

The Sleep Center Is 'Booming'



Rachel Salas and Charlene Gamaldo bring an uncommon perspective to a common problem.

approach to sleep medicine, a young discipline that has only recently been acknowledged by the American Board of Medical Specialties. Once the sole domain of pulmonologists, sleep medicine now involves neurologists, psychiatrists, otolaryngologists, pediatricians and even dentists.

"What's really interesting about sleep medicine is that by having those different backgrounds, specialists can bring their unique perspective to the research and clinical aspect of sleep," says Assistant Director **Charlene Gamaldo**, who was recruited in 2006 as the first neurologist at the Sleep Disorders Center. She was joined two years later by neurologist **Rachel Salas**.

Sleep apnea is one of the most common reasons patients are seen in the sleep center. People with sleep apnea stop breathing repeatedly during the night, often waking up multiple times without being aware of it. During each apnea event, their lungs collapse like a deflated balloon, and blood oxygen levels can drop. "So in the morning, they don't feel rested and restored because throughout the night, they're basically suffocating," says Gamaldo. Not only

does sleep apnea result in extremely fragmented and poor-quality sleep, it may be linked with risk factors for heart disease, hypertension and stroke.

Most often, patients are diagnosed with a combination of sleep issues. "We treat patients with narcolepsy, restless legs syndrome, periodic limb movements, circadian rhythm disorders," says Salas. "Many patients who come in for sleep apnea end up having one of these other conditions. We tackle the whole picture."

They start by performing a thorough sleep history on each patient. If they suspect sleep-disordered breathing, they may order a sleep study. In that case, patients spend a night at the center, bringing along

Sleep: the Next Vital Sign

Most people don't associate a hospital stay with a good night's rest. Hospital staff, beeping monitors and other disruptions can disturb patients at all hours. And sleep deprivation is not only annoying. It's been linked to increased blood pressure and anxiety, and can affect immune function and pain tolerance.

Charlene Gamaldo and Rachel Salas, together with Sleep Disorders Center Director Nancy Collop and other members of the neurology faculty (Robert Hoesch, Romer Geocadin and Katherine Thomas) are aiming to improve patients' sleep by studying environmental sleep disorders in the hospital as part of an initiative dubbed Sleep: The Next Vital Sign.

"We're looking at things that could be modified to improve patients' sleep and maybe even decrease their length of stay in the hospital," says Gamaldo. Modifications they're investigating include designated quiet time, requiring that pagers be turned to vibrate, and having volunteers do "sleep rounds" to help patients get to sleep. "By improving quality of sleep in the hospital and improving patient satisfaction," says Salas, "we'd be hitting two birds with one stone." ■

their usual things from home, like their toothbrush and pajamas. In a private room, they're hooked up to EEG leads on their head and face to monitor muscle tone and eyelid movements, and to other monitors that examine airflow, respiratory efforts and leg movements.

Sometimes, a patient presents such a textbook case of sleep apnea that it can be diagnosed in a couple of hours. Treatment is often the therapeutic CPAP breathing device, which stands for continuous positive airway pressure.

"If we suspect a patient may possibly have narcolepsy or idiopathic hypersomnia [sleepy all the time for no apparent reason], we do an overnight sleep study followed the next day by a series of nap challenges so we can gauge the degree of sleepiness," says Salas. No matter what issues a patient comes in with, treatment always includes not only diagnostic components, but education and counseling as well.

"As physicians and particularly as neurologists, we may not always have a cure or treatments for the medical conditions that we diagnose," says Gamaldo. "But that's not the case with sleep medicine, which now offers excellent options—ranging from behavioral,

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Are you already on your third cup of coffee this morning? Can't remember a time you felt well-rested? It's no wonder: We're a sleep-deprived society.

Most Americans get less than seven hours of sleep per night, according to the Johns Hopkins Sleep Disorders Center. Yet current research indicates most people require seven and a half to eight and a half hours of sleep nightly to function their best—emotionally, cognitively and physically. Furthermore, sleep deprivation can magnify the severity of other sleep disorders, including sleep apnea and restless legs syndrome.

The Sleep Disorders Center takes a wide-ranging

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Like so many medical subspecialties, neurology and neurosurgery remained for decades the near-exclusive domains of men. Yet, even the most casual glance at this issue of *NeuroNow* shows that at Johns Hopkins, such is hardly the case today.

