

## Aging Well with Autism

**C**arol Orth embraces a stuffed turtle that vibrates as she grasps it tighter. It's just one of the props the psychotherapist and clinical supervisor of the Johns Hopkins Adult Autism and Developmental Disorders Center encourages patients with autism spectrum disorder (ASD) to pick up when they feel agitated. Murals with beach scenes offer calm. Whiteboards encourage interaction during therapy sessions. Reams of Bubble Wrap entice clients to pop plastic mounds to release tension.

Demand for services such as these at the spacious new outpatient facility adjacent to the Johns Hopkins Bayview Medical Center campus continues to rise, given the increasing prevalence of ASD among children: 1 in 59—versus 1 in 166, in 2011. Yet little is known about ASD in adults, a population that continues to grow as these children age and need additional psychiatric and medical care over time.

Now, a new longitudinal study on aging and ASD led by Johns Hopkins clinicians looks at co-occurring illnesses and behavioral and neuropsychiatric symptoms that arise with advancing age.

The retrospective study, which analyzed data collected between 1981 and 2015, is the first to have a relatively large sample size (74 individuals age 30 and older), says geriatric psychiatrist **Elizabeth Wise**, who co-authored the report with **Peter Rabins**, former director of the Division of Geriatric Psychiatry and Neuropsychiatry; and Marcia Smith, a local psychologist. The study, published in the *Journal of Autism and Developmental Disorders*, focuses on a sample of adults who have been part of the same community program—offering early intervention and support—for 20 to 35 years.

The research focused on these clients' medical, behavioral and neuropsychiatric symptoms during that time. At least three-quarters of the participants have some degree of language impairment, and almost a third



**Carol Orth, left, clinical supervisor of the Johns Hopkins Adult Autism Center, and geriatric psychiatrist Elizabeth Wise begin an interactive session with patient Jared Green, 27, in the center's sensory room. Pictured at right, Eric Samstad—the center's medical director.**



needed an oral sedative before medical or dental appointments. More than three-quarters have intellectual disability.

"I think it's a sign that we highlighted a pretty impaired group of people," says Wise. Still, the prevalence of challenging behaviors, including self-injury, aggression and wandering, declined significantly. "Whether it was through medication or behavioral programs, we found that behavior problems can be reduced over time." Twenty years ago, 90 percent engaged in one or more challenging behaviors, compared with 52.7 percent in 2015, says Wise.

Many of these approaches are also underway at Hopkins Bayview's adult autism center and have proven successful in easing symptoms. Dozens of patients with ASD have been coming to the clinic since the 1990s. Some were initially diagnosed as children at Kennedy Krieger Institute, which has long-standing ties to Johns Hopkins. "It's been really rewarding to watch these individuals transform over time," says Orth.

"What sets us apart," she says about the center

that serves some 300 patients, "is that the people we work with have an autism disorder and are treated for mental illness and disability. It's a very complex picture." In addition to psychotherapy, medication management and psychosocial rehab, the center offers specialty clinics for schizophrenia, substance use disorder and anxiety. Resources are also available to family members.

### Caring for Patients Across the Spectrum

The need for tactile and sensory stimulation is heightened in people with ASD, says Orth. So, it's not uncommon for her to throw a ball back and forth to a person with ASD—even during an initial meeting with a family. "It's a nonthreatening way to connect with them and offers them sensory stimulation in the areas of sight, sound and touch," she says. In small group meetings, people with ASD discuss such things as how to handle an interview or other new situation.

Wise notes that adults with ASD often have severe symptoms, such as aggression and self-injury, that can persist. And recent studies, she says, show that most adults with ASD live in supervised accommodations with fair to poor social outcomes. Few are employed full time, and there's great demand for more services for aging adults on the spectrum.

But many adults with ASD, says Wise, are highly intelligent and accomplished. She and



"Whether it was through medication or behavioral programs, we found that behavior problems can be reduced over time."

—ELIZABETH WISE

(continued on back page)



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

### Advances and Triumphs

As I embark on my second year at the helm, let me reflect on the great year we just completed in the department.

