Hopkins Brain Wise
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Bedside Psychiatry Team Screens Patients, Improves Outcomes

Behavioral Intervention Team nurse practitioner Maureen Lewis, left, talks to a newly admitted patient on a medical unit about potential mental health concerns. The program is directed by psychiatrist Pat Triplett, at patient's immediate left, and aided by psychiatric social worker Deborah "Sunny" Mendelson, far right.

One day last winter, **Pat Triplett** received an urgent page: A patient who'd been on a medical unit for two weeks started lashing out at everyone in his path. By the time the Johns Hopkins psychiatrist arrived, it was too late to connect with the patient. Security staff members had already pinned him down. "It exacted a huge toll on the unit," says Triplett, "and stuck in my mind as just what we are trying to avoid."

That incident—and others—moved Triplett to fast-track a plan to screen all newly admitted inpatients—not just those headed for psychiatric units. The idea, he says, is for a psychiatrist, nurse practitioner and psychiatric social worker to assess medical unit patients for mental health concerns early on, "before they escalate."

The need is dire, he adds. Roughly 38 percent of medical admissions to Johns Hopkins have psychiatric disorders such as depression, bipolar disorder or schizophrenia. Also, up to 20 percent of the hospital's admissions are linked to opioids.

Now, however, with the debut of the Behavioral Intervention Team (BIT) in April 2016, at least one team member sees a patient, often within hours of admission to a medical unit. "Not everyone will need psychiatric assessment," Triplett says, "but some will, and the sooner they're identified, the quicker they will be treated."

The Johns Hopkins BIT model is still a work in progress. Currently, the team covers three medical units—about 70 beds. By next spring, Triplett aims to roll out two more teams and a broader reach. He credits the model as the brainchild of former Johns Hopkins colleague Hochang "Ben" Lee, now at Yale New Haven Hospital, where it has proven successful.

Here's how the approach works: Every weekday morning, one BIT member meets to review patient charts that medical-surgical staff members have prepared. Afterward, all three BIT members—each specialized in psychiatric evaluation—decide which patients will be seen and by whom.

Triage is tiered, says Triplett: Patients arriving after a suicide attempt, for example, are seen immediately; those co-burdened with schizophrenia and poor medical outcomes are also assessed more rapidly.

BIT nurse practitioner **Maureen Lewis** begins each visit by scanning the electronic medical record for any history of psychiatric illness or substance abuse. After introducing herself, she says, "We're just checking in to see if you're taking any antidepressants." This surprises some patients, Lewis says, "but even the mildly troubled can benefit from the program and have been receptive to our efforts." When necessary, she arranges transfers to inpatient psychiatry.

Signs of depression on medical units aren't rare, often surfacing after a major medical event. But they can be subtle, says BIT psychiatric social worker **Deborah "Sunny" Mendelson**. She describes an elderly patient admitted with a massive stroke. "Everything was swirling around for him," she recalls. Though he'd lost major abilities, "he felt especially vulnerable and sad about not seeing well enough to read the white board or adjust his bed. I told him that it takes a while for the brain for adapt, but you have the ability to communicate." The conversation cheered the man, as did the vision consult she recommended, which led to new eyeglasses.

Often, Mendelson digs deeper. She asks how patients cope with new perceptions of themselves, particularly if they'll need more surgery or have advanced cancer. Simply the chance to talk about their situations, she says, "can be liberating."

But challenges abound. Many inpatients have a complex mix of medical and psychiatric problems, notes Triplett, such as those who develop delirium after joint replacement surgery. Or, new medication changes can make a huge difference in mood.

Complicating matters further are patients admitted for medical problems who also have chronic mental illness. Many of these patients have high rates of diabetes, obesity and smoking.