In fact, the physicians and surgeons we feature in these pages represent only a smattering of the women on our faculty, and at that we're able to give only a glimpse of the clinical and research contributions these outstanding doctors are making. To cover the full spectrum of the work of all our women colleagues would require something more akin to a book than a newsletter.

Still, we are confident that you will enjoy the articles we present here. Besides reading on the cover about the ways Charlene Gamaldo and Rachel Salas are bringing their expertise to bear on disordered sleep, be sure to take note of the path-breaking stroke research (story, right) of Argye Hillis and Rebecca Gottesman and how that connects to the surgical intervention provided by Judy Huang. In the clinic and in the lab, Jaishri Blakeley and Lori Jordan are making strides against the potentially devastating inherited disease neurofibromatosis (page 3). And make no mistake: The brain cancer research now being led by Betty Tyler (page 3) is first-rate.

Finally, if you're tempted to think our abundance of talented women is a fluke, don't miss the story on page 4. We are proud indeed that so many of today's up-and-coming neurologists and neurosurgeons have chosen to train with us.

Henry Brem

Harvey Cushing Professor and Director of Neurosurgery

Justin McArthur

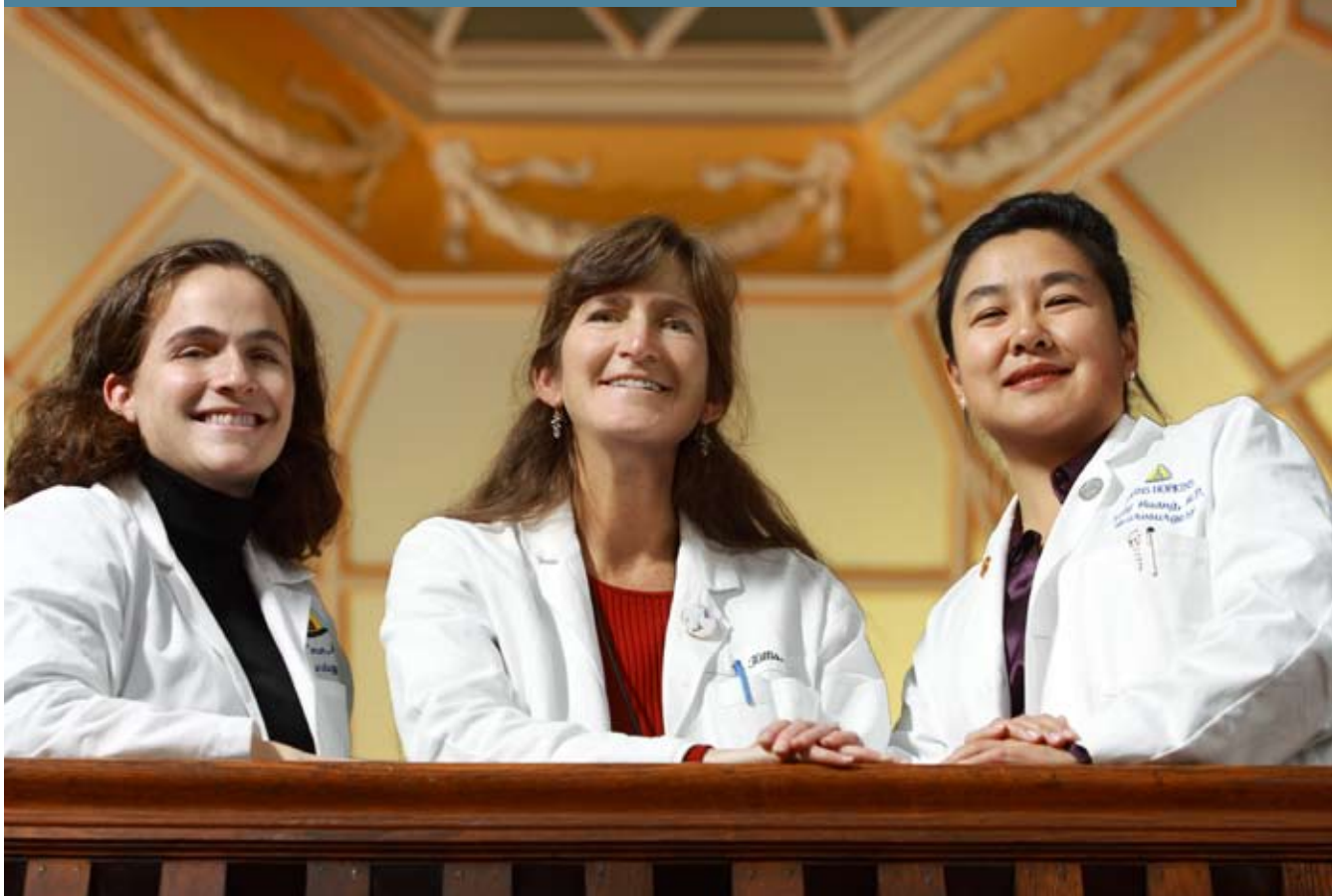
Interim Director of Neurology

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pharmacologic and surgical techniques—for all of the sleep conditions that we treat. In many cases our treatments can even be curative, as in the case of CPAP therapy for sleep apnea or treating iron deficiency in restless legs syndrome. Regardless of the condition, we help patients make considerable improvements in their quality of life and overall well-being." ■

For more information: 443-287-3313 or hopkinsmedicine.org/neuro



To improve outcomes, Rebecca Gottesman, Argye Hillis and Judy Huang are concentrating on less obvious but still devastating consequences of stroke.

A New Take on Two Effects of Stroke

It's one thing to survive a stroke. Recovering afterwards is another matter.

To improve the odds that patients can emerge from stroke with both mind and body intact, neurologists **Argye Hillis** and **Rebecca Gottesman** have been focusing on two sometimes subtle indicators and/or consequences of stroke: aphasia and hemispatial neglect. Though the two disorders have vastly different manifestations—aphasia affects written and verbal language cognition, while hemispatial neglect “erases” visual fields on one side of the body—what they share is the potential to severely affect a stroke patient's quality of life.