We landed another stellar crop of interns as new trainees. An impressive seven of our 10 interns have published first-author papers, indicating an academic orientation. An important change we have set in motion is the creation of academic tracks within the residency: for research, public mental health, child psychiatry and clinicians-educators. The idea is to provide mentorship, enrichment and academic opportunity in each of these areas. These changes will help us attract the most talented medical students entering the field. You will read herein about the work of a terrific M.D./Ph.D. student, **Seva Khambadkone**—first author on a striking study implicating nitrate-cured meats regarding mania.

This year has seen much national recognition of our faculty's accomplishments. **Traci Speed**, another Johns Hopkins M.D./Ph.D. student, received an award for early-career psychiatrists from the Association of Women Psychiatrists. **Kay Jamison**, our Dalio Professor of Mood Disorders, was named a Pulitzer Prize finalist for her biography of celebrated poet Robert Lowell, whose bipolar disorder both informed and disrupted his literary productivity. Alzheimer's disease expert **Kostas Lyketsos** was given the Award for Research in Geriatric Psychiatry by The American College of Psychiatrists.

We have also had an impact on the field this year through national leadership. **Anita Everett**, former head of our Hopkins Bayview Medical Center Community Psychiatry Program, served this year as president of the American Psychiatric Association. Former faculty star **Ben Lee** took the reins as chair of the Department of Psychiatry at the University of Rochester Medical Center. Substance abuse researcher **Elise Weerts** was named president of the College on Problems of Drug Dependence. As we celebrate the 75th anniversary of our department's most notable contribution to the field—**Leo Kanner's** discovery of childhood autism—we are also pleased to be breaking new ground in the study of adults with autism. Seasoned geriatric expert **Peter Rabins** has worked with new faculty member **Elizabeth Wise** in this intriguing area.

Thanks to everyone for your interest in our work. My warmest wishes to you.

## Processed Meats and Mania: A Connection?

As a medical student, **Seva Khambadkone** was speaking with psychiatry researchers **Timothy Moran** and **Kellie Tamashiro** about potential research projects when they gave her an interesting proposition—to see if nitrates used in processed meats such as hot dogs and beef jerky induce mania in rats.

Moran and Tamashiro had been approached by Johns Hopkins neurovirologist **Robert Yolken**, who noticed in his own studies that patients hospitalized for acute mania were significantly likely to have eaten nitrated meat products. To assess potential cause and effect, Yolken asked the researchers to study nitrate consumption in laboratory animals.



**“Due to the diet, there might be changes in the microbiome that may then feed into brain function and behavior.”**

—KELLIE TAMASHIRO

Their results, published recently in the journal *Molecular Psychiatry*, demonstrate that within two weeks of exposure to nitrates, rats were more hyperactive throughout the day. The behavior changes were accompanied by alterations in some brain pathways as well as microbes in the gut.

The research team set up three experiments. First, they fed some rats regular rodent chow, and others the same chow plus one piece of store-bought beef jerky every other day. “We were really surprised to see that within two weeks, rats eating the jerky were hyperactive compared to our control rats,” says Khambadkone, now a cellular and molecular medicine graduate student. This occurred even during the day, when the nocturnal animals are normally less energetic.

In a second experiment, researchers gave some rats standard chow; others, chow plus a piece of store-bought



beef jerky every other day; and a third group, chow plus a piece of custom jerky, prepared without nitrates, every other day. Rats eating the custom jerky behaved like typical rats, whereas the ones given nitrated meats were again more hyperactive. Extra activity was observed when rats were in their regular cages or exposed to a novel environment apart from their regular cages.

A third experiment divided rats into three groups, with one getting standard chow, one getting custom chow laced with beef protein, and a third getting custom chow formulated with beef protein and sodium nitrate. Once again, the rats consuming nitrates were more hyperactive than the others in both their normal and novel environments.

“I wouldn't want to say that beef jerky causes mania or bipolar disorder—we're definitely not showing that,” says Khambadkone. “But, overall, it's clear that bipolar disorder is a very complex psychiatric illness that likely emerges from a combination of genetic and environmental vulnerabilities. It's possible that a nitrated, cured meat could be one of these environmental risk factors that could contribute to the emergence or severity of mania.”

