

## Dementia: More Than Memory Alone

*Therapy? For now, we make the best of what we've got.*

**F**or a week, a frail woman in her 80s has waited just inside her room, ready to sock anyone coming through the door.

A 72-year-old man wakes up at night and, seeing a stranger in his bed (it's his wife), he flees the house, clutching a blanket.

"We used to think some people with dementia might be spared psychotic or mood symptoms," says psychiatrist **Constantine Lyketsos**, "but now we know that's not the case."

Lyketsos has made a career point of investigating the hallucinations, agitation, depression, apathy, sleeping and eating disorders—the especially difficult face of Alzheimer's and other dementias—that arise in the course of disease. For some 14 years, he's headed Hopkins' arm of the seminal Cache County study that monitors an apparently healthy subgroup of Utah residents who slip into dementia and decline. And as director of the new Johns Hopkins Memory and Alzheimer's Treatment Center (column, right), Lyketsos is quick to apply what's found, as are his colleagues.

The last few years, however, have brought discouraging news for these patients. Recent Cache County work showed that most of the just-diagnosed get neuropsychiatric symptoms—delusions and depression, especially—in as little as 18 months and, worse, that all have them within five years. Added to that are recent FDA warnings for some antipsychotic drugs often used for the problems.

Given the aging population and the huge damage these symptoms wreak, "studies that

better the ways we use existing therapies for neuropsychiatric symptoms or that search for new ones are *crucial*," Lyketsos says.

If, for example, psychosis or agitation pulls at life's seams, the Hopkins clinicians have had to weigh risk against benefit more rigorously for traditional antipsychotics. With them, the mortality risk is real. At the same time, national studies Lyketsos co-authored justify their use, especially for persistent agitation that plagues patients and tries caregivers. "So we use a much higher standard for the drugs,"

A new \$7.8 million NIH grant to try the safer antidepressant citalopram could tell if that's a solution.

At the same time, there's renewed emphasis on good practice—routinely ruling out urinary tract infections, for example, that can spark swift changes in behavior, or considering environment. One such example: An observant nurse discovered that a patient who punched visitors had accidentally bumped her thermostat to an uncomfortable high.

Also, there's no substitute for

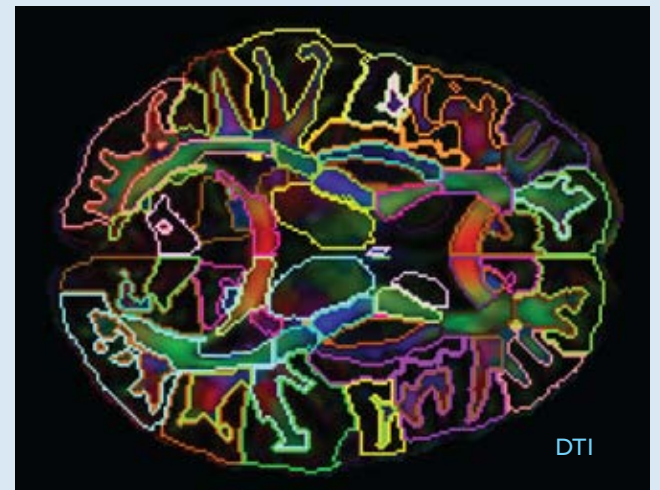


says Lyketsos, "and pick our patients very carefully."

Because earlier research alerted the clinicians to antipsychotics' drawbacks for AD patients, they're now testing alternatives. Hopkins trials proved antidepressants' worth for Alzheimer's patients with major depression. "We're hoping they could also step in for antipsychotics to treat agitation," Lyketsos adds.

training caregivers or having a 24-hour help pipeline in place, Lyketsos says. He recalls phoning a woman whose now-agitated husband had loved Greek dancing. A little bouzouki music at sundown, Lyketsos suggested, might work wonders. The husband grew calmer at nighttime awakenings. ■

*For information: 410-550-6337*



Neurophysicist Susumu Mori's atlas of the brain's white matter helps reveal early dementia's telltale losses.

## Synergy At Last

Hopkins' Memory and Alzheimer's Treatment Center is new, just opened last fall, and it's something of a phoenix—having risen, not out of ashes, but from a welter of clinics, patient units and research projects across three departments and as many campuses. "We kept bumping into each other while Alzheimer's explodes as a public health problem," says **Constantine Lyketsos**, director of the center. Yet with ample clinic space now available on Hopkins' Bayview campus and funding freed up, the value of sharing what's best became amazingly obvious.

