatment or cognitive training in adolescents." ■

Learn more about adolescent stress at [bit.ly/jhmadolesc\\_childpsych](http://bit.ly/jhmadolesc_childpsych).

## ADDICTIONS PSYCHIATRY

### Broadway Center for Addiction Stats

#### PEOPLE

**377** Individuals served per year

**174** New admissions per year

**147** New admissions who come from inpatient hospital units **(87%)**



#### HOUSING

Patients provided housing each year



**42** Women (Wilson House)

**250** Men (Helping Up Mission)

Source: Kenneth Stoller, The Johns Hopkins Hospital

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rently enrolled at the center while receiving buprenorphine from their primary care or psychiatric physician, extending to them the reach of a Johns Hopkins-tested rewards approach to recovery, which includes store gift cards.

Over the years, the Broadway Center's profile has risen, thanks in part to fate. Just after Stoller took the helm, the program lost some block grant funding. Suddenly forced to promote the program to shore up revenue sources, he began visiting primary care and psychiatric sites. Today, with a deeper understanding of the center's tactics, he says more M.D.s in the surrounding community are open to using medications and referring patients. Nationwide,

interest is growing in replicating the Broadway Center model.

Federal help could be forthcoming: After the government's drug control policy office singled out the center "as a model for improving the quality of and access to much-needed opioid addiction services," Stoller was heartened.

Still elusive, however, is a better public opinion of maintenance therapy. Many people consider medically assisted treatment a moral failing or a crutch. Yet, Stoller counters, "If you broke your leg, what would be your best approach—sit on a couch and be immobile or engage in daily life using crutches?" ■



Learn more about the Broadway Center for Addiction at [bit.ly/broadwaycenterforaddiction](http://bit.ly/broadwaycenterforaddiction).



## Extended Help—and Hope—for Women with Mood Disorders

Back in 2004, when the Johns Hopkins Women's Mood Disorders Center opened, its goal was to help women grappling with unstable moods at all stages of life. That goal hasn't changed, but the need for such services grows ever stronger. The center has tripled its volume of visits from women who are pregnant, postpartum, or facing a menstrual cycle-related mood or anxiety disorder. And its staff handles approximately 250 new consultations a year—up from about 75 a year when the program began.

Now center staff members are in the midst of launching programs to accommodate even more women, says **Lauren Osborne**, its assistant director. Licensed clinical psychologist **Tamar Mendelson**, a researcher in the Johns Hopkins Bloomberg School of Public Health, has joined the practice a half day a week, working with social worker **Samantha Meilman** to provide individual cognitive behavioral therapy to pregnant or postpartum patients and lead a six-week group cognitive behavioral therapy program for new mothers.

In addition, the center started a two-year fellowship program in reproductive psychiatry. **Katherine McEvoy**, a former chief resident in the psychiatry department, became its first fellow on July 1. In addition to working in the Women's Mood Disorders Center and Harriet Lane Maternal Mental Health Clinic, McEvoy will spend time with two new services to be located within obstetrics clinics: a resident clinic in the Johns Hopkins Outpatient Center and a maternal-

fetal medicine clinic in The Johns Hopkins Hospital.

Many obstetric providers, says Osborne, are not that comfortable treating even low-level depression and anxiety in pregnancy—or if they are, they don't know what doses of medications to give. “Dr. McEvoy will be there as a resource to those who want to manage patients themselves or to treat patients with more complex needs,” she says.

“With other problems, you may be able to wait a couple of months to see a doctor,” adds Osborne.



Center Director Jennifer Payne, left, and Assistant Director Lauren Osborne lead efforts to improve the quality of life for women with mood disorders.

“But pregnancy has its own issues, and these women need to be seen before they deliver. We think these clinics will allow us to get these patients in faster by being right on-site.” ■

Learn more about the Women's Mood Disorders Center at [bit.ly/jhwomenmooddisorderclin](http://bit.ly/jhwomenmooddisorderclin).

### Taming Postpartum Depression

In research news, **Jennifer Payne** and **Lauren Osborne**, Women's Mood Disorder Center director and assistant director, respectively, have found that measuring levels of the hormone allopregnanolone during pregnancy could help predict the risk of developing postpartum depression. Allopregnanolone, measured in nanograms per milliliter, is a metabolite of progesterone. Known for its calming effects, it hits the same brain receptors targeted by benzodiazepines and alcohol. In a study of 62 women diagnosed with mood disorders and followed through pregnancy and the postpartum period, the researchers found that every additional nanogram per milliliter of allopregnanolone measured during the second trimester resulted in a 63 percent reduction in the risk of developing postpartum depression.

Furthermore, the change in allopregnanolone from the second to third trimester was associated with DNA methylation levels of a biomarker in the HP1BP3 gene, previously identified by Payne and epigenetic researcher **Zachary Kaminsky** to predict postpartum depression. Additional work found that higher levels of the inflammatory cytokine GM-CSF correlated with depression in the third trimester. Osborne and Payne are now looking to replicate the findings in a new cohort of women going forward.