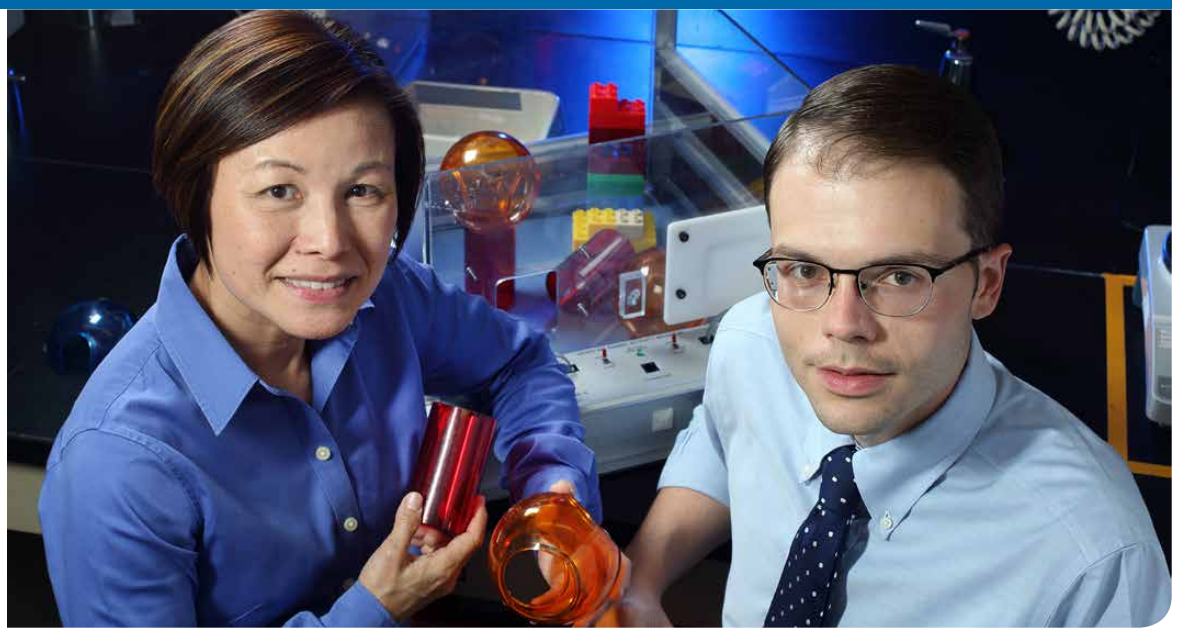
In its short existence, the program has won accolades for reducing psychiatric crises and length of stay. "We don't have data yet," says Triplett, "but if we can cut length of stay for patients getting psych consults by two-thirds of a day, as Yale has, it will have a huge financial impact." The BIT program has also raised morale, especially among nurses. "Having the psych team on the unit or nearby," says Triplett, "lets them focus fully on their medical nursing."

But the biggest payoff for the Behavioral Intervention Team, says Triplett, has been how this approach improves patients' peace of mind far sooner than later. ■

"This approach screens medically unstable patients for psychiatric problems so we can provide an intervention before things escalate."

—PAT TRIPLETT

Aging Brains, Stress and Alzheimer's: A Correlation?



In their studies on the cognitive effects of stress in aging brains, psychiatry researchers Kellie Tamashiro and Zachary Cordner have found that stress may increase the risk of Alzheimer's in later life.

As a medical student, **Zachary Cordner** was struck by a study co-authored by **Peter Rabins** indicating that spouses of Alzheimer's disease patients were at a twofold risk of developing the condition themselves.

"The spouses were facing an incredible amount of stress day in and day out providing care," says Cordner, "but exactly how that led to an increased risk of Alzheimer's disease was entirely an open question." Then, when he joined Johns Hopkins' M.D./Ph.D. program and the lab of stress expert **Kellie Tamashiro** a couple of years later, he quickly realized that the effects of stress on the aging brain were things he could address through research using mouse models.

Lab mice live for about two years, says Cordner. To simulate the unpredictable stressors faced by spousal caregivers of Alzheimer's disease patients, he and Tamashiro exposed young adult and aged (18 months) mice to two weeks of chronic variable stress—one day the lights might be left on overnight, or another day, they might be placed in an overcrowded cage. Memory tests given to the mice after the two-week period demonstrated that while stress exposure led to some cognitive impairment in all of the mice, the aged mice were profoundly more affected.