While the center still spans Hopkins Hospital, Bayview Medical Center and The Copper Ridge Institute in Sykesville, it now pools expertise. Diagnosis, therapy, dementia care—as outpatient, intermediate or long-term—and experience in educating caregivers continue but without duplication.

Benefits to research are clear. "If you see enough patients under clinical care—our objective for next year is 1,000—a substantial number enter studies, raising our ability to find cures," Lyketsos explains. But the new center isn't research-driven, he points out. "We offer a continuum of care from diagnosis to death whether or not patients are in a research protocol. We're likely unique in the extent of that. Our studies are grounded, however, in that top-shelf clinical care."

What Lyketsos calls "little pieces of added value" are typical:

- When an Alzheimer's diagnosis is especially difficult, center clinicians apply advanced imaging techniques originally developed for research. Working with radiologists, they've developed a dementia-specific protocol for the 3 Tesla MRI scanner. The scanner's high magnetic field strong-arms needed resolution into images—enough, for example, to detect microbleeds that underlie some dementia. Combining this with more traditional PET scans brings a new capability to expose brain damage. Combined MRI and PET make diagnosis more trustworthy.

- With Alzheimer's being a most demanding disease, ongoing care is hard to do well. Years of research and patient contact has let center staff develop the Johns Hopkins Dementia Care Needs Assessment, an 86-item checklist and explanatory manual: *Is it time to stop driving? Are you on too many medications? Are guns in the house?* The approach keeps patients and caregivers from falling through the cracks. ■

### Womb With a Whew:

Can stress in utero play a part in obesity?

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### Desire, Pixellated

Intriguing clues to anorexia's inner drives

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### When Gender Doesn't Sit Right

Hopkins clinic aims to ease psychic pain.

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Creative Alternatives wraps around the sickest of patients.

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# Desire, Pixellated

Visual clues to anorexia's biology may guide future therapy.

Two young women of similar age and education undergo separate sessions in an MRI scanner. For both, the words *bacon* and later, *celery* flash before them. But there the similarities end: One woman finishes, saying, "I'm *hungry*." The other, however, reports a rising sense of anger and rage at the first word, peace and calm at the second.

"We've long approached eating disorders with a focus on the *meaning* of patients' behaviors," says psychiatrist **Graham Redgrave**. An example might be young women saying a need for control underlies their bingeing and purging. But newer studies, he says, examine the behaviors themselves.

"We see them as motivated by something fundamental in the brain," he explains. They could stem, in part, from a genetically paved predisposition to slip into certain circuits, from hormonal differences or a number of things biological—all with environment involved and none, as yet, confirmed.

In a field where therapy has come from trial and error, the push now is to understand eating disorders' basic science. So Redgrave hopes first to confirm the affected brain areas. His most recent study, for example, aims to map the seat of the two desires that consume people with anorexia nervosa: wanting to be thin and wanting not to be fat. Though this work is very much a pilot study with its six patients and six controls, the results are interesting, he says; and are driving more work.

But how do you translate desire accurately into an image? Today, functional MRI images brain activity in a way not possible a decade ago. Yet imaging what's meaningful is fraught with problems:



Graham Redgrave's fMRI work is a first: Nobody's used it before to show potentially key brain areas for what drives anorexia.

Thoughts around food are complex. They often trail clouds of confounding personal memories. *Birthday cake. Brussel sprouts.* To try to get at the core, then, Redgrave turned to the Stroop task. Devised in the 1930s, it involves a simple activity that requires attention. Show test-takers the word *red* printed in blue and ask that they select the blue push-button from four others. Measure how quickly. Vary the colors and words.

The value in the Stroop is that words with emotional significance cause people to pause a heartbeat before pushing the button; it's a nice, quantifiable property called the Stroop effect. While they were in the MRI scanner, both long-term anorexia nervosa patients and controls viewed colored, potentially loaded words such as *gaunt* or *burger* interspersed with

neutral nouns like *stapler* or, more simply, four Xs.

A clear Stroop effect surfaced only for patients. And the resulting images revealed two brain sites of interest. One, active in patients seeing the "thin" words, is an area used in language, craving and task-planning. A second distinct planning area was active only in the controls when they viewed "fat" words.