Hillis, who was a speech pathologist before becoming a neurologist, says aphasia is an acquired language impairment due to some kind of neurologic brain damage. Most commonly caused by stroke, aphasia short-circuits the brain's language center, leaving some people painfully aware that they can't find the correct words to express their thoughts (Broca's aphasia). Others, with Wernicke's aphasia, have no grasp of their cognitive difficulties. “They think they've asked you to bring them some coffee,” says Hillis, “when they actually said bring me a pillow.”

Hemispatial neglect is no less

confounding. “Some people with right hemisphere stroke tend to ignore things on their left,” says Hillis. “So they don't eat food off the left side of their plate, they don't brush the left side of their hair, they don't shave the left side of their face. They have absolutely no recognition they're doing this. You can even say, Look to the left; have you missed anything? And they'll say, Nope, I think I got everything.”

Hillis and Gottesman see early testing for aphasia and hemispatial neglect as being vital to better overall stroke care. Such tests are generally not part of conventional assessment of stroke risk; physicians instead tend to focus on motor and muscular issues such as slurred speech, partial paralysis and limb weakness. Yet Gottesman notes that the additional testing is quick and easy.

“I found,” she says, “that when you add two simple tests of hemispatial neglect, one looking at visual fields, the other crossing out lines on a page—if people are neglecting, they won't cross out all the lines—you can calculate their error rate and add that to the current NIH stroke scale [a rating of stroke severity]. “I also found that that the combination was a better predictor of the actual stroke volume, as measured by MRI, and functional outcomes

than the NIH stroke scale alone.”

Gottesman hopes that such studies will convince the National Institutes of Health to give more weight to cognitive issues when evaluating stroke outcomes.

While both aphasia and hemispatial neglect respond to various forms of language and ocular therapies, and often somewhat resolve as the brain constructs new neural pathways, the most promising treatment is to bring blood flow back to affected areas. This is where neurosurgeon **Judy Huang** comes in. By testing for aphasia and hemispatial neglect, which can occur from mini-strokes or transient ischemic attacks (TIAs), Hopkins neurologists can bring Huang into the picture before disaster occurs.

“If my colleagues see patients who have symptoms and they're found to be good candidates for surgery—the source of their TIA is a blockage in a carotid artery—they know to call me and I'll do a carotid endarterectomy,” says Huang.

