Hopkins BrainWise
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FALL 2015

Angela Guarda discusses healthy approaches to food and social eating skills with patients.

A Weighty Approach to Anorexia Nervosa

Amid all the debate about how to help patients with anorexia nervosa gain weight, Johns Hopkins psychiatrist **Graham Redgrave** says he always keeps one thing in mind: Starvation changes the brain. "It impairs judgment and makes patients more obsessional," explains the assistant director of the Johns Hopkins Eating Disorders Program. As one patient told him, "the more weight I lose, the more I want to lose." And that spells trouble, as anorexia nervosa is the most lethal of psychiatric diagnoses—with a seven- to nine-fold increased risk of death, compared with healthy, matched controls.

The observation that starvation worsens anorectic thinking—and the reality that weight restoration is necessary for recovery from anorexia—have pushed program director **Angela Guarda** and Redgrave to ramp up "refeeding" efforts for dangerously underweight patients.

Now, a new study of Johns Hopkins patients hospitalized with anorexia offers good evidence that rapid weight gain during inpatient treatment is safe and effective and can restore weight to the majority of patients over a relatively brief hospital stay.

Guarda, Redgrave and colleagues collected data over eight years from 361 Johns Hopkins patients with anorexia and related disorders. The average length of stay was six weeks in a combined inpatient and partial hospitalization program focused on helping patients gain weight and normalize their eating behavior. Most patients started on a diet of 1,500 calories a day (1,200 if they were extremely malnourished). On hospital day three, the total calories were increased by 500 and then stepped up every other day by another 500—up to 3,500 to 4,000 calories a day.

By discharge from the program, more than 71 percent of adults had reached a body-mass index of 19, and 80 percent of adolescents came within five pounds of their target weight.

"We were able to get patients with anorexia to gain around four pounds a week," says Redgrave. "That's twice the national average." Studies show that patients who gain more weight in treatment, he adds, are less likely to relapse in the first two years after treatment, when they're most vulnerable.

Careful medical monitoring remains a hallmark of the Johns Hopkins program, especially since an initial drop in serum phosphate when patients begin to consume more calories puts them at risk for refeeding syndrome—potentially fatal shifts in fluids and electrolytes that can cause serious complications, like heart arrhythmia.

Up to now, "slower is safer" has been the clinical view, says Guarda, senior author of the study. "But at what price? If a patient needs to gain 50 pounds but only gains 10 pounds in the hospital, the result is only a temporary improvement." Furthermore, she adds, recent studies under traditional protocols demonstrate that people can actually lose weight in the hospital during the first few weeks and that low weight at admission, rather than rate of weight gain, is the main predictor of low phosphate levels and refeeding syndrome.

A hallmark of the Johns Hopkins program, says Redgrave, is a highly structured team approach with a focus on behavioral, cognitive and supportive therapies—both one-on-one and in groups. Family therapy also plays an important role. The key, he says, is to strike a balance between confronting patients and providing reassurance and encouragement to help patients change ill patterns of behavior and counter anorectic thinking.

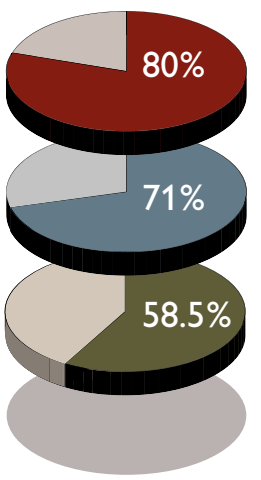
Redgrave is confident that the program's refeeding strategy will withstand the test of time. He cites 19th century British physician William Gull's advice that doctors shouldn't spend too much time asking patients what they want to eat. "Just feed them," Gull said. "Patients have to eat to get better."

Learn more about the Johns Hopkins Eating Disorders Program—watch a video at **bit.ly/jhmeatingdisordersprogram**.

"We were able to get patients with anorexia to gain around four pounds a week."