"Drawing conclusions isn't always wise in a small study," says Redgrave, "but one possible idea is that food matters more to healthy people and thinness matters more to patients."

If broader studies show that the brain area holds true for very ill patients, more work could show if activity there fades with treatment. Eventually, says Redgrave, we may be able to tell who does best with a therapy—a holy grail of sorts in his field. ■



Fatty ratty: stress and/or diet could be at work, says Tamashiro.

## Birth of a Ration

In 1944, after the Nazis blocked supply lines, Holland suffered a famine that, naturally, affected that country's pregnant women. As the war ended, newly born but underweight babies were able, at last, to have normal nutrition. But ultimately, all was not well. A follow-up years later found a high proportion of the "famine babies" had become obese adults suffering diabetes, hypertension and cardiovascular disease.

Psychiatry's **Kellie Tamashiro**, in Hopkins' Behavioral Neuroscience Lab, says that example has partly informed her research to understand what's behind the tripling of obesity worldwide in the last 30 years. "Like the Dutch situation, some specific interplay of environment and behavior is at work. It has to be more than genes."

Intuition says *it's basically behavior: Everybody knows people now eat more and exercise less.* But that's not as precise as translating a specific environmental factor or eating behavior into metabolic pathways gone wrong. And that, she explains, is where her studies are leading.

Tamashiro focuses on the effects of having less-than-optimal environments

either in utero or just after birth. A solid body of animal research and human epidemiological studies suggest that such early problems create adults who avoid mirrors and populate hospitals. It's called the Barker hypothesis: A bad early environment somehow sets metabolism to favor later obesity and diabetes.

Most existing research has centered on giving pregnant rats too-high or too-low nutrition. But Tamashiro has taken it a step beyond diet to factor in effects of added stress. She aims to reflect the human condition in inner cities where obesity is epidemic.

"In 1944," Tamashiro explains, "the Dutch babies' bodies were programmed to be more efficient than normal at saving energy." Animal models shore this up: Short-changing maternal diet does indeed lead to obesity as pups mature. But the other extreme is true as well. An ultra-high energy diet during pregnancy also brings problems: In Tamashiro's latest study, mother rats on fatty animal chow produced lardy pups at risk of abnormal adult metabolism.

That study helped clarify underlying physiology. Starting with pregnant

rats fed high-fat chow, Tamashiro noted that as little as a month after birth, their fat pups—also high-calorie noshers—had the elevated levels of the leptin hormone that parallels onset of metabolic disease. And glucose intolerance that foreshadows diabetes had also begun.

But stress, she found, did the same thing—unsurprising, she says, because the neural pathways that regulate mammals' stress responses are also active in guiding metabolic balance. So pregnant rats mildly upset by varying stressors such as bright lights or small quarters also have high-risk fat pups. It's these early changes, she says, that may prime animals—or humans, perhaps—for later disease.

"Of course, it's dangerous at this point to generalize to people," Tamashiro adds, acknowledging her work as a step. "But it still lets us hope that intervening early in life could sidetrack disease." For example, plump rat pups kept to a healthy diet, she found, see their sluggish metabolism even out. If future studies would lead to low-stress-pregnancy programs in inner cities or more enlightened infant formulas, all the better. ■



## An Eye on Suicide

Her tactics are as broad as improving education—repeatedly coaching residents to recognize gathering clouds of violence in patients or to assess suicide risk. Or they're as pointed as telling observers to make sure at-risk patients' hands are in full sight.

Recently, however, partly because Hopkins' Peter Pronovost put a systems approach to medical safety in the national spotlight, but also because there's institutional support, Jayaram and colleague Jeff Janofsky (below) initiated more formal steps to reduce suicide risk. While colleagues in surgery locked in new protocols to stop wrong-site operations, for example, Psychiatry has adopted the proactive FMEA (failure mode and effects analysis) approach to safety.

Last fall, a rare brainstorming session with unit nurses, social workers, occupational therapists, physicians and patient observers let them pinpoint and rank 91 things routinely done or left undone that could put patients at risk.

What did they designate as the weakest link in suicide prevention?

As new chair of the American Psychiatric Association's patient safety committee, Jayaram's in a good place to explain:

52,712. That's how many patients have passed through Hopkins hospital's psychiatric inpatient units since 1979, amassing what surely must be some kind of record for a large inner-city medical center: no suicides.

