

neurotransmitter

A MAGAZINE OF THE GEORGE WASHINGTON INSTITUTE FOR NEUROSCIENCE AND
THE GEORGE WASHINGTON UNIVERSITY HOSPITAL'S NEUROLOGICAL INSTITUTE



summer 2017

R

oughly three years ago, the joint enterprises of the George Washington University (GW) School of Medicine and Health Sciences, the GW Hospital, and the GW Medical Faculty Associates (MFA) launched *Neurotransmitter* to highlight our expertise in the treatment of patients with disorders of the brain, spinal cord, peripheral nerve, and muscle. This magazine also highlights our greater mission to address these illnesses through a bold application of basic and clinical research with the intent to turn laboratory discoveries into improved patient care.

Since *Neurotransmitter's* inception, our award-winning publication has covered groundbreaking work in epilepsy treatment using deep brain stimulation, clinical success stories from our Comprehensive Stroke Center, and our innovative use of electronic and magnetic stimulation to treat depression. We have also featured basic and translational science initiatives on Zika vaccines, neural developmental disorders, and the influence of stress on the brain and immune system. One thing we've discovered in these early years of *Neurotransmitter* is that we have many great stories to tell. This edition marks our transition from an annual publication to a biannual format, a continuing effort to further share our successes.

In the pages that follow, you can read about our clinical efforts, such as the MFA's Headache Center, which seeks to ease the pain of patients suffering from migraine headaches, a condition that costs the U.S. economy \$17 billion annually in treatments and lost productivity. There also is the dramatic story of a woman with a 20-year history of back pain who was aided by our Comprehensive Spine and Pain Center. For these patients, the partnership between GW Hospital and the MFA forms a multidisciplinary team to apply modern treatment approaches to optimize care.

Like clinical care, collaboration is a key aspect of discovery. Chiara Manzini, PhD, turned to internet service Gene Matcher to identify collaborators in the United States and abroad to accelerate her work identifying a new genetic variant of muscular dystrophy, a disease that produces muscle weakness, intellectual abnormalities, and cataracts. Also featured in this edition is coverage of basic research conducted by Mary Ann Stepp, PhD, on small nerve fibers of the cornea, which one day will tell us more about neuropathy, a disease of the nerves that affects millions of Americans and produces severe pain.

Beyond our clinical spaces and laboratories, GW continues to fill a leadership role facilitating the exchange of ideas throughout the clinical and scientific world. The GW Institute for Neuroscience hosted recently its annual symposium, focusing on the role of the sensory system in social behaviors. GW investigator Linda Kusner, PhD, led the world's most important meeting dedicated to myasthenia gravis, a devastating autoimmune disease.

Reading these and other stories in the pages of *Neurotransmitter*, we believe it's evident that GW is at the forefront of basic and clinical neurosciences. We hope you agree and that you enjoy a good read.

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THE NEUROSCIENCES INSTITUTE (NI) at the George Washington University Hospital is a premier neurological center. Patients come for comprehensive interdisciplinary care by the Institute's internationally recognized team of experts. The team treats patients for a wide range of neurological problems and provides expert care for patients with the most complex disorders that affect the nervous system. The NI consists of neurosurgeons, neurologists, emergency room physicians, critical care specialists, physiatrists, psychiatrists, neuro-radiologists, neuro-pathologists, and neuro-interventional specialists as well as outstanding allied health service providers in nursing, speech therapy, physical therapy, occupational therapy, and neuro-rehabilitation. The NI combines medical and surgical services, along with research and education, under unified leadership to optimize the health of our patients now and into the future through a multidisciplinary approach, state-of-the-art technology, and innovative treatment trials. To learn more, visit www.gwhospital.com/hospital-services/the-neurosciences-institute-at-the-george-washington-university-hospital.

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Spine Center
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Stroke Treatment Center
Translational Research Center



GW FACULTY MEMBER LINDA KUSNER LEADS INTERNATIONAL CONFERENCE ON MYASTHENIA GRAVIS

Linda Kusner, PhD, associate research professor in the Department of Pharmacology and Physiology at the George Washington University's School of Medicine and Health Sciences (SMHS), co-chaired the 13th International Conference on Myasthenia Gravis and Related Disorders, along with Ted Burns, MD, of the University of Virginia, May 15-17.

The conference, presented by the Myasthenia Gravis Foundation of America and the New York Academy of Sciences, provided a forum for basic scientists and clinical researchers to discuss, disseminate, and highlight the advances and challenges of therapies for myasthenia gravis (MG) – a rare, acquired autoimmune syndrome resulting in severe muscle weakness and fatigue, significant disability, and decreased life expectancy.

In addition to her role leading the three-day conference, Kusner chaired the session titled "Acetylcholine Receptor Animal Models," during which she presented the address, "Acetylcholine Receptor Animal Models and Complement."

Henry Kaminski, MD, chair of the Department of Neurology and Meta Amalia Neumann Professor of Neurology at SMHS, also chaired a session at the conference, titled "Clinical Trials Update (Other than MGTX)," and presented "Clinical Trials for Myasthenia Gravis."

During the final session of the conference, "Treatment Guidelines from Around the World," Kaminski led the panel discussion "Comparing and Contrasting Treatment Strategies Around the World," featuring experts from Argentina, Japan, the United Kingdom, and the United States.

LINDA KUSNER, PhD, associate research professor in the Department of Pharmacology and Physiology at the George Washington University School of Medicine and Health Sciences, co-chaired the 13th International Conference on Myasthenia Gravis and Related Disorders, May 15-17.

The conference serves as a forum for scientists and clinical researchers to discuss, disseminate, and highlight the advances and challenges of therapies for myasthenia gravis.

A DIRECTOR OF DISTINCTION

Perry Richardson, MD, professor of neurology and of neurological surgery at the George Washington University School of Medicine and Health Sciences (SMHS), and Clinical Neurophysiology Fellowship Director, received this year's American Academy of Neurology (AAN) Program Director Recognition Award during the 2017 AAN Annual Meeting in Boston, Massachusetts, April 22-28. The honor is presented each year to a pair of neurology program directors in acknowledgement of their excellence administering their residency programs through leadership, creativity, and innovation, skills crucial in ensuring the future of neurology.

"Perry is a role model for residents and faculty," said Henry Kaminski, MD, chair of the Department of Neurology and Meta Amalia Neumann Professor of Neurology at SMHS. "He has developed novel programs for teaching core competencies and procedures, from lumbar puncture and botulinum toxin injection simulations, to the annual medical error 'scavenger hunt.'"

"Perry is a role model for residents and faculty. He has developed novel programs for teaching core competencies and procedures."