GRAHAM REDGRAVE, ASSISTANT DIRECTOR, JOHNS HOPKINS EATING DISORDERS PROGRAM

PATIENT PROGRESS AT DISCHARGE FROM THE PROGRAM



The research was funded by The Steven and Jeanne Robinson Fund for Eating Disorders and internally by the Johns Hopkins Medical Institutions.

A Nose for Schizophrenia Risk

Of all the sensory systems, olfaction is most closely linked to the frontal and temporal brain regions implicated in schizophrenia. Measuring potential olfactory dysfunction may therefore provide a window into schizophrenia pathology.

And the earlier in life these symptoms are identified, the better, says Johns Hopkins neuropsychologist **Vidya Kamath**—ideally, before a patient's first psychotic episode.

Kamath recently published findings about the relative specificity of olfactory deficits in individuals with schizophrenia, healthy family members and young people at clinical or genetic risk for psychosis but who have not yet been diagnosed with a specific disorder. Clinical risk subjects are those individuals without a first- or second-degree relative with schizophrenia who are experiencing attenuated symptoms of psychosis. Genetic risk subjects have a first-degree relative (parent or sibling) with a diagnosis of schizophrenia and may be experiencing early symptoms.

To Kamath's knowledge, this is the first study to show that youth at clinical risk are impaired on both odor identification and odor discrimination, similar to observations of adult schizophrenia patients.

These findings are important, says Kamath, because they may represent a genetic marker not only of vulnerability for schizophrenia, but possibly of a neurodevelopmental biomarker associated with the actual development of psychosis.

Kamath's work draws on insights from her research on the First Episode Psychosis Project, a five-year study focused on the longitudinal changes that occur over the early course of psychosis. Led by Johns Hopkins Schizophrenia Center Director **Akira Sawa**, the study examines how aberrant brain changes in late-adolescence contribute to the onset and early progression of schizophrenia.

Vidya Kamath adjusts electrodes on a research assistant's head in preparation for measuring cortical responses in the brain as the subject describes an odor. Sniffin Sticks (foreground) are also used.

Typically, Kamath and her team see two research participants a week. A thorough olfactory evaluation includes measures of odor identification, detection threshold, discrimination and judging the pleasantness or unpleasantness of an odor.

In this most recent study, using Sniffin' Sticks odor identification and discrimination tests, Kamath and her colleagues found that patients and relatives were impaired on odor identification, but odor discrimination impairment was limited to the patient group. In these patients, olfactory impairment was correlated with negative symptoms, such as flat affect.

A similar pattern emerged in at-risk youth: Genetic-risk youth were impaired on odor identification, while clinical at-risk youth were impaired on both tasks.

"When you're looking for biomarkers," says Kamath, "you want measures that differentiate between those who will develop schizophrenia and those who are unlikely to develop the illness. Olfactory dysfunction may be an early warning sign of disease vulnerability. Our goal is to come up with a predictive measure."

That requires rounds of exhaustive tests, Kamath says. Participants are asked to smell an odor and name it. Then she and her team chart the minimum concentration at which they can identify different scents. Finally, participants are asked to rate the pleasantness and intensity of pleasant and unpleasant odors. Other investigators perform a biopsy using a small skin sample from the nasal area to correlate cellular and molecular changes with behavioral olfactory measures.

Many of these at-risk youths, notes Kamath, are also grappling with negative symptoms, such as apathy and social withdrawal. But the ability to predict schizophrenia onset earlier in

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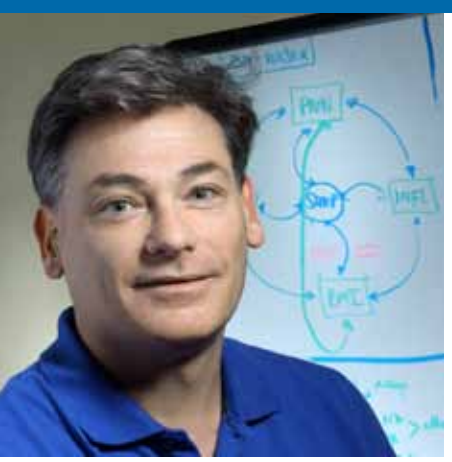
Schizophrenia Center Annual Symposium

Nov. 6, 2015
8:30 a.m. to 2 p.m.