"We don't know that ours is a record; we're looking into it," says psychiatrist **Geetha Jayaram**. "but it would help confirm what we believe, that steps we're taking are right ones to keep patients safe."

Jayaram has been instrumental in that safety. For 19 years, she's worked to improve the overall welfare of those on the Meyer units under her administrative and clinical care, giving equal weight to their status as both patients and sufferers of psychiatric illness. As the psychiatry department's physician advisor, a gritty role that, in part, demands scrutiny of anything gone wrong, Jayaram has pushed for built-in safeguards and review. She embraced root cause analysis—solving problems by digging down to an incident's source—before it became routine.

**Suicide is, of course, a horror and a wound to humanity. But there's value in viewing it dispassionately.**

As a signal, you mean? Yes. You learn quickly, when seeing different hospitals as a consultant, that an inpatient suicide is the tip of a wedge. The base reflects a system that's damaged.

**What has helped Hopkins so far?**

In part, I think, a lot of looking over our shoulders. We've tried to address every problem area the Joint Commission has singled out. So you assess patients thoroughly and often. All at-risk patients who come on the unit are immediately held under heightened observation, for example, until there's collateral information to help us evaluate them. Our attending physicians must interview every patient daily and write notes. Also, we've created a patient safety plan that our nurses use to rate risk of violence. It lays down defusing tactics, should the need arise, that partly come from asking patients, *How can we make you feel calm?*

**What else?**

Hopkins has intense sit-down rounds that involve a patient's entire treatment team. When the occupational therapist tells you, *I saw Mr. Jones today and he talked a great deal about death*, that's crucial. And you hit home that every visitor, even

VIPs, are treated politely but as potential sources of lethal agents. A security guard oversees each unit.

**Close calls?**

Yes. Every hospital has them. Fortunately, there are few enough for me to remember them all. Determined patients can think of a million things: One patient snatched a trash bag and put it over her head, even as an observer was watching. We've eliminated trash bags.

**Which brings us to the brainstorming session. What was the weakest link?**

It centered on the observers, those hired to keep varying degrees of watch on patients at risk. We all agreed, even the observers, that communication between them, nurses and patients wasn't always clear and orderly. Now observers are vetted and trained by nurses. We document hand-offs to the next shift. And everyone's patient observations are set down electronically.

**So your aim is a culture of safety.**

Yes. It's a shift in thinking to see errors properly as flaws in the system. You remove processes that rely on employee endurance or memory. You stop blaming and shaming people. That frees everyone to become truly invested in patient care. ■

For more information: [gjayara1@jhmi.edu](mailto:gjayara1@jhmi.edu)

## Preventing Suicide May Stem From How We Watch

Since 1995, when this country's Joint Commission charged hospitals with reporting sentinel events as part of being accredited, inpatient suicide on medical and psychiatric units has been the second most common hospital error, after wrong-site surgery. "Though the numbers of hospital suicides are still tiny," psychiatrist **Jeffrey Janofsky** told a Psychiatry grand rounds gathering last month, "any are obviously too many."