The work, published in *Translational Psychiatry*, also found that stress exposure was associated with increased expression of a gene called beta-secretase, or Bace1, which is involved in the development of plaques that build up in the brain during Alzheimer's disease. In young mice, there was a 1.5- to twofold increase of Bace1 in the hippocampus, the center of learning and memory; in aged mice, Bace1 was increased not only in the hippocampus, but also in the prefrontal cortex and amygdala, areas that regulate thoughts, actions and emotional behavior. In addition, the researchers noted that increased expression of Bace1 was associated with decreased addition of chemicals or methyl groups in the promoter region of DNA for Bace1.

"Our work suggests that the aging brain appears to be more susceptible to the cognitive effects of stress, and stress may increase the risk of Alzheimer's disease, especially in aging individuals," says Cordner, now a psychiatry intern at Johns Hopkins Bayview Medical Center.

In a second set of experiments, Cordner and Tamashiro exposed two additional groups of young adult and aged mice to environmental enrichment—such as increased bedding, toys to play with or tunnels to crawl through—a week before and during a two-week chronic variable stress period. "What we found was we were able to prevent all of these negative effects of stress on learning and memory through environmental enrichment," says Cordner.

There is a fair amount of interest in enriched environments—including exercise, brain training and social activity—in people, Cordner notes, and some data to suggest those activities help prevent adverse consequences in late life. "The tricky part is there is probably a lot going on in the brain from environmental enrichment, and exactly how that prevented the effects of stress in our study is a big question," he says. Studying this is his next step. ■

Reducing Restraints for High-Risk Youths

Restraints and seclusion have generally been viewed by child psychiatry staff as unpleasant but sometimes necessary tools to manage aggressive behavior among hospital patients. Professionals agree that alternatives are needed, but there's been little research on evidence-based behavioral interventions to reduce restrictive practices—until now.

Modeling a proven prevention strategy that has been implemented in more than 7,500 schools nationwide to reduce disciplinary actions and suspensions—Positive Behavior Interventions and Supports (PBIS)—Johns Hopkins child psychologist **Elizabeth Reynolds** and colleagues in a four-year prospective study were able to meaningfully reduce, from 543 to 253 events, the use of restraints and seclusion on their inpatient unit. Also, the percentage of inpatients who were placed in seclusion or restraints markedly decreased during the study period, and the mean duration of seclusion and restraint incidents decreased from 20.43 to 8.18 minutes per episode.

Given the concern that a reduction in seclusion and restraint can lead to an increase in administering medications "pro re nata" (PRN)—or as needed—to treat acute agitation or aggression, the researchers also monitored the use of PRN medications. After implementation of the PBIS model, there was a reduction in the number of uses of PRN meds from 1,705 to 1,014. The percentage of patients who received a PRN medication decreased from 41.6 to 29.4 percent.

"We were able to reduce the rates of seclusion and restraints, and the use of PRNs, significantly," says Reynolds.

How? The proactive PBIS model, Reynolds explains, employs positively worded behavioral expectations for patients—"be safe," "be responsible" and "be respectful"—and a reward system that reinforces appropriate behavior. In this program, staff members stamped patients' "passports" with rewards that could be accumulated and reimbursed with physical products or privileges. Punitive actions were not included in the model.

Elizabeth Reynolds

"Rather than focusing on the behavior we don't like, we focus on the behavior we want to see," says Reynolds. "When that behavior is demonstrated, we praise it and reward it."

Key to success, Reynolds adds, is training for the nursing staff that includes education and role-playing, and buy-in from staff members significantly challenged in managing high-risk patients.

"Obviously, this is a very difficult population to work with," says Reynolds. "You see kids with significant trauma histories, poor home environments and lots of parental loss. It can be a really challenging place to work."

But staff members on the Johns Hopkins Child and Adolescent Psychiatry Inpatient Service, Reynolds stresses, often look for ways to create a more therapeutic and caring environment—a place where patients feel more supported.