Owens Auditorium
Johns Hopkins Medical Campus
Baltimore, Maryland

This symposium brings together world-renowned experts in schizophrenia and other mental illnesses. Speakers will present their cutting-edge and multidisciplinary approaches, including those in clinical psychiatry and neuropsychology, molecular and system neuroscience, as well as public outreach. Registration deadline: Oct. 23, 2015.

Learn more: **bit.ly/Jhschizophrenia symposiumdetails**.



Sleep loss, says Michael Smith, impairs pain modulation, "but treating insomnia in the short term can keep pain at a manageable level."

Insomnia Makes Pain Worse: New Hope for Patients with Knee Osteoarthritis

Sleep disturbance isn't merely a *consequence* of pain, says Johns Hopkins sleep researcher **Michael Smith**. "Insomnia makes pain *worse*." This is especially true, he adds, in patients with knee osteoarthritis (OA), 81 percent of whom report having trouble maintaining sleep.

A recent study Smith spearheaded, however, shows that cognitive-behavioral therapy may improve both insomnia and clinical pain. Published in the May 2015 issue of *Arthritis and Rheumatology*, the study is the largest to date examining the effectiveness of cognitive behavioral therapy as a sole treatment for insomnia related to chronic pain and the only study that's included polysomnography—tests to diagnose sleep disorders–among the outcome measures.

Smith and his colleagues conducted the randomized, double-blind, active placebo-controlled clinical trial with 208 participants in four groups: people with insomnia and OA; people with joint problems only; people with insomnia only; and healthy adults with neither disorder. Seventy-two percent of the participants were women.

The active treatment Smith and colleagues used was a standardized cognitive behavioral therapy intervention that included sleep restriction therapy, stimulus control therapy, cognitive therapy for insomnia and sleep hygiene education. For the control, they used behavioral desensitization, which Smith says was shown to be a credible placebo in a primary insomnia study. In addition to using in-home polysomnography, the researchers measured outcomes with sleep diary assessments and sensory tests of pain modulation at baseline, post-treatment, three months and six months.

Results showed that patients in the cognitive-behavioral therapy group had significantly greater reductions in wake

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Quincy Samus, left, reviews a patient's care plan with memory care coordinator Kelly Marshall outside a client's home.

"This program has the potential to reshape current dementia care delivery by linking medical and community-based care services."

—CONSTANTINE LYKETSOS, DIRECTOR, THE JOHNS HOPKINS MEMORY AND ALZHEIMER'S TREATMENT CENTER

Making the Most of Dementia Care at Home

From the moment the care team stepped into the private home, they saw signs of dementia. "There were so many piles of papers," says **Quincy Samus**, a Johns Hopkins behavioral gerontologist, "that the team [which includes a dementia care psychologist, nurse and occupational therapist] had difficulty finding a path into the living room."

A team member had received a call from a distraught woman whose father, a retired lawyer recently diagnosed with dementia, refused to discard any papers, official or otherwise. Concerned about his escalating paranoia, the daughter, who lives out of town, called the Johns Hopkins program.

Called MIND (for maximizing independence) at Home, the comprehensive program assesses the needs of people with memory disorders living at home—and those of the family caregivers. It aims to keep patients at home longer, a preference for most of them, and to reduce unmet care needs, such as evaluation of home and personal safety, and management of neuropsychiatric issues.