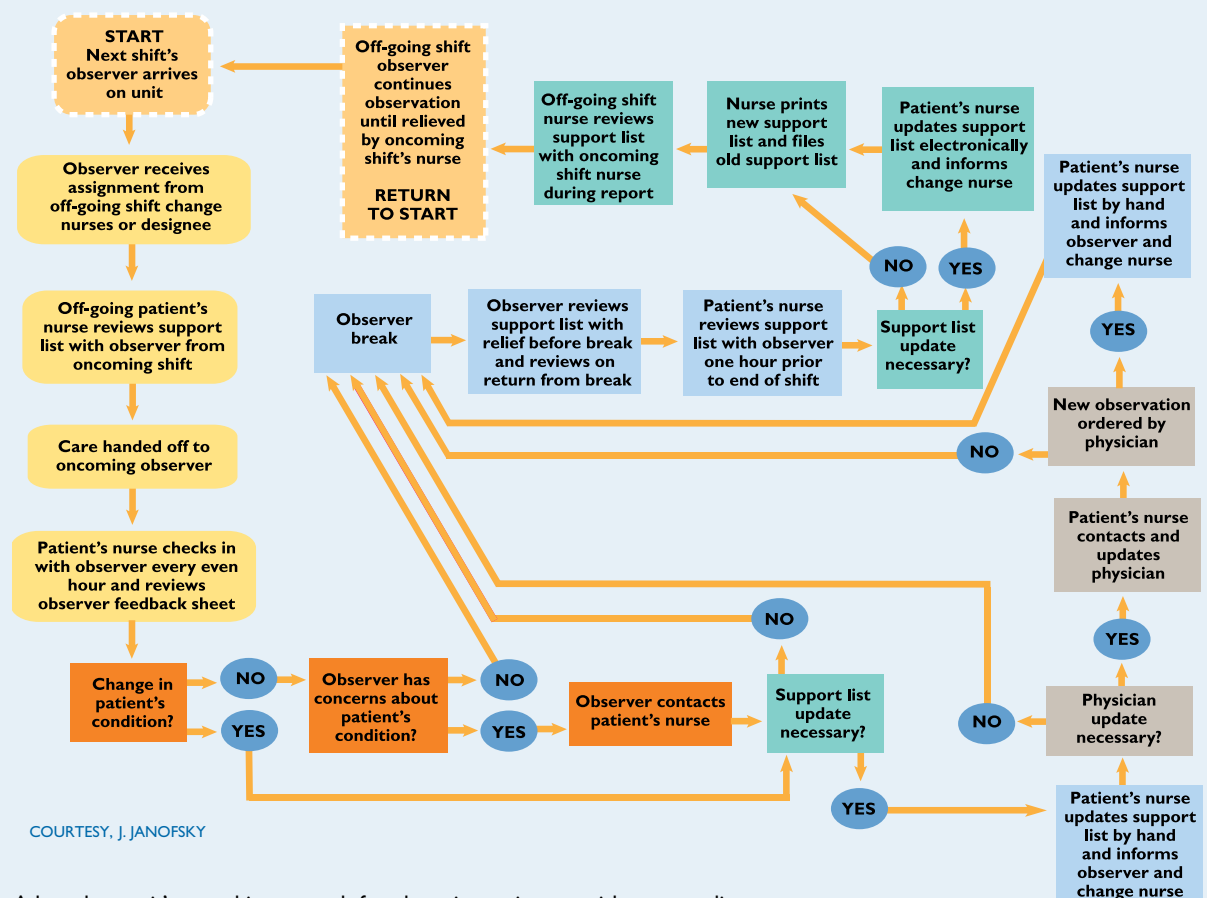
What to do? Results of a recent Harris poll said the general public believes it's mostly a matter of singling out those health care providers who're "at fault," while using better training and malpractice or licensing litigation as medicine's uplifting and punishing arms. But the nation's Institute of Medicine—and Janofsky and his Hopkins colleagues—think otherwise. "We've come to realize that medical errors are best reduced by improving the system and not by focusing on individual errors," he says. And being proactive is key.

To that end, the psychiatry department is first targeting a weak link, namely, the way at-risk patients are monitored on hospital units: deciding who's monitored and how best to monitor, all while improving communication between observers, nurses, doctors and patients.

It's the system that takes the heat.

Recently, Psychiatry put three solutions in place:

- They analyzed the monitoring process and standardized it (see right) to make it turn less on vigilance and memory and more on communication.
- Nurses and observers now write computerized patient notes for each other at each shift change and at set intervals.
- A new feedback form documents observer impressions and suggestions.



COURTESY, J. JANOFSKY

A board game it's not; this new path for observing patients at risk can save lives.

## Whatever It Takes

*Creative Alternatives refuses to let illness define patients*

There's a groundedness about Quentin Fisher that's disarming, a quiet certainty about where his life is going that would be uncommon even outside of a place set up for some of a city's sickest patients.

The Baltimore man wouldn't hesitate to say that he's centered, in large part, from his connection with Creative Alternatives, a program that, for 14 years, has wrapped around people with enduring mental illness, resolutely blanket-ing them with support until their lives improve.

The Hopkins program defies the usual approaches nationwide.

Fisher had been living with a foster family when his schizophrenia led to a five-year stay at Spring Grove state psychiatric hospital. He grew better under therapy and the constancy of medication; his illness was attended to. "But I didn't have anything to hope for," says Fisher; "they weren't so interested in where my life was going. I wanted to work. And I wanted to *do* something."