The surgery, which scrapes plaques and potential clots from the artery, greatly reduces the chance of a larger stroke occurring, while the suddenly increased blood flow may lessen or alleviate aphasia and hemispatial neglect. “If all goes well,” says Huang, “the patient can go home the next day.” ■

To Conquer Neurofibromatosis

Neurofibromatosis badly needs a PR campaign. Ask most people to name a disease that's passed from parent to child and their response is likely to be cystic fibrosis, muscular dystrophy, sickle-cell anemia, Tay-Sachs disease—any or all of these pop to the front of the mind.

But not neurofibromatosis. Yet NF, as it's also known, is among the most common inherited disorders, affecting more kids than cystic fibrosis. One in 3,500 children, roughly half of all people who develop NF, get it from their parents.

NF is an extraordinarily challenging disorder for neurologists to treat, partially because it's so unpredictable. NF wreaks havoc on nerve tissue, and NF-1, which accounts for 90 percent of NF cases, can be involved with everything from bone deformities to brain tumors. It's also a capricious disorder: Parents with NF who have nothing more than a few light "café-au-lait" brown spots on their skin can bear children who have exactly their mild symptomology or an exacerbated version of NF that may cause scoliosis, learning disorders, early or delayed puberty, blindness, disfigurement. The list is staggering.

This wide range of potential outcomes makes comprehensive and continuous care a must, which is where Johns Hopkins' Comprehensive Neurofibromatosis Center comes into play. Di-

rected by neurologist **Jaishri Blakeley** and staffed by neurologist **Lori Jordan**, neurosurgeon **Allan Belzberg** and genetic counselor **Amanda Bergner**, the monthly clinic is a one-stop shop for NF care.

"Sometimes we see an affected parent and multiple children," says Jordan, who usually treats pediatric patients and transfers them to Blakeley when they reach adulthood. "These families have all their records in one place, and in one half-day, the entire family can be seen. Coming to the center allows families to streamline their health care."

Although two-thirds of NF-1 cases are mild, many parents, especially after a trip around the Internet, come in fearing the worst for their child. "A lot of what we do is examine the child and talk about what we find," Jordan says. "Most of the time, the child is doing well."

While there's currently no cure for NF, regular visits can limit the impact of emerging physical and mental issues, and Jordan impresses upon parents that continued vigilance is important, even in mild cases.

By catching scoliosis early, for example, "you can intervene surgically before it causes major complications," she says.

For more severe cases where tumors grow along nerves, Blakeley, who specializes in neuro-oncology, works with



Jaishri Blakeley, left, and Lori Jordan say their work with patients and families is equal parts education and medical management.

Allan Belzberg to perform microsurgeries that can reduce pain and functional impairment. Blakeley's medical management of a patient's tumors are critical. Although most NF tumors are benign—and there can be hundreds of such tiny tumors in severe cases—there's still a 5 percent to 10 percent risk that some may turn malignant.

Blakeley is also researching drugs to combat NF-2, the rarer form of the disease that mainly attacks the central nervous system and currently can only be treated surgically. The work has other

potential applications as well. NF, she says, "is a very predictable model for studying nerve structure and changes in structure that happen during neuropathic pain," especially pain that occurs after nerve resection. That work has the backing of a Department of Defense grant, which Blakeley says isn't surprising, because "it matters hugely to soldiers who have so-called phantom pain after amputation."

Controlling amputation pain by studying NF? Now there's something worthy of a press release. ■

BRAIN TUMOR RESEARCH

The Neuroscientist With a Bachelor's Degree

When **Betty Tyler** joined the Department of Neurosurgery as a laboratory technician in 1990, she wanted to do challenging research and to know that the product of her labors could readily be used to help patients. She got her wish.

For the past 19 years, Tyler has worked in the lab of Neurosurgery Director **Henry Brem**, seeking new treatments for brain tumors, including glioma, one of the most intractable forms of cancer. And, little by little, her work has truly helped patients.

Numerous hurdles confront researchers in their search for brain cancer treatments. First, there's the infamous blood-brain barrier, the protective mechanism that shields the brain from toxins and other harm, but also means that scientists can't rely on the bloodstream to deliver brain cancer drugs. Then there is the extremely delicate nature of the brain. An experimental drug might do an extraordinary job of destroying brain tumor cells but kill healthy brain cells as well—and with them, a vital function such as language or vision.

To circumvent the blood-brain barrier, Brem developed a drug-delivery device called the Gliadel wafer. Implanted into the brain during surgery, the dime-size wafer gradually releases a cancer-fighting drug. In the lab, Tyler helped to fine-tune and test Gliadel in animal studies, while Brem applied her findings in patients. Several studies have shown that Gliadel extends patients' lives by several months and increases the percentage of longer-term survivors.