Henry Kaminski, MD



PERRY RICHARDSON, MD, professor of neurology and of neurological surgery at the George Washington University School of Medicine and Health Sciences, received this year's American Academy of Neurology Program Director Recognition Award.



CONNECTIONS IN RESEARCH: GW TAPS VITTORIO GALLO, PhD, TO SERVE AS THE ASSOCIATE DEAN FOR CHILD HEALTH RESEARCH

Vittorio Gallo, PhD, has been selected for a newly established position within the school to enhance research relationships between the George Washington University (GW) School of Medicine and Health Sciences (SMHS) and Children’s National Health System (Children’s National), starting on July 1, 2017.

VITTORIO GALLO, PhD, has been selected for a newly established position within the school to enhance research relationships between the George Washington University School of Medicine and Health Sciences and Children’s National Health System, starting on July 1, 2017. Gallo will support faculty in their pursuit of child health research funding and provide overall coordination of the school’s child health research efforts.

In this new role as associate dean for child health research, Gallo will support faculty in their pursuit of child health research funding by identifying appropriate funding sources and providing educational opportunities to enhance grant-seeking skills. He will also provide overall coordination of the school’s child health research efforts and will provide general administrative leadership for the operation of strategic projects in child health, in coordination with Robert Miller, PhD, senior associate dean for research, Vivian Gill Distinguished Research Professor, and professor of anatomy and regenerative biology at SMHS.

“By establishing this position, we will ensure that all of the resources necessary for collaboration are readily available to our researchers and that there is a steady flow of communication between both institutions,” said Miller.

Gallo’s research focuses on understanding development and regeneration of a brain region that plays a crucial role in brain function – the white matter. White matter abnormalities are associated with many neurodevelopmental and behavioral disorders, as well as neurological disorders of the adult. Gallo and his team have made outstanding contributions to the understanding of the cellular and molecular mechanisms that lead to the formation of the white matter.

In addition to his new role, Gallo will serve as chief research officer at Children’s National, and will continue his appointment as professor of pediatrics and of pharmacology and physiology at SMHS. He will also continue in his role as director of the District of Columbia Intellectual and Developmental Disabilities Research Center based at Children’s National.

Gallo has been on the faculty of SMHS and Children’s National since 2002 and has held many key research and administrative positions, including director of the Center for Neuroscience Research and the Wolf-Pack Chair in Neuroscience at Children’s Research Institute.

In addition to his new role, Gallo will serve as chief research officer at Children’s National.

GW HOSPITAL HOSTS SUMMIT ON TRAFFIC FATALITY PREVENTION

In March, the George Washington University (GW) Hospital hosted the Washington Area Bicyclist Association’s inaugural Vision Zero Summit, focusing on ending traffic deaths and serious injuries through education and information sharing.

Babak Sarani, MD, director of the Center for Trauma and Critical Care at GW Hospital and associate professor of surgery and of emergency medicine at the GW School of Medicine and Health Sciences, gave the opening address at the daylong event.

Sessions at the summit focused on topics such as developing road safety strategies, the effects of dangerous driving on pedestrians and people with disabilities, public perceptions of speeding and impaired driving, and law enforcement priorities. Speakers included D.C. Mayor Muriel Bowser; Lucinda Babers, director of D.C.’s Department of Motor Vehicles; and Anneta Arno, MD, director of the Office of Health Equity, District of Columbia Department of Health.



VISION ZERO SUMMIT

The Washington Area Bicyclist Association’s inaugural Vision Zero Summit, which was hosted by the George Washington University Hospital, focused on ending traffic deaths and serious injuries through education and information sharing.

Seventh Annual GWIN Symposium Highlights Senses, Social Behaviors

George Washington University (GW) scientists, students, and faculty gathered on April 27 for a daylong celebration of the study of the brain during the 7th Annual Neuroscience Symposium, a chance for attendees to learn about research being done around the United States – and in their own backyard.

"This really is not only an opportunity for us to have the renowned and truly fantastic neuroscientists from across the country come and share their work with us, but it's also an opportunity for us to become more aware of the work that's being done by our colleagues," said Anthony-Samuel LaMantia, PhD, director of the GW Institute for Neuroscience (GWIN), which sponsors the symposium, and professor of pharmacology and physiology at the GW School of Medicine and Health Sciences (SMHS).

At this year's event, "New Sensations: Exciting Insights in the Chemical Senses and Social Behaviors," attendees heard from two nationally renowned neuroscientists, along with students and presenters from SMHS and Children's National Health System (Children's National).

"Over the last few years, we've seen a real growth in both the recruitment interest and expertise in neuroscience. [If] you look at what's happened over the last 3-to-5 years ... we've recruited fantastic faculty, both at the junior level, with people coming in and starting their careers, but also at the more senior level, which I think is important to give it balance," said Robert Miller, PhD, senior associate dean for research, Vivian Gill Distinguished Research Professor, and professor of anatomy and regenerative biology at SMHS.

After an opening round of presentations by SMHS students and faculty members, the first keynote speaker took the stage. Catherine Dulac, PhD, Higgins Professor of Molecular and Cellular Biology at Harvard University and investigator at the Howard Hughes Medical Institute, spoke about her research on "Neurobiology of Social Behavior Circuits in the Mouse Brain."

"Starting with our interest in pheromone detection and then moving into more social behavior research, over the last decade or so, my lab has been trying to understand the symptoms that underlie social behavior in mice," she said.

Much of Dulac's research centers on investigating the neural mechanisms that control social responses in relation to parental care as well as maternal and paternal behaviors in mice.

In addition, with the human brain, which is geared toward social interaction, Dulac and her colleagues seek to better understand the neurobiology of instinctive social behavior.

Charles Zuker, PhD, professor of biochemistry and molecular biophysics and of neuroscience at Columbia University College of Physicians and Surgeons and an investigator at the Howard Hughes Medical Institute, delivered the second keynote, which focused on understanding taste.

Zuker deviated from his original presentation, and instead took the attendees on a journey of the senses with a talk called "Symphony of the Senses." He challenged the audience members to consider the different ways animals see, hear, and taste; the audience chuckled at learning that mice are indifferent to Diet Coke – they don't taste aspartame. He also stressed the essential relationship between sensory perceptions and the brain circuits that ultimately account for them.

"Each species lives in its own sensory world, of which others might be tied partially, or may be completely unaware of," he said.

But taste was the sense of the day, with Zuker outlining his work to identify receptors and cells for sweet, bitter, umami (the Japanese word for "yummy"), salty, and sour, and through that understand how the brain transforms sensory signals into actions and behaviors.