When he'd improved enough for discharge, a Creative Alternatives interviewer laid out the benefits of coming to their voluntary program, which now serves 175 "members" from Baltimore city. "Creative Alternatives is based on hope," says Program Manager **Sheila Goldscheider**, R.N. As its name implies, CA offers a change from the constant cycle of hospital visits, returns to psychiatric institutions, being on the street or in jail that often dogs those with persistent schizophrenia, bipolar disorder or unrelenting major depression.

"We're the proverbial one-stop shopping," Goldscheider explains. When Fisher first came to CA in 2006, for example, a personal service coordinator sat him down: *What do you want to do with your life?* Then she and other staff



Sheila Goldscheider was one of the first to spot a spark in Quentin Fisher.

united as Team Fisher, working with the 42-year-old to lay paths to his goal: to live independently and have a job.

CA has a Hopkins psychiatrist and psychotherapist to keep Fisher and other members on an even keel, medically. There's substance abuse therapy. A housing coordinator aims for the best fit between living quarters and personal need. An entitlement coordinator helps members with Social Security, medical assistance and such. The community integration person engineers ways to let members grow roots, arranging shared dinners or TV evenings, for example, if they live close to each other. Other staff teach life skills: getting along, shopping, cooking, keeping house, sticking to a budget. CA once set up a tab for a member at a lunch counter in Fells Point and got him a subscription to a nearby community theater. "We have fun," says Fisher.

"We try to be 'real world,'" Goldscheider says. "And we do whatever it takes."

As for Fisher, his self-esteem shot up after he took and passed a community college course in

real estate. Then CA's employment staff helped him find and hold a job. Currently, some 17 percent of members work—good stats for that population.

CA began in 1993 as a demo project within Hopkins Community Psychiatry program at Bayview, a response to a request from the state of Maryland for capitated services for the slip-through-the-cracks group. It hasn't disappointed. "In addition to meeting our goals to turn peoples' lives around," Goldscheider adds, "we've saved the state money hand over fist." State hospitals are hugely expensive to run.

A required independent review each year gives CA highest marks. *Do more members live independently? Are they content? Are hospitalizations down?* Success comes from the relationships built with members, Goldscheider says. "We often see if things are wrong before they can themselves. We become family." Fisher says it best: "I've been helped every moment I've been here." ■

*For information: 410-631-6021.*

## A Beautiful Partnership

The scientist and the beauty queen. It's a fine match.

Psychiatrist **Gerald Nestadt**, who heads the Hopkins hunt for genes underlying obsessive compulsive disorder (OCD), has made the quest for targets for therapy his life's research. Peers say Nestadt's studies are impeccable; his team is making headway.

**Linda Marshall** is a beauty queen, though in a broader sense. Attractive, accomplished, she heads Elysée Scientific Cosmetics, Inc. Their president since 1975, she's shepherded the family-run company to become a successful corporation with discerning, loyal customers nationwide.

Marshall has seen no conflict between high standards and prosperous business. Case in point: she quit an early job in the business after the owner said *It doesn't matter what we put in our bottles; Women just want hope.*

Elysée's products contained natural antioxidants long before their buzz-word status. A portion of sales underwrite a program to bring beauty to women recovering from breast cancer.

Since 2002, with her real and "second family"—generous industry colleagues—Marshall has raised roughly half a million dollars for Nestadt through *Beyond Beauty*, what she calls the elegant, celebrity-endorsed dinners that advance OCD research.

Her altruism is deeply personal. "Once, I had no idea what OCD was," she says. Her oldest son, James, spent an inordinate amount of time on grooming—every hair checked twice—even for a teenager. Before he married, there were fears of food contamination, a possible segue into the anorexia he disguised well under three layers of clothing and jolly reassurances.

Two things burn in Marshall's memory of her son's last conversation. "I will always carry my love for all of you in my heart," he said, and, "I do so want to make a difference."

Marshall and her family founded the James E. Marshall OCD Foundation in 2003, with help from the cosmetic industry. They've already made a difference. ■



We call it *Beyond Beauty* says Linda Marshall, because we tap the beauty inside.

## Hopkins **BrainWise**

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Department of Psychiatry  
100 North Charles Street, Suite 410  
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**Keith Weller**, Photography

Editorial Office  
901 South Bond Street, Suite 550  
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