Hoping to do even better, Tyler and Brem then began examining whether adding a second drug might improve their results. One drug they've studied is temozolomide (TMZ). In a recent study, Brem and colleagues in neurosurgery and oncology reported that glioma patients receiving a combination of oral TMZ, Gliadel and radiation therapy lived an average of twice as long as patients receiving only Gliadel and radiation. Tyler is thrilled by these results. "It's very rewarding to see that what you do in the lab can help to improve a person's life," she says.

As the team's research has advanced, so has Tyler's



Working with Henry Brem, Betty Tyler is giving new hope to patients diagnosed with brain cancer.

career. She is now the principal investigator on a study funded by the American Cancer Society that extends her research on TMZ. And in 2005, Tyler, whose highest degree is a B.A., became an assistant professor—a rare accomplishment for a scientist without a Ph.D., but a well-deserved one, says Brem. "When she first came on board, I saw that she was very bright, very analytical," he says. "She's become recognized as a great teacher and mentor to Hopkins medical students and fellows." ■

Breaking Into an Old Boys' Club

During her seven years as a neurosurgery resident, Violette Recinos has frequently been typecast. "I'll walk into a patient's room with a medical student who is a man," says Recinos, "and the patient will assume the student is the doctor and I'm the nurse."

"It's not a big deal." In fact, it's a logical assumption. Women neurosurgeons are a rarity—only 6 percent of all neurosurgeons in the United States. In neurology, women account for a slightly larger fraction, but still only about 22 percent.

Several factors have kept women away from these specialties. An entrenched "old boys' club" mentality is one factor, says George Jallo, residency director for the Department of Neurosurgery. But lifestyle factors—especially long work hours that can conflict with raising a family—have also discouraged some women from even trying to join the club.

Johns Hopkins, however, has been especially successful in recent years at attracting women into its neurology and neurosurgery programs. In this year's senior neurology class, all six residents are women, and the ratio of women in subsequent years is significantly higher than the national average. In neurosurgery, three of 21 residents are women—a minority, but more than in most other neurosurgery residencies.

What's drawn women to these programs?

Recinos knew she would be only the third woman to enter the Hopkins neurosurgery program, but it did not deter her. She had always wanted to be a doctor

and loved studying science, especially the science of the brain. Majoring in neuroscience as an undergraduate at Hopkins confirmed her interest, and when, as a medical student she decided to apply to neurosurgery programs, Hopkins was her first choice.

"It had everything I was looking for in a neurosurgery program," says Recinos. "The residents receive great training by specialists who are at the top of the field. They start operating early in their training, and the research opportunities are limitless. Above all, the faculty and staff are top-notch."

Recinos and other female residents also say their programs have cultivated an atmosphere of congeniality and respect between faculty and residents that has helped all residents.

"The Hopkins neurology program has been incredibly supportive of women in neurology," says Karen Hirsch, who is completing her third year in the residency. Faculty, for example, make it a point to include spouses and children in all social events hosted by the program.

Balancing an intensive medical career with the rest of life's obligations is a challenge, says Hirsch, but she has been encouraged by witnessing the success of the several women who hold senior positions on the Hopkins neurology faculty. Her mentors have included Argye Hillis, who directs the neurology residency program, and Andrea Corse, both of whom are married with children. "They are people I look up to" says Hirsch. "When you see women who do it successfully, it is encouraging." ■



Just a few of tomorrow's Johns Hopkins-trained neurologists: clockwise from left, Rooman Ahad, Melissa Motta, Liana Rosenthal and Yolanda Chik

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Departments of Neurology and Neurosurgery

Justin McArthur, M.B.B.S., M.P.H., *Director of Neurology*
Henry Brem, M.D., *Harvey Cushing Professor and Director of Neurosurgery*

Marketing and Communications

Dalal Haldeman, Ph.D., *Vice President*
Mary Ann Ayd, *Managing Editor*
Mat Edelson, Abigail Green, Melissa Hendricks, *Writers*
Maxwell Boam, *Design*
Keith Weller, *Photography*

Info: hopkinsmedicine.org/neuro

Neurology: 410-516-6250
Neurosurgery: 410-516-6234

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