"There's less tension in the air when you're not getting into power struggles all day," says Reynolds, "and it's much easier for patients to engage in their treatment." ■

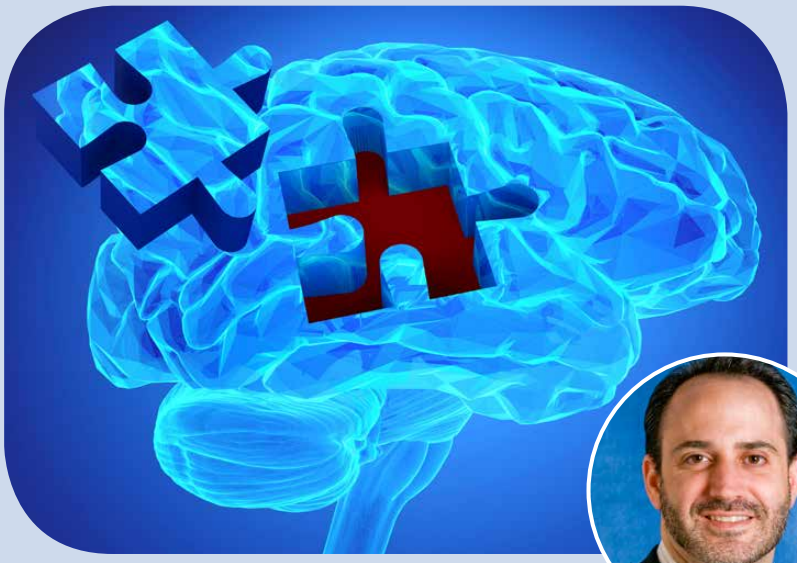
Of Protein, Neurodegenerative Disorders **and Schizophrenia**

Frederick Nucifora's background in neurodegenerative disorders has made him wonder if some of the same mechanisms contributing to these diseases could also occur in schizophrenia or other mental illnesses.

Changes in stress-related cascades, including inflammatory and endocrine processes that have been linked to schizophrenia, can disrupt normal protein quality controls or modify proteins, Nucifora explains. In fact, protein insolubility has been implicated in many disorders, including cancer, cardiac and pulmonary disease, and neurodegenerative disorders. In Alzheimer's disease, protein builds up as plaque; in Huntington's disease, it presents as occlusions or blockages; and in Parkinson's disease, it presents as Lewy bodies, abnormal proteins occurring in brain nerve cells.

"We hypothesized that there may be either disruption of protein quality control or misfolded proteins also occurring in schizophrenia," says Nucifora.

His team studied autopsied brains from 19 patients with schizophrenia and 19 healthy controls. Separating out the brain's proteins through a process called fractionation, the researchers measured levels of total and insoluble protein. They observed an increase in the amount of insoluble protein in a subset of patients with schizophrenia. The investigators then studied the samples looking for ubiquitin, a known marker for protein insolubility in neurodegenerative disorders and a signal for protein insolubility, according to Nucifora's prior research. They saw an increase in ubiquitination, the bonding of ubiquitin to proteins in the same subset of schizophrenia patients who had more insoluble protein.



Frederick Nucifora

> "If we understand [these pathways], **we could try to develop therapeutic targets** that could be directed at this process."

"What's interesting is this provides novel insight that protein insolubility can be a pathological mechanism leading to schizophrenia, at least in a subset of patients," Nucifora says. Schizophrenia is thought to be a diverse disease, he adds, so it makes sense that this mechanism would be found in just some patients. Because the samples were from autopsy brains, his team didn't have enough information to link the finding to patients with any particular clinical presentation.

Understanding the molecular mechanism of this subtype of schizophrenia could lead to a better understanding of the pathways, circuitry and behavioral symptoms seen in patients with mental illness.

"This could cut across diagnoses," he says, perhaps also occurring in bipolar disorder or major depressive disorder. "If we understand that, we could try to develop therapeutic targets that could be directed at this process."

Ultimately, Nucifora would like to study this in additional cases. Meanwhile, follow-up studies planned in olfactory neurons—nerve cells taken from the system regulating sense of smell—will test different stressors to see which ones may contribute to protein insolubility and the development of schizophrenia. ■

Managing Chronic Pain in Patients with Sickle Cell Disease: Beware of Opioid Effect

Recent research from **C. Patrick Carroll** highlights a Catch-22 in the treatment of adults with sickle cell disease. Such patients are frequently prescribed opioid pain medications to manage chronic pain and recurrent painful crises. However, research suggests that opioids can, paradoxically, increase pain sensitivity in some cases, and work by Carroll and others demonstrates that people who regularly take opioids often report more severe pain than those who don't.

