neurotransmitter

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

fall 2016

This latest edition of *Neurotransmitter* represents another step forward in our effort to communicate the progress taking place among the clinical partners at the George Washington University (GW). Inside these pages, we illuminate the rich tapestry of the neurosciences and the broad expertise of the GW Institute for Neuroscience (GWIN) and the GW University Hospital Neurological Institute.

This third magazine deals with subjects that overwhelm daily headlines. Douglas Nixon, M.D., Ph.D., chair of the Department of Microbiology, Immunology, and Tropical Medicine and Walter G. Ross Professor of Basic Science Research at GW's School of Medicine and Health Sciences (SMHS), leads a group of investigators from across the University who are exploring how the Zika virus may produce devastating abnormalities in brain development and identifying other likely areas of nervous system infection. *Neurotransmitter* also discusses the psychiatric ramifications of the global refugee crisis.

We are excited to announce a major recruitment to GW. Kevin Pelphrey, Ph.D., a world-renowned investigator on autism, will lead the GW Autism and Neurodevelopmental Disorders Institute. Pelphery will build collaborations across several GW colleges, including SMHS, the Columbian College of Arts and Sciences, and the Milken Institute School of Public Health, as well as with clinical partners the GW Hospital, the GW Medical Faculty Associates, and Children's National Health System.

Collaborations are key to excellence in science and medicine. The Joint Commission recently acknowledged our collective efforts by designating GW Hospital as a comprehensive stroke center. The commission noted how well the GW Hospital administration, staff, and physicians worked together to provide advanced stroke care. We offer a personal account of the impact modern stroke care has had on one of our patients. In addition to this success story, we provide an update on the groundbreaking research of Mohamad Koubeissi, M.D., and Donald Shields, M.D., Ph.D., FACS, in dramatically reducing the frequency of seizures among patients with epilepsy.

Beyond the research conducted at GW, we feature pieces on scientists who visited us to present their work. At GWIN's 6th Annual Neuroscience Symposium, investigators from across the country presented discoveries in multiple sclerosis and Alzheimer's disease. GW also welcomed back former psychiatry resident Brandon Kohrt, M.D., Ph.D., RESD '13, who gave the prestigious Seymour Perlin, M.D., lecture.

We hope you enjoy this edition of *Neurotransmitter*.

Please go to **smhs.gwu.edu/neurotransmitter** to view or share a copy of this or previous editions of *Neurotransmitter*.

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contents

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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THE NEURO-IMMUNE INTERFACE: GLIA, NEURONS, AND DISEASE

Stephen Hauser, M.D., found in his research that antibodies targeting cells that promote antibody production reduced disease activity within weeks of treatment. "This discovery ... enabled a paradigm shift in understanding how the inflammatory phase of MS develops."

Neuro-immune diseases – particularly Alzheimer's, multiple sclerosis (MS), and myasthenia gravis (MG) – took center stage at the 6th Annual Neuroscience Symposium, a day-long event sponsored by the GW Institute for Neuroscience. "The Neuro-Immune Interface: Glia, Neurons, and Disease"-themed symposium featured two keynote speakers, as well as presenters from the GW School of Medicine and Health Sciences (SMHS) and Children's National Health System (Children's National).

"This [symposium] is a wonderful thing to do," said keynote speaker Carla Shatz, Ph.D., Sapp Family Provostial Professor, David Starr Jordan Director of Stanford Bio-X, and professor of biology and neurobiology at Stanford University.

Shatz, in "Saving the Synapse: Developmental Critical Periods and Alzheimer's Disease," asserted that if researchers could better understand the cellular and molecular mechanisms underlying developmentally critical periods, then they could use the mechanisms in the adult brain to help repair injuries in stroke and Alzheimer's patients.

The second keynote speaker, Stephen L. Hauser, M.D., Robert A. Fishman Distinguished Professor and chair of the Department of Neurology at the University of California – San Francisco, focused on MS.

Hauser, whose research targeted B cell-based therapies and their impact on the disease, found that antibodies targeting cells that promote antibody production reduced disease activity within weeks of treatment. "This discovery … enabled a paradigm shift in understanding how the inflammatory phase of MS develops," he said.

LINDA KUSNER, Ph.D.

STEPHEN L. HAUSER, M.D.

CARLA SHATZ, Ph.D.

Robert Miller, Ph.D., senior associate dean for research and Vivian Gill Distinguished Research Professor at SMHS, who presented "Cellular Interactions Regulating CNS Myelination, Demyelination, and Early Myelin Repair in Vertebrate CNS," also focused on MS, namely the role of astrocytes, or star-shaped glial cells in the brain and spinal cord, in myelination, the creation of the fatty insulation protecting nerves.