The faculty and student presentations sprinkled throughout the day covered topics including neural control of liver degenerative disease associated with obesity, stress and fear memory, altered brain circuits in mouse models of neurodevelopmental disorders, neurological deficits from molecularly targeted chemotherapeutic drugs that target pediatric cancers, and building a circuit for feeding and swallowing. The event also featured a poster presentation session, a lunch, and a concluding reception.

"As we look toward the future, neuroscience is going to continue to put out tentacles to many other programs [at GW]," Miller said. "The future looks very exciting."

GWIN is jointly supported by SMHS, the GW Office of the Vice President for Research, and the Columbian College of Arts and Sciences at GW, and works in partnership with the Center for Neuroscience Research at Children's National.



A CELEBRATION OF THE STUDY OF THE BRAIN

The 7th Annual Neuroscience Symposium offered attendees a chance to learn about research being done around the United States.

Free From Falls



Free From Falls, an eight-week, National Multiple Sclerosis (MS) Society-designed course, offers those with MS the chance to learn and implement strategies for reducing their risk of falling – and also gives second-year Doctor of Physical Therapy (DPT) students at the George Washington University (GW) School of Medicine and Health Sciences (SMHS) the opportunity to hone their clinical skills in a unique group environment.

“It’s working really nicely because it’s a win-win, for the participants and the students,” said Sue Leach, PhD, PT, assistant professor of physical therapy and health care sciences at SMHS, who leads the program. “The clients work in a safe environment on reducing their risk of falling, and the DPT students have the benefit of working closely with an at-risk population.”

Since the 2014 inception of the joint venture between the SMHS physical therapy program and the Greater D.C. and Maryland chapter of the MS Society, DPT students have assisted during the course’s two components: a one-hour lecture on various aspects of fall awareness, and an hour of Building Better Balance exercises.

Within the first hour, participants share their personal experiences with one another, allowing them to develop a support network that, in some cases, lasts well beyond the program. “What I remember most about those sessions was that I sometimes laughed so hard, the muscles in my face hurt,” said former participant Angela Matysiak. “I stayed in touch with this group because I wanted to carry all that I had learned during the study into the future. I wanted to continue to surround myself with bubbly and excited people who understand the seriousness of MS and who can make me laugh. And me them.”

The second hour, during which Matysiak also recalls laughing as she practiced various exercises, includes physical training designed to increase balance confidence and reduce the risk of falling. Each DPT student attends two of the eight sessions, first performing a weekly check-in with clients such as Matysiak, and then providing the appropriate physical assistance. The idea, Leach said, is for students to build on their clinical judgment skills, tailoring activities to the needs and abilities of each participant based on the Balance Control Systems Framework. To this end, each student designs an appropriate balance exercise or activity specific to a client and assesses its effectiveness. This one-on-one student-client model within a group context has proved successful during five Free From Falls sessions at GW, Leach said.

In addition to helping clients and providing opportunities for students, the Free From Falls program has allowed SMHS researchers to gather valuable data. For example, the school’s research team demonstrated that a two-minute walk test provides an efficient alternative to the six-minute walk test for people with MS.

“That means for people who experience fatigue, which is a common symptom with MS, you can actually reduce the time of the testing and the demands on clients and still have an accurate measure,” Leach explained, adding that most participants who complete the program report higher balance confidence.

As a result of the training, the team also found differences in the gait patterns of program participants, suggesting greater walking stability that may indicate a lower risk of falls.

For more information about the Free From Falls program, please contact Sue Leach at leachs@gwu.edu.

“I stayed in touch with this group because I wanted to carry all that I had learned during the study into the future. I wanted to continue to surround myself with bubbly and excited people who understand the seriousness of MS and who can make me laugh.”

Former Free From Falls participant **Angela Matysiak**



A New Disorder

GW RESEARCHER IDENTIFIES NEW FORM OF MUSCULAR DYSTROPHY

BY CAROLINE TRENT-GURBUZ

The case of the INPP5K mutation traces back to a group of muscular dystrophy patients referred from an Italian collaborator, says M. Chiara Manzini, PhD, assistant professor in the George Washington University (GW) Institute for Neuroscience and the Department of Pharmacology and Physiology at the GW School of Medicine and Health Sciences. Her research into congenital muscular dystrophy, a neuromuscular disorder that causes progressive muscle weakness, allowed her to collect several cases for her genetic studies – but a few were different.

In this group, “the patients were very short, and they had skeletal deficits,” Manzini explains. Those deficits, she adds,

were something new; in the severe forms of muscular dystrophy she studies, mutations in the genes that produce proteins for muscle development also affect the brain and eyes, resulting in intellectual disability and vision issues such as cataracts. The patients also had unique skeletal features in their skull and their face, she says. “We weren’t absolutely sure of what they were.”

Curious, Manzini followed protocol, sequencing each gene in her patients’ genomes. She found two instances of mutations of the INPP5K gene. “INPP5K was different from the other genes related to that type of mus-

cular dystrophy,” she says. “It is very important for muscle function, and for response to insulin in the muscle. We were intrigued, but we really didn’t know what to do with it.”

Manzini entered the gene in “Gene Matcher,” a website she jokingly refers to as “Match.com for scientists.” It took a year, but early in the summer of 2016, she matched with a case in the United States, as well as with a group in England and a lab in Germany. “[Matching] is very important for rare diseases, because we may find one or two [patients] with a genetic mutation, but you really want to find more and more to get a full-fledged idea of what the disease looks like,” she says.