Rats fed the nitrate-laced custom chow also had dysregulation in several functional pathways of the hippocampus, the area of the brain responsible for processing long-term memory and emotional response. In addition, they had increased levels of two types of gut bacteria.

“It is clear that the gut does communicate with the brain somehow through these bacteria,” Tamashiro says. “Due to the diet, there might be changes in the microbiome that may then feed into brain function and behavior.”

What's still unclear is what causes either manic or depressive episodes in patients, adds Moran: “One implication here is that environmental factors could be one of the things that can bring on a specific episode.” ■

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

## Addressing Cognitive Problems That Arise from Cancer Treatment

As cancer treatments improve, the number of survivors is expected to reach 20 million by the year 2026, says neuropsychologist **Tracy Vannorsdall**. But cancer and its treatment can lead to changes in brain structure and function, resulting in reduced cognitive and mental health for survivors.

Vannorsdall, who studies cancer-related cognitive impairment, says many associate this with chemotherapy. But that's just one potential trigger. Radiation, endocrine treatments, pain medications and fatigue can also affect cancer patients' cognition. Rated by cancer survivors as one of the most problematic post-treatment symptoms, cognitive dysfunction can last for years, contributing to lower quality of life.

During a recent Grand Rounds talk at Johns Hopkins, Vannorsdall discussed two of her intervention studies. The first is evaluating noninvasive brain stimulation to improve cognition

and lessen fatigue among breast cancer survivors.

Chemotherapy is associated with structural and functional changes in the brain's dorsolateral prefrontal cortex, an area that mediates complex cognitive function, says Vannorsdall. For this study, she is using transcranial direct current stimulation (tDCS)—a treatment that delivers a very low current via two electrodes placed on the scalp—while study participants complete a working memory task called a dual n-back test. Participants, seated at a computer, are presented with a series of shapes and sounds, then asked to determine if a shape or sound is identical to one presented one, two or three times back in the sequence. They complete five 30-minute sessions over a week.

“The notion is this will increase the likelihood that neurons underlying the electrodes will fire in response to cognitive stimulation,” Vannorsdall says. “It's a very challenging task, but it's adaptive. If patients are having difficulty, the task gets simplified. Once they reach a level of success, it goes up a degree of difficulty.” Prior studies have shown that tDCS improves working memory and reduces fatigue in multiple sclerosis patients.

In another study, Vannorsdall and radiation oncologist **Kristin Redmond** hoped to

prevent cognitive deficits in patients with brain metastases. Prior studies indicated that sparing the hippocampus, which is involved in learning and memory, from radiation can help preserve memory. Vannorsdall and Redmond looked for other areas to be spared.

Redmond found that the genu, a “relay station” in the corpus callosum packed with neurofibers and involved in executive functioning, attention and processing speed, can be easily damaged by radiation. In a pilot study, Vannorsdall and Redmond are adapting radiation given to patients to shield the genu, and monitoring participants through cognitive testing; brain imaging to study their white matter; and questionnaires about participants' quality of life, moods and functioning.

Through this work, says Vannorsdall, “I think we have the possibility of helping preserve a wide array of cognitive skills.” ■

Learn more about cancer treatment and fuzzy thinking: [bit.ly/chemobrainhelp](http://bit.ly/chemobrainhelp).

The effort is supported by the psychiatry department's Venture Discovery Fund.



**This approach—using tDCS—will increase the likelihood that neurons will fire in response to cognitive stimulation.**

—TRACY VANNORSDALL



### Cancer Treatments' Link to Cognition

1. Poorer outcomes for patients with pre-existing mental illness
2. Related to the development of mental health problems
3. Associated with reduced cognitive functioning

## National Curriculum Aims to Fill Gaps in Reproductive Psychiatry

Throughout her residency, **Lauren Osborne** noticed how little training some of her colleagues were getting in reproductive psychiatry—the assessment and treatment of psychiatric symptoms arising in women during hormonal transitions such as pregnancy or perimenopause. It hit home while Osborne pursued a research fellowship in women's mental health.