Carroll, director of psychiatric services for the Johns Hopkins Sickle Cell Center for Adults, and colleagues recently evaluated pain experiences among adult sickle cell disease patients who were prescribed long-term opioids. These participants reported significantly higher pain, fatigue and curtailed daily activities than those not taking these drugs.

The study recruited 83 people with sickle cell disease with an average age of 39; 29 patients had been prescribed daily, long-acting opioids to manage their pain. Patients completed daily electronic pain diaries for 90 days, including self-reported levels of pain, physical activity, fatigue and pain-related daily activity interference. Patients also recorded levels of pain relief and medication satisfaction.

Sickle cell patients on long-term opioid treatment reported noncrisis pain intensities that were more than three times higher than those not taking opioids. During crisis pain days, patients on long-term opioids reported 32 percent higher pain levels. Overall, patients prescribed chronic opioid therapy were more impaired, with more than three times greater pain interference and twice the fatigue on noncrisis days, and 20 percent more pain interference and 33 percent higher fatigue.

Carroll's group also performed standard measures of pain processing, such as how intensely participants experienced unpleasant heat and pressure. They were particularly interested in central sensitization, in which the central nervous system amplifies painful sensations. Central sensitization is a potential mechanism for both chronic pain and opioid-induced hypersensitivity to pain, says Carroll. Patients on long-term opioid therapy showed higher levels of central sensitization.

C. Patrick Carroll and colleagues have found that patients with sickle cell disease on long-term opioid treatment for pain experience pain intensities more than three times higher than those not taking opioids.

In participants not on chronic opioid therapy, central sensitization levels correlated with levels of noncrisis pain; however, this correlation vanished in patients taking chronic opioids, who had higher levels of central sensitization and pain at the outset.

"We need to be careful and skeptical about giving increasing doses of opioids to patients with sickle cell disease who are in chronic pain if it isn't effective," Carroll says. While the work is preliminary and should not lead physicians or those with sickle cell disease to eliminate opioids from a treatment regimen, he says this suggests that the mechanisms of pain in sickle cell disease patients taking long-term opioids may be different from those who don't take the medications.

Medication timing might play a role, he notes, since some research suggests that opioids relieve pain immediately but then cause hypersensitivity later. What's needed next, he says, are challenge studies "to see if we can figure out exactly what causes both reduction to pain and increased pain [with opioids]." ■

Learn more about the study: **bit.ly/scdopioids**

Shedding New Light on the Role of **Inflammation and Oxidative Stress in Schizophrenia**

Schizophrenia, the devastating mental illness characterized by delusions, hallucinations or disorganized thoughts, afflicts about 1 percent of the population, with onset typically in late adolescence. Its causes are still not well understood, and for the past 50 years, antipsychotic medication has remained the treatment of choice. But an increasing number of studies find abnormalities in inflammation and oxidation in affected individuals.

Recently, an international group of scientists have summed up this emerging field in a special issue of *Schizophrenia Research*. Edited by Johns Hopkins psychiatrists Akira Sawa and Thomas W. Sedlak, the journal highlights the wide ramifications of these discoveries. While risk of schizophrenia has been tied to a variety of factors, including genetics, brain injury, drug use and prenatal infections, the emerging insights on inflammatory alterations may be a common thread and lead to new treatments for this pernicious malady.

Johns Hopkins' contributors to this effort include **Akira Sawa; William Eaton; Mikhail Pletnikov; Crystal Watkins; Emily Severance; Robert Yolken; Sarah Andrews;** and **Thomas Sedlak**.

View the full issue at: **bit.ly/schresjourn**

New Books by Faculty

Still Down: What to Do When Antidepressants Fail
by Dean F. MacKinnon, M.D.
JHU Press

Committed: The Battle Over Involuntary Psychiatric Care
by Dinah Miller, M.D., and Annette Hanson, M.D.
JHU Press

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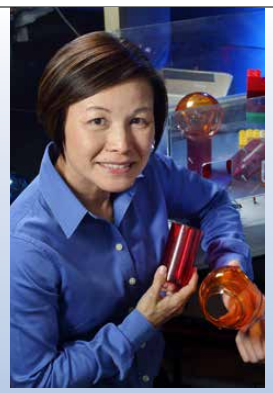

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