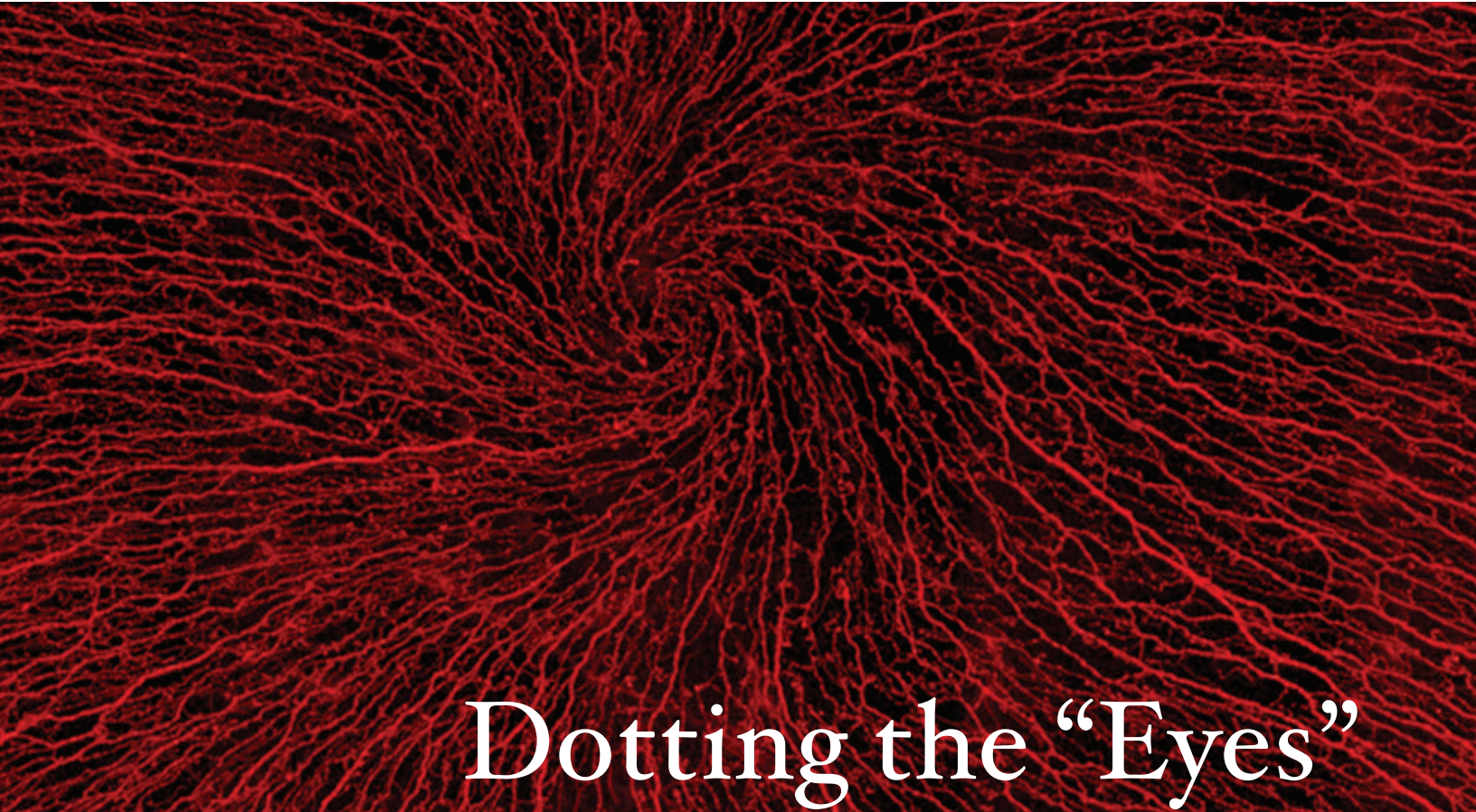
The researchers, all of whom had been exploring the nature of the INPP5K gene independently, joined forces and shared information. “We started talking, and that’s what exponentially sped up the research, because suddenly it was, ‘No, this is real,’” Manzini says. “There are so many different cases, and the presentation is always the same: muscular dystrophy with cataracts, intellectual disability, and short stature.”

Each of the labs, using a zebrafish animal model, replicated what Manzini had suspected: the removal of the gene caused muscle disruption, lens disruption, and a smaller brain, suggesting they had discovered a new type of congenital muscular dystrophy. By October 2016, the researchers had collaborated and submitted two papers, “Mutations in INPP5K, Encoding a Phosphoinositide 5-Phosphatase, Cause Congenital Muscular Dystrophy with Cataracts and Mild Cognitive Impairment” and “Mutations in INPP5K Cause a Form of Congenital Muscular Dystrophy Overlapping Marinesco-Sjögren Syndrome and Dystroglycanopathy,” to the prestigious American Journal of Human Genetics. The articles appeared in the journal in March 2017.

“It was very fast,” Manzini says. “It was an incredibly busy summer.”

JOINING FORCES

In her research, M. Chiara Manzini, PhD, assistant professor in the GW Institute for Neuroscience and the Department of Pharmacology and Physiology at the George Washington University School of Medicine and Health Sciences, found two instances of mutations of the INPP5K gene. Research labs in the United States, England, and Germany, which had been conducting similar research, replicated what Manzini had suspected: the removal of the gene caused muscle disruption, lens disruption, and a smaller brain, suggesting they had discovered a new type of congenital muscular dystrophy.



Dotting the “Eyes”

EXPANDING KNOWLEDGE OF THE UNDERLYING PATHOLOGY OF CENTRAL NERVOUS SYSTEM DISORDERS THROUGH CORNEAL NERVE RESEARCH

BY **CAROLINE TRENT-GURBUZ**

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ary Ann Stepp, PhD, professor of anatomy and regenerative biology at the George Washington University (GW) School of Medicine and Health Sciences, views her work in corneal wound healing as a bridge – not just to researchers in other disciplines, but also to the public.

“We want to convince the rest of the neuroscience field that they have this extra tool they could use in their research,” says Stepp, who recently received a \$2.8 million, five-year R01 grant from the National Institutes of Health to continue her research. Her work, she explains, involves the sensory nerves that innervate the cornea.

The cornea is densely innervated, with more nerves on the surface than any other part of the body. When the cornea is injured – which can happen as easily as a fingernail scratch – it’s relatively simple to capture an image of the nerves after they’ve grown back during the healing process. That accessibility is unique, given that other nerves in the peripheral nerve system (PNS) are deep within the body and much harder to image. Although the eye tissue is more specialized, Stepp says, it’s easily manipulated, so researchers can get a better grasp on PNS regeneration during wound healing. Stepp’s

IN THE EYES OF A MOUSE

The cornea is densely innervated, with more nerves on the surface than any other part of the body. The graphic above shows a forward-facing view of the corneal sensory nerves of a mouse.

career has focused on what she refers to as “beautiful tissue,” and her work continues to lead to more discoveries.

One research area that has branched out of what Stepp calls the “corneal model” is small-fiber neuropathy. Small fibers, or sensory fibers, appear in the fingers, in the skin, and on the surface of the cornea; as people develop diabetes or simply age, those fibers, especially in the fingers and toes, decrease. It’s not clear why they do, but through the use of a confocal microscope, researchers can observe these nerves in a non-damaging, non-invasive way.

“By studying these nerves, we’re not only getting insight into small-fiber neuropathy in peripheral disease, but we’re also seeing changes in the corneal nerves in central nervous system diseases – for example, Parkinson’s disease,” she says. “The question is whether or not that can be a diagnostic tool.”

Stepp likewise is looking into how the arrangement or innervation of the nerves is restored during corneal wound healing and is altered in dry eye. The condition, she says, has been considered a disease of the glands that synthesize and secrete tears; now, she’s hypothesizing that the pathology associated with the innervation of the cornea by sensory nerves causes some forms of dry eye. “It’s a new way of thinking of dry eye,” she explains. “The way you would treat this type of dry eye would be similar to how you would treat other peripheral small-fiber neuropathies and other pathologies that involve the central nervous system.”