Currently, about 35 million people worldwide have dementia, says **Constantine Lyketsos**, director of the Johns Hopkins Memory and Alzheimer's Treatment Center, and that number, doubling every 20 years, is projected to reach 115 million by 2050. To help address what he calls "this staggering reality," Lyketsos and Baltimore philanthropist Roy Hoffberger conceived MIND at Home, which debuted in 2012 as a $2.5 million privately funded pilot study.

Led by Samus and Lyketsos, the 18-month clinical trial included 303 participants, ages 70-plus, with dementia and mild cognitive impairment and 290 caregivers. A dementia care coordinator came into each home to address living and care issues before they could spiral out of control.

At least once a month, MIND at Home coordinators contacted households, checking on home safety, medical and mental health care, nutrition and food availability, as well as whether patients were participating in meaningful activities, like exercise or regular interaction with a friendly visitor. Based on needs, the program provided referrals to day programs, education, informal counseling and problem solving.

At 18 months, study participants who received these interventions were likely to remain at home—nearly two months longer than participants who received usual care. This gain extended to an average of about nine months when follow-up continued for up to 41 months. In other words, says Samus, "we were able to help people age in place, and without sacrificing their quality of life."

"We don't pretend we can keep people with dementia in their homes forever," says Lyketsos, "but for much longer than expected—all because we can link those in need of care to appropriate resources and services." Most contacts were phone-based, he notes, addressing problems like nutrition, which implies that benefits can be achieved in a cost-efficient way.

Though the study hasn't calculated cost savings, Lyketsos says delaying admission to a nursing home or a rehab facility likely saves families thousands of dollars.

But the most satisfying outcomes, says Lyketsos, have been patients' improved self-rated quality of life and the benefits to caregivers. The pilot study showed that the program over time freed up as much as 16 hours of caregiving time per week compared with control caregivers.

So successful was the trial, says Lyketsos, that its leaders were able to obtain $9.8 million in additional government funding to find a better and less costly way to keep dementia patients at home. Now he and his colleagues are working to package MIND at Home as an affordable commercial product tailored to diverse clinical, socioeconomic and racial populations.

In the former lawyer's case, the team met with the family and enlisted the help of a professional organizer. "Over time," says Samus, "we saw major changes."

Whether it's regulating the temperature at home, making sure the patient is groomed or sending a nurse to investigate a potential urinary tract infection, "there's always something we can do to improve enjoyment of life" says Samus. "It's been extremely rewarding." ■

Worthwhile Results

The study shows that the MIND at Home intervention

- is feasible
- is low-risk (no intervention-related adverse events)
- can delay transition out of the home
- reduces unmet care needs
- improves self-reported quality of life

Learn more about the program at mindathome.org. Watch a video **bit.ly/MINDatHomeoverview**.

Insomnia

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time after sleep onset. In that group, most patients also reported significant and comparable reduction in pain over six months—with a third reporting a 30 percent reduction in pain severity. Furthermore, diary and polysomnography measurements of sleep improvement predicted decreased pain at each study end point, indicating, says Smith, that better sleep has at least some beneficial effects on pain.

Smith considers these findings strong evidence that cognitive behavioral therapy should be used as a first-line treatment for chronic insomnia in most patients with knee osteoarthritis. "The best part," he adds, "is that there are relatively minor side effects associated with CBT-I, unlike many sedative hypnotics, which put older adults with knee problems at risk for falls and hip fractures." ■

Learn more about Johns Hopkins Medicine's behavioral sleep medicine clinics: **hopkinsmedicine.org/psychiatry/sleep_clinic.html or call 410-550-6337**.

Schizophrenia

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its course—through nasal clues—can open the door to further interventions, sooner rather than later. These include social and community support and low doses of medication to lessen the severity of symptoms.

The next step, says Kamath, is to look at electrophysiological responses to odors to examine whether at-risk youth display neurophysiological impairments in early olfactory sensory processing.

Meanwhile, with each suspicious finding in patients at risk for schizophrenia, says Kamath, "the most important question we can ask is, how do we help those who have the illness improve their quality of life?" ■

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