“Ten of the 11 other people I went to residency with called me within their first three months of practice to ask me a question about treating a pregnant

woman,” says Osborne, assistant director of Johns Hopkins' Women's Mood Disorders Center. “What that said to me was that all of these people entering all areas of psychiatry felt unprepared to manage pregnancy-related issues.”

Now, Osborne and some 40 colleagues across the country are looking to turn things around, through the creation of a national curriculum on reproductive psychiatry. The program, aimed at prescribers and established by the National Task Force on Women's Reproductive Mental Health (chaired by Osborne),

covers 15 topics, including perinatal depression and bipolar disorders, eating disorders in pregnancy, infertility and perinatal loss. Materials are packaged into three modalities: comprehensive, downloadable guides that can be taught to residents in a classroom, even if the facilitator has no expertise in women's mental health; supplemental videos and interactive exercises a trainee can complete through self-study; and short exams, offering continuing medical education (CME) credit, on each of the 15 areas. The materials will be pilot-tested at five residency programs, including Johns Hopkins, then made available online. The only charge will be for the CME exams.

The project arose from a 2013 national perinatal mental health conference, when Osborne and colleagues summarized the state of education in reproductive psychiatry and went on to survey residency directors about program requirements and

attitudes. They discovered that the biggest barriers to teaching reproductive psychiatry to residents were lack of time and faculty expertise. It was a “light bulb” moment, recalls Osborne, whose group realized it could provide that expertise from afar. All of the classroom materials have a facilitator's guide containing an answer key and references, which enables any psychiatric provider to lead the discussion. Osborne received the 2018 Educational Innovation Award from Johns Hopkins' Institute for Excellence in Education for the project.

“I want every general psychiatrist to have some minimum knowledge of how to treat a woman during pregnancy and the postpartum period, so I can avoid the disasters that come into my office regularly—women whose medications have been stopped erroneously during pregnancy and who then become very ill,” says Osborne. While managing some conditions requires advanced

skills, she notes, psychiatrists should at least be able to handle basic concerns and know where to refer patients if they need additional assistance.

Another goal is getting the psychiatric community to recognize that reproductive psychiatry is an important subspecialty, she says: “We require every general psychiatrist to learn something about how to treat children, older adults and those with substance use disorders, but we don't require them to learn how to treat women. I hope the existence of this curriculum and surrounding buzz will get people talking and change some of those attitudes.” ■



Lauren Osborne

**Aging Well with Autism** *(continued from cover page)*

Orth recently started working with a retired surgeon with ASD, for example, who's had trouble adjusting to the social world after leaving the workplace. In every situation, the center's team of psychiatrists, psychotherapists and occupational therapists work in concert with the individual and/or that person's care team to assess severity of symptoms and level of function, and to create treatment plans and interventions to meet his or her specific needs. The plan includes both individual and group sessions.

"There's never a dull day here," says **Eric Samstad**, medical director of the center. "We need to accept that we're not going to cure anyone, but overall, we are improving quality of life." And, though lack of engagement can be intimidating, he adds, "If you make the effort to get to know these patients, they warm up to you. They really appreciate it."

For Orth, success comes when she's made a connection, "or when they recognize me and feel safe—giving me a high-five, or a wave," she says. "Tuesday afternoons are the best; the group session begins at 3, but people show up at 2 and start engaging in the lobby." ■



Child and Adolescent Psychiatry presents  
**Autism Scientific Symposium**  
 Marking 75 Years since Leo Kanner first identified autism.

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**Tuesday, September 25, 2018**  
**2:30pm - 5:00pm**  
**Hurd Hall - Johns Hopkins Hospital**

More information: [hopkinsmedicine.org/psychiatry/Leo\\_Kanner\\_autism](http://hopkinsmedicine.org/psychiatry/Leo_Kanner_autism)  
 Event is free and open to the public



**JOIN US AS WE MARK THIS MILESTONE**

Seventy-five years ago, Johns Hopkins child psychiatrist **Leo Kanner** defined autism as "an innate inability" of a child to relate to those around him or her, and an "all-powerful need to be left undisturbed." Join us as we honor Kanner's legacy. **Contact:** [jellio26@jhmi.edu](mailto:jellio26@jhmi.edu).

**Hopkins Brain Wise**

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