By better understanding the corneal nerves, Stepp adds, researchers will get a better sense of the pathology underlying these medical issues. “It’s an exciting way not just to link our research on the cornea to the greater community, but [also] to think about what the cornea could do for them in terms of their research objectives.”

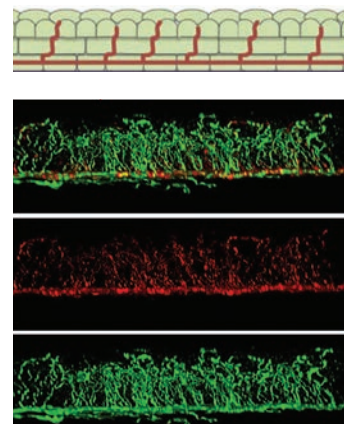
Stepp discovered that within the cornea, nerves – rather than a vascular system – help to provide trophic, or cellular, support for growth factors. Those nerves, Stepp says, are also free nerve endings, which transfer sensory information such as pain, heat, and

cold from the periphery to the brain, a discovery she found with support from GW neuroscientists.

“It’s pretty special that these are free nerve endings that are able to exist and persist and stay stable and function for long periods of time in healthy circumstances,” she explains. The reasoning behind her hypothesis is that epithelial cells, which make up the corneal surface, have taken over the neural protection functions of glial cells. “This changes the way the [cells] respond to different drugs and different treatments,” she says. “It’s an

interesting dynamic to think about what we could propose with respect to treatments.”

In the meantime, Stepp continues to be fascinated by the eye. “It literally is fun to come into work every day and look into the microscope and see something new and cool that nobody’s ever seen before. I mean, what a life,” she says. “It’s so wonderful to know that there’s still stuff that needs to be sorted out and that maybe, someday, it’s going to help people live better lives. That’s what it’s all about.”



UNDERSTANDING THE CORNEAL NERVES

By better understanding the corneal nerves, researchers will get a better sense of the pathology underlying these medical issues, says Mary Ann Stepp, PhD. The graphic above shows a cross-section of the corneal sensory nerves of a mouse.



A MAJOR GRANT TO STUDY THE CORNEA'S SENSORY NERVES

Mary Ann Stepp, PhD, recently received a \$2.8 million, five-year R01 grant from the National Institutes of Health to continue her research. Her work involves the sensory nerves that innervate the cornea.

Living Life Pain-Free

GW SPINE AND PAIN CENTER PUTS PATIENTS BACK INTO ACTION

BY KATHERINE DVORAK

In July 2015, Martha Jones had just returned from a trip overseas when her back completely “crashed,” she recalls. After 20 years of experiencing increasing back pain, she had reached the point where she didn’t know where to go or what to do, but she knew something had to change.

She had heard George Washington University (GW) Hospital had a spine and pain center. Jones says her experience at GW, which culminated in surgery, “absolutely” changed her quality of life. Jones had one of the most severe spinal deformities known and needed to undergo a T2-iliac spinal fusion and deformity correction, procedures performed by Michael Rosner, MD, vice chair of the Department of Neurosurgery and professor of neurological surgery at the GW School of Medicine and Health Sciences (SMHS).

“The further away I get from the surgery, the more I can appreciate and begin to understand the magnitude” of what was done, she says. “I really didn’t know how bad I was.”

Jones’ comprehensive care ran the gamut of what GW’s Spine and Pain Center has to offer, including physical therapy sessions with Mariam Hameed, MD, assistant professor of anesthesiology and critical care medicine at SMHS; the surgery itself; and rehab in an acute rehabilitation unit through Sibley Memorial Hospital.

About 31 million Americans experience low back pain at any given time, according to the American Chiropractic Association, though most people won’t need surgical intervention as Jones did.

“Everybody has back pain sometime in their life, but it shouldn’t be expected to be chronic,” says Anthony Caputy, MD, chair of the Department of Neurosurgery and Rizzoli Professor of Neurological Surgery at SMHS. “Most patients who come here don’t need surgery, and they’ll get better with non-surgical techniques, which include physiotherapy at the Spine and Pain Center or various other interventional treatments.”

From their offices at 2131 K Street, NW, staff at the Spine and Pain Center take a multidimensional approach to spine care, with clinicians from numerous specialties working with patients to reduce pain and improve their quality of life.

Often, physical therapy is the first step toward easing back pain. Patients are sent to the Spine and Pain Center after a primary care referral or after being seen by a neurosurgeon who recommends they try more conservative measures before moving on to surgery, says May Chin, MD, co-director of the GW Spine and Pain Center and professor of anesthesiology and critical care medicine at SMHS.

Chin says the center’s approach to spine care is “almost like an algorithm.” The staff use a multimodal approach, blending different types of therapies to see what best eases a patient’s pain. “You start with the more conservative ways to treat [patients], and if the conservative measures don’t add up, then you get more aggressive,” Chin says.