Kaminsky was recently awarded a Maryland Innovation Initiative grant by Tedco for the development of a commercial blood test to identify biomarkers in the HP1BP3 and TTC9B genes that can predict postpartum depression. First up, says Kaminsky, is replicating his and Payne's research results in a larger patient cohort, with the idea of turning it into a commercial business.

### PEDIATRIC PSYCHIATRY

## Clues to Latino Parents' Anguish: A First Step

When Johns Hopkins pediatric psychiatrist **Rheanna Platt** meets with Latino children grappling with behavioral problems, she's often pondered: Could the ways their parents adjust to life in America be playing a role?

That's hard to tell, but needs to be known. Current psychosocial research on U.S. immigrants is scant, she says, and studies of Latino families even rarer. Yet more than 80 percent of Johns Hopkins Bayview Medical Center's pediatric patients and 45 percent of its obstetric patients are Latino. Anecdotes from the center's pediatric social workers attest to traumatic events in these parents' countries of origin, as well

as discrimination locally. Such experiences, she says, likely trickle down emotionally to the children.

Fortunately, Platt spotted a prime opportunity to follow Latino parents: well-baby visits. Parents' being there is nearly guaranteed, she explains. “They may neglect their own health, but most bring their children for the requisite six visits during the first year of life.”

So in 2015, with psychiatric researcher **Elisabet Arribas-Ibar**, Platt launched a necessary first study of 100 parents of the youngest children—newborns to age 5—to examine possible risk factors and mental health symptoms.

Using surveys, in-depth interviews and childhood records, Platt and Arribas-Ibar gathered data on

immigration status, health care access and contextual risk factors. They also explored parental stress in the pediatric primary care setting. Finally, the study aimed to gauge the willingness of parents to meet as a group to discuss risk factors and mental health.

Their findings point to a host of stressors for these parents. Chief are financial struggles, documentation status, fear of violence and relationship discord. Health problems like obesity and asthma may complicate matters, says Platt. Among patients referred to community psychiatry's Latino Family Clinic, other learning disruptors, like ADHD, are common.

With time, Platt often sees relationships between children and

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Rheanna Platt says Latino parents grappling with their children's mental health struggles can tap into social and psychological support at pediatric clinics.

### Adversities Confronting Recently Immigrated Parents

- Violence in country of origin
- Violence during immigration process
- Discrimination, acculturative stress and poverty in receiving country
- Increased risk for parenting stress and parent mental health problems

## A Sampling of **Brain Research and Thinking** Underway at Johns Hopkins

Polygenic risk of schizophrenia and cognition in a population-based survey of older adults. **D.T. Liebers, Mehdi Pirooznia, F. Seiffudin, K.L. Musliner, Peter P. Zandi, Fernando S. Goes.** *Schizophrenia Bulletin* 2016 Jul;42(4):984-991.

Oxytocin receptor DNA methylation in postpartum depression. **M. Kimmel, M. Clive, F. Gispen, J. Guintivano, T. Brown, O. Cox, M.W. Beckmann, J. Kornhuber, P.A. Fasching, Lauren M. Osborne, E. Binder, Jennifer L. Payne, Zachary Kaminsky.** *Psychoneuroendocrinology* 2016 Jul;69:150-160.

Outcome measurement in ICU survivorship research from 1970 to 2013: a scoping review of 425 publications. **Allison Turnbull, A. Rabiee, W.E. Davis, M.F. Nasser, V.R. Venna, R. Lolitha, R.O. Hopkins, O.J. Bienvenu, K.A. Robinson, Dale M. Needham.** *Critical Care Medicine* 2016 Jul;44(7):1267-1277.

Mindfulness-based approaches for children and youth. **Carisa Perry-Parrish, N. Copeland-Linder, L. Webb, E.M. Sibinga.** *Current Problems in Pediatric Adolescent Health Care* 2016 Jun;46(6):172-178.

### PAPER TRAIL



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parents deteriorate. “Many Latino parents,” she says, “have trouble advocating for their children’s needs in the school setting because of language barriers.” In families where parents immigrated years before their children did and sent hard-earned money back home, tensions can mount. It’s not uncommon to hear parents, their resentment bubbling up, ask a struggling adolescent, “How can you be depressed after everything we’ve done for you?”

Though many Latinos are beginning to tap the hospital’s health seminars and social services—three Spanish-speaking therapists are available at Johns Hopkins Bayview’s pediatric clinics—“lots of folks are afraid to do so or don’t know where to turn,” Platt says.

All the mothers interviewed for the study expressed interest in a pediatric primary care-based intervention—encouraging news, says Platt, as the survey showed a high prevalence of symptoms like anxiety, PTSD and depression in those with minimal social support.

“Our best hope,” Platt says, “is to learn more about Latino parents’ struggles and design programs to promote their well-being—and in turn, their children’s.” ■

Learn more about the study at [bit.ly/latinoparentspsych](http://bit.ly/latinoparentspsych).

## Hopkins **BrainWise**

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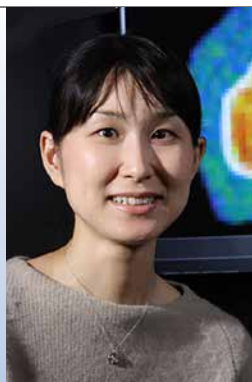
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