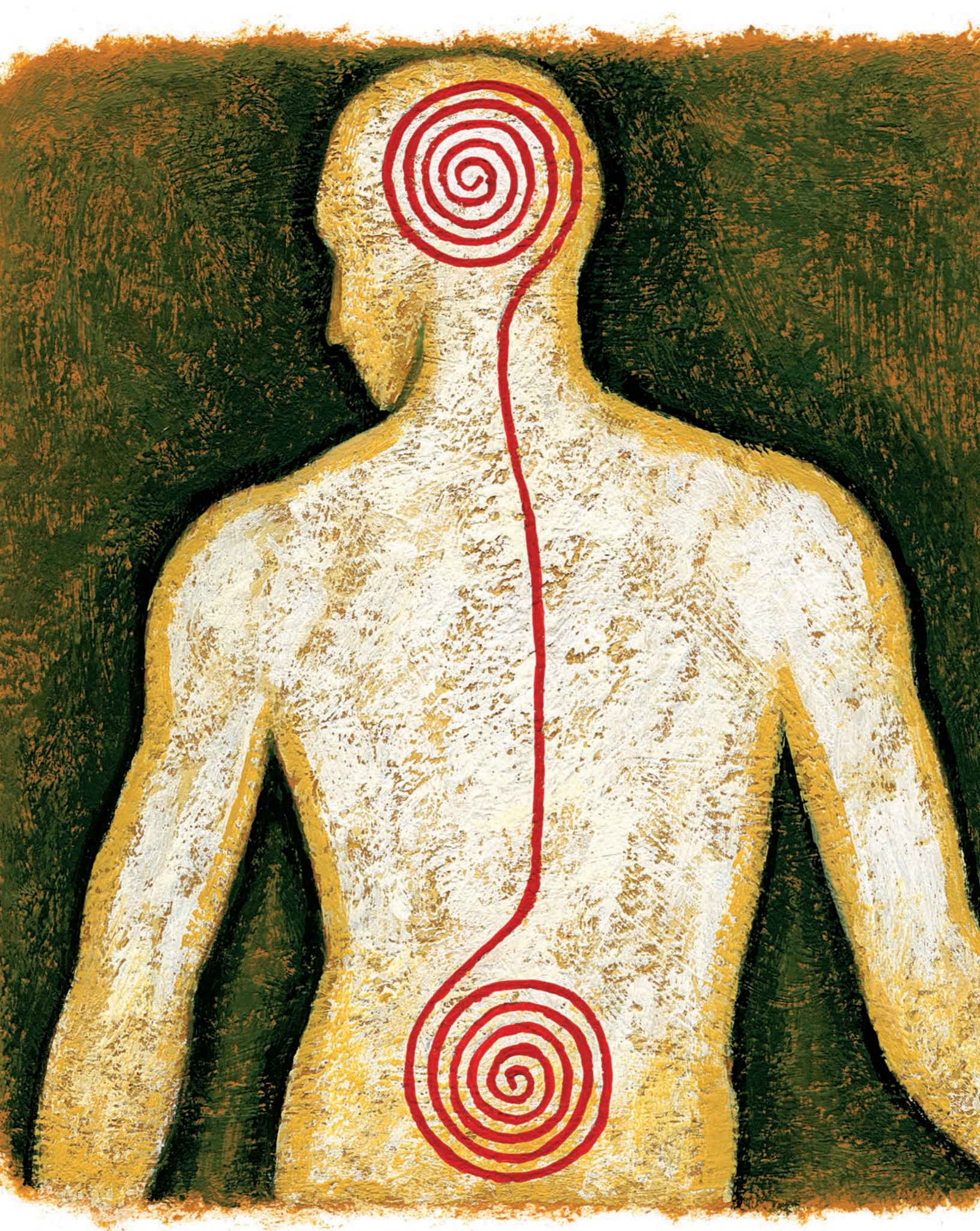
Studies have shown that a multimodal approach has the best outcome, according to Hameed. “A combination of physical therapy, anti-inflammatory medications, muscle relaxers, or nerve pain medications in addition to injection therapy is typically employed,”



IMPROVING THE QUALITY OF LIFE FOR BACK PAIN PATIENTS

ABOVE: Michael Rosner, MD, is vice chair of the Department of Neurosurgery and professor of neurological surgery at the George Washington University School of Medicine and Health Sciences (SMHS).

About 31 million Americans experience low back pain at any given time, according to the American Chiropractic Association. Most patients can be helped by non-surgical techniques, which include physiotherapy, but some require surgery.



“Everybody has back pain sometime in their life, but it shouldn’t be expected to be chronic. Most patients who come here don’t need surgery.”

Anthony Caputy, MD

she explains. The center also uses a tailored approach to care for each patient to ensure not only pain relief, but also improvement in back function, she adds.

If these conservative measures prove ineffective, a patient may need further care, which can include a trip to GW Hospital for minimally invasive surgical intervention.

That’s where Wayne Olan, MD, director of interventional and endovascular neurosurgery and associate professor of neurological surgery at SMHS, and his team come in.

The minimally invasive spinal surgery unit “fits in the middle,” Olan says. It’s for patients who aren’t necessarily surgical candidates, but who are past the realm of physical therapy or medication.

“This is the widest-growing portion of the spine care continuum, as everything in medicine goes toward being less invasive and less traumatic, and toward a quicker recovery,” he explains.

Minimally invasive neurosurgery started out with needle-based procedures to help repair spine fractures and has expanded into intradiscal therapies, in which materials such as stem cells, blood products, or fibrin sealant are injected into the disc space to help regenerate the disc, Olan says. GW is well-known for its minimally invasive osteoporotic fracture fixation, in which the fractured area is filled with a cement-like material that hardens quickly to stabilize the bone.

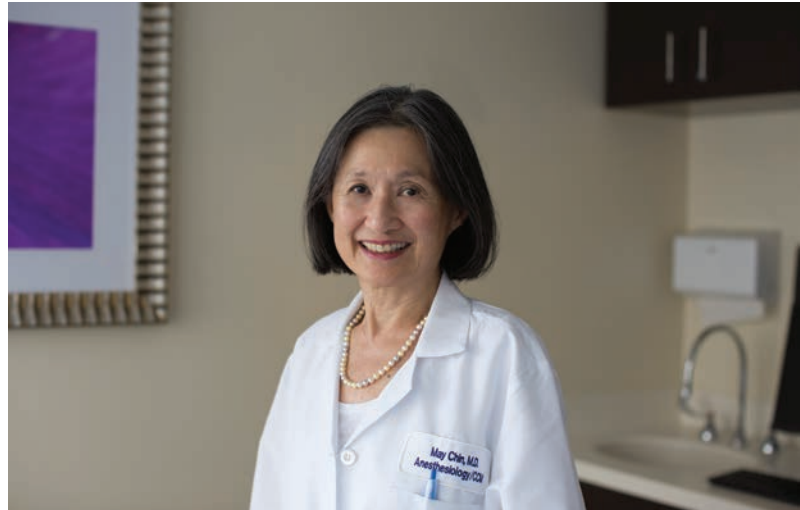
With various specialties working together – including orthopedic specialists, pain management specialists, and neurosurgeons – Olan says when a patient comes to GW, he or she is “walking into a system that has the opportunity to provide every possible treatment option.”

Specialists can walk down the hall to get a second opinion on a patient’s condition or pick up the phone to speak with a physical therapist; at GW, insists Olan, no stone is left unturned to ensure the patient is getting the treatment that best fits his or her needs.

“We manage patients based on their activities. ‘Return to play’ is very big for us,” Olan says. “I can make you pain-free lying in a bed, but my job is to make you pain-free doing what you love to do.”

Some spine issues, however, are more severe than others. For Jones, the road to recovery after surgery continues almost two years later, and the procedure that started her on that path was one of the last-resort treatments.

But it proved to be “a miracle,” she says.



“Patients always ask me when they should go forward with surgery,” says Rosner. “The answer is: ‘You’ll know when it’s time.’ When their life is so bad that they can’t get up, can’t walk around, can’t do anything ... that’s when we take that step.”

Rosner specializes in spine deformity correction. Patients undergoing the procedure receive the entire continuum of care – from a pre-operative assessment in which the patient works with staff from the Spine and Pain

“You start with the more conservative ways to treat [patients], and if the conservative measures don’t add up, then you get more aggressive.”

May Chin, MD



A MULTIDIMENSIONAL APPROACH

The staff at the GW Spine and Pain Center take a multidimensional approach to spine care, with clinicians from numerous specialties working with patients to reduce pain and improve their quality of life. Often, physical therapy is the first step toward easing back pain. The center is staffed by May Chin, MD (top left), Wayne Olan, MD (bottom left), and Anthony Caputy, MD (above).

Center to the OR, where a deformity correction team is waiting to help, and then on to rehabilitation.

Most often, Rosner says he sees spine deformities that are degenerative. They can be caused by the simple act of aging or be a result of previous surgeries. “These things don’t develop over a month, or a couple of months, or a year; they take a decade or two to form,” he explains.

Each surgery takes about two days, he adds, and recovery typically lasts one to two years.

To rate the success of their surgery after two years, patients are asked two questions: Would you do the surgery again? Are you back to doing what you thought you were going to be able to do?

Jones hasn’t quite reached the two-year mark, but she already knows the answer to the first question. It’s been the “test of a lifetime,” she says, but there’s no doubt in her mind that she’s made a great deal of progress from where she was in July 2015.

LEARNING FROM PATIENT OUTCOMES

The story doesn’t end once a patient has initially recovered from back surgery. Tracking overall patient outcomes two years following surgery is critically important in helping medical professionals better understand how to help people manage pain, find ways to improve rehabilitation post-operation, and work to decrease complication rates.

Capturing data on patient outcomes started for Michael Rosner, MD, vice chair of the Department of Neurosurgery and professor of neurological surgery at SMHS, while he was on active duty with the U.S. Army. Its military spine team developed the spinal surgery database for outcomes over a decade ago, Rosner says, as he was serving as chief of neurosurgery at Walter Reed National Military Medical Center. During his transition to retirement from active duty and starting at GW, Rosner took steps to collaborate with Walter Reed and extend the military spinal deformity database to the civilian sector.

The database records patient outcomes, which from “a research standpoint is the best thing we’re going to be able to bring to the system,” says Rosner. Definitive data for spine deformity correction surgery comes at about the two-year mark, he explains.

The benefits of tracking patients over time, says Rosner, can extend beyond patient satisfaction, and into lowering health care costs.

“The surgeries are expensive, but if we’re able to decrease pain medication usage and get patients back to being able to function beyond their expectations when they were bedridden before, that has a pretty positive impact [in terms of] cutting down on the costs that other medical problems can cause,” he says.

Rosner says the data collected so far has informed the decisions now made in surgery at GW. That includes the length of surgery, which used to be completed in one day but is now split into two procedures.

“We found that patients had longer ICU stays and overall longer hospital stays with one-day surgery,” he says. “It isn’t always intuitive. [People think] ‘Oh, two days of surgery, it must take longer to recover,’ but they actually recover sooner.”



Getting Centered

GW'S HEADACHE CENTER PINPOINTS SOLUTIONS FOR MIGRAINE SUFFERERS

BY **ERIC BUTTERMAN**

The coffee has brewed, schedules have been checked, and hellos have been exchanged. Now you shift your attention to tackling the day's tasks, but then it happens – a migraine headache strikes. It's a soul-crushing start to the day.

Of course, for those who have never experienced a migraine, it can be tough to relate. With an average headache, one might turn to an over-the-counter remedy, such as aspirin or ibuprofen, and be in the clear in no time. But for those who suffer from migraines – approximately 12 percent of the U.S. population, according to the National Institutes of Health (NIH) – the experience can be nothing short of debilitating.

Migraines are a disorder, says Amanda Michael, MD, assistant professor of neurology at the George Washington University (GW) School of Medicine and Health Sciences (SMHS). They're often misunderstood, which leads to a lot of pain and suffering for patients. The GW Medical Faculty Associates (MFA) Headache Center wants to be part of the solution. "We help [patients'] quality of life and have a commitment to research," explains Michael, who, along with John Rothrock, MD, professor of neurology at SMHS, co-directs the Headache Center, which opened its doors in July 2015. "We're building a tradition here. We're involved in several multicenter trials, looking at efficacy and safety for multiple new medications to treat acute migraine as well as to prevent migraine in the first place."

Rothrock believes the center is a clear asset to the community and the university, and there are four good reasons to take him at his word: Four is the number of headache centers at universities that he has previously led, including at the University of California at San Diego and the University of South Alabama.

"The Headache Center assists people with headache problems in the region and will raise the standard of care through research, providing excellent service to patients and encouraging others to do the same," Rothrock explains. "It wants to be a voice for those dealing with this and give them strategies to feel more in control and, just as important, hopeful."

WHAT COMMONLY TRIGGERS A MIGRAINE?

People who get migraines may be able to identify triggers that seem to kick off the symptoms. Possible triggers include the following:

- > Stress and other emotions
- > Biological and environmental conditions, such as hormonal shifts and exposure to odors
- > Fatigue and changes in one's sleep pattern
- > Glaring or flickering lights
- > Weather changes
- > Certain foods and drinks

The American Headache Society suggests documenting triggers in a headache diary. Taking this information with you when you visit your health care provider helps him or her identify headache management strategies.

At the heart of the center's philosophy is the fact that the best providers of relief can be the patients themselves. "If we can educate patients to see the warning signs and teach them how to help themselves, then they can often stop the problem right in its tracks, sometimes having more effect than a member of the medical profession ever could," Rothrock says. "It comes down to respecting our patients enough to let them have an active role. They know their bodies; they've often been here before. They can help us help them."

The Research Role

Unlike many other clinical enterprises, the MFA's center isn't just benefiting from research – it's at the forefront. Although Michael and Rothrock don't do basic laboratory research, they regularly collaborate with NIH-funded scientists. "Most of what we're doing is clinical or

"Migraines are often misunderstood, which leads to a lot of pain and suffering for patients. The GW Medical Faculty Associates Headache Center wants to be part of the solution. We have a commitment to research."

Amanda Michael, MD

A DEBILITATING DISORDER

According to the National Institutes of Health, approximately 12 percent of the U.S. population suffers from migraines. For those who suffer, the experience can be nothing short of debilitating.

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A ROOM FOR IMPROVEMENT

Every 10 seconds, according to the Migraine Research Foundation, someone in the United States goes to the emergency department (ED) complaining of head pain. Of those visits, approximately 1.2 million are for acute migraine attacks. The bright lights, noise, and close confines of an ED waiting room, however, can be especially tough for someone already suffering from a migraine attack. Amanda Michael, MD, believes a more therapeutic environment should be made available for migraine sufferers.

Michael, assistant professor of neurology at the George Washington University (GW) School of Medicine and Health Sciences and co-director of the GW Medical Faculty Associates Headache Center, says overwhelming need led the center to establish a "headache rescue room" for patients suffering from therapy-resistant acute migraine headaches. "We give IV fluids and targeted migraine medications to stop the migraine attack," she says. "We can also adjust home medications if we need. This combination of comprehensive care often leads to strong clinical outcomes."

translational research," Rothrock says. He adds that the center is working to expand the body of knowledge on migraines and, using that knowledge, to design more effective means of treating patients and developing new therapies. "Part of the multicenter trials are focused on experimental therapies for cluster headaches, but we are more specifically focused on migraines," he says.

Among the topics clinicians at the Headache Center are interested in is neuropeptide CGRP, or calcitonin gene-related peptide, antagonists. Scientists believe CGRP could play a role in targeting the circuitry behind migraines.

"We are now starting the first trial at GW looking at an antagonist to calcitonin-related protein, a promising new therapy in the field of migraine medicine," Michael says. "No one is ready to submit to the FDA yet, but all five have track records of published trials. They all are promising when you consider safety and being effective."

Michael says the center is also trying to launch a study of transcranial magnetic stimulation (TMS) to treat migraines. TMS uses magnets to stimulate the brain's nerve cells. Once funding is in place, the study would cover a two-week

RAISING THE STANDARD OF CARE

Amanda Michael, MD (top) is an assistant professor of neurology at the George Washington University (GW) School of Medicine and Health Sciences (SMHS). She is also the co-director of the GW Medical Faculty Associates (MFA) Headache Center, together with John Rothrock, MD, professor of neurology at SMHS (bottom). Rothrock has previously led four headache centers at universities, including at the University of California at San Diego and the University of South Alabama, before co-directing the MFA Headache Center, which opened its doors in July 2015.



treatment period using TMS, and patients would keep monthly headache diaries about their symptoms.

The Headache Center's philosophy of growing patient education isn't just a hope. It's all part of a plan to keep the patient formally rooted in the research mix. "We want to be looking at the effect on intensity of patient information on clinical outcome," Rothrock says. "Does a better-informed patient do better clinically?"

The latter question neatly meshes with another of the center's objectives, "Headache School," for which its staff recently submitted a grant proposal. "We are passionate about developing this school [for] comprehensive headache education," Michael says. "It would be a three-hour session, where patients can learn about migraines: how to treat one [while it is occurring] and how to try to prevent it from happening to begin with. It would be interactive – with probably six to eight patients suffering with migraines – and would include the aid of instruction experts in migraine and headaches overall. If patients understand better why they are having something prescribed, it helps them to take meds accordingly. It's an important part of understanding the disorder better."

The Psychological Side of Migraines

Although the numbers may seem unbelievable to those who have never had a migraine headache, they are the sixth most debilitating illness in the world, according to the Migraine Research Foundation. A startling 12 percent of the U.S. population – 18 percent of women, 6 percent of men, and 10 percent of children – experience migraines, and nearly one in four U.S. households has at least one member who experiences migraines.

James L. Griffith, MD, Leon M. Yochelson Professor and chair of the Department of Psychiatry and Behavioral Sciences at the George Washington University School of Medicine and Health Sciences, says that beyond the physical triggers of migraines, an underlying psychological component can trigger the painful attacks. “This [cause] often can be overlooked,” says Griffith, adding that the National Institutes of Health reports that migraine sufferers typically experience recurring attacks prompted by factors such as stress, anxiety, hormonal changes, and lack of food or sleep.

“Treatment for those who fall into this category can be very effective,” he explains. “You have to remember that you’re treating the whole person. Migraine patients often have psychological factors that trigger headaches, as well as co-morbid mood or anxiety disorders that compound their suffering.”

Half of all migraine sufferers have an anxiety disorder, such as panic disorder, generalized anxiety disorder, or obsessive-compulsive disorder, and a third have major depression. “Depression rates increase two- to fourfold among migraine patients, and the rates increase to 60 percent among those migraine patients who [experience] daily chronic headaches,” Griffith adds. “It is a bidirectional relationship – depression patients also have 20 to 35 percent prevalence rates for migraine headaches.”

What is important to understand, Griffith says, is that psychological problems or stressors are not the cause of migraines as a neurological disorder. Rather, migraine headaches and mood and anxiety disorders reflect different types of instability in the serotonin system of the brain. “Psychological issues that create a stress response within the nervous system can trigger a migraine headache in a vulnerable individual. This can happen by dwelling on thoughts that stir feelings of helplessness, resentment, shame, or other negative emotions,” he says.

Dealing with these issues, psychiatrists often combine patient education on a healthy lifestyle with cognitive-be-

BEYOND PHYSICAL TRIGGERS

An underlying psychological component can trigger painful migraine attacks, says James L. Griffith, MD.



havioral psychotherapy, which has been effective for both migraines and depression. Cognitive-behavioral psychotherapy teaches patients to recognize thought patterns that generate negative emotions, particularly helplessness, hopelessness, and feelings of desperation. “Patients learn to challenge those thoughts and to replace them with thoughts that foster hope, optimism, and confidence,” explains Griffith. “A cognitive-behavioral psychotherapist,” he adds, “works with a patient in a manner akin to a coach training an athlete, practicing over and over the focusing of attention on thoughts generating positive attitudes and emotions. This cognitive training has secondary effects upon the body’s endocrine and autonomic systems that are protective against both migraine headaches and mood and anxiety disorders.”

In addition to cognitive-behavioral psychotherapy, activities such as mindful meditation, yoga, and aerobic exercise have been shown to have beneficial effects for certain patients. Even though medications remain the core element of treatment, Griffith says it’s vital to think beyond pharmaceuticals.

“The potency of psychological interventions in treatment of migraines is not widely understood,” he says. Griffith believes that neurologists and psychiatrists both need to be educated during their residency training about the importance of diagnosis and conjoint treatment of both migraine and co-morbid mood and anxiety disorders. “We need to ... present migraine headaches and depression treatment as two different expressions of problems involving the brain’s serotonin system, so patients are less likely to feel that depression symptoms represent personal inadequacy.”

But the goal, as much as anything else, is to offer understanding to those who suffer from migraines and who may not feel any emotional support. “Migraine is a lonely illness,” Griffith says. “Pain is invisible. The head pain that is most present in your awareness can’t be adequately explained to another person. It’s hard for other people to feel empathy – you can see a broken leg in a cast, but you can’t see a headache. ... But we see them.”

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