In addition to the research on Alzheimer's and MS, Linda Kusner, Ph.D., associate research professor of pharmacology and physiology at SMHS, discussed MG, a rare and debilitating autoimmune disorder that causes muscle weakness. Through her work, Kusner discovered that the expression of the protein survivin could be part of a mechanism that keeps cancer cells alive, thereby linking cancer and autoimmune disease in MG and other autoimmune disorders.

This year's symposium also included discussions from SMHS Ph.D. candidates and postdoctoral fellows as well as poster presentations from SMHS and Children's National researchers.

Through her research, Linda Kusner, Ph.D., discovered that the expression of the protein survivin keeps cancer cells alive, thereby linking cancer and autoimmune disease.

KEVIN PELPHREY, Ph.D. Director of the Autism and Neurodevelopmental Disorders Institute and professor of pharmacology and physiology at the GW School of Medicine and Health Sciences

SPANNING THE SPECTRUM OF AUTISM

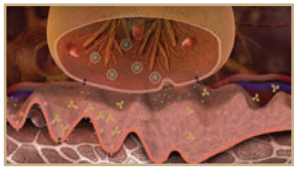
The George Washington University's research portfolio has recently begun to expand thanks to the expertise of Kevin Pelphrey, Ph.D., new director of the Autism and Neurodevelopmental Disorders Institute (ANDI) and professor of pharmacology and physiology at the GW School of Medicine and Health Sciences.

Pelphrey will connect the University's full research spectrum, including faculty members representing six GW colleges, with clinical partners GW Hospital, Children's National Health System, and the GW Medical Faculty Associates. The goal is to create a one-stop resource for families affected by autism in the Washington, D.C. metropolitan area.

Pelphrey, who is the parent of a child with autism, has more than 15 years of experience in autism and neuroscience research. He specializes in cognitive neuroscience and developmental disorders and currently holds seven active grants, including a $15 million National Institutes of Health grant from the Autism Centers of Excellence Program. Pelphrey will also be the first to hold the endowed title of the Carbonell Family Professor in Autism and Neurodevelopment Disorders.

At ANDI, which received $5 million from GW and will be located on the University's Virginia Science and Technology Campus in Ashburn, Virginia, Pelphrey and his team will focus on adults with autism and women with autism.

TAKING AIM AT NEW TARGETS FOR MYASTHENIA GRAVIS TREATMENT



IN MYASTHENIA GRAVIS the immune system makes antibodies that damage or block many of the muscle's acetylcholine receptors on the surface of muscle cells, preventing the chemical from binding to the damaged receptors and reducing muscle contractions, leading to weakness and fatigue.

Linda Kusner, Ph.D., associate research professor in the department of pharmacology and physiology at the GW School of Medicine and Health Sciences, received a multi-year Muscular Dystrophy Association research grant totaling nearly $300,000 to provide a new fundamental understanding of the basic mechanisms of autoimmunity and validating a new therapeutic target for myasthenia gravis (MG).

Kusner aims to develop a therapy for MG that might eliminate or lessen the need for corticosteroids, the current standard of care. With colleagues, she has discovered a protein called survivin present in MG-affected cells that the group believes supports the presence of autoreactive immune cells by allowing them to escape cell death. In studies that targeted the protein, Kusner and her team observed a reduction in the levels of antibodies in the MG disease process.

In her new work, Kusner will analyze thymus tissue from MG patients as well as from healthy individuals to determine whether the survivin protein is present in both instances. Kusner's team also will evaluate survivin-based therapeutics in an MG rodent model to assess the therapeutics' ability to improve observable weakness, decrease the expression of autoreactive immune cells, decrease acetylcholine receptor-specific antibodies, and decrease damage to the nerve-muscle junction.

THYMECTOMIES AND MYASTHENIA GRAIVS

Henry Kaminski, M.D., chair of the Department of Neurology and Meta Amalia Neumann Professor of Neurology at the GW School of Medicine and Health Sciences, has found that removing the thymus effectively reduced patients' muscle weakness, as well as the need for immunosuppressive drugs and hospitalizations.

"While surgery is expensive and not without risk, this research will empower patients and their doctors to make informed decisions regarding treatment," said Kaminski.

Previous studies have suggested that removing the thymus may reduce MG symptoms – droopy eyelids; blurred or doubled vision; difficulty talking, breathing, and swallowing; and neck and limb movement problems – but Kaminksi's study, published in the New England Journal of Medicine, is the first randomized study of thymectomy in MG patients, providing clinical evidence of the benefits of the surgery.

Beyond the Buzz

GW RESEARCHERS JOIN INTERNATIONAL ACTION ON THE ZIKA VIRUS

BY **C.J. TRENT-GURBUZ**

The countdown at the University of Wisconsin-Madison (UW) began on March 7, 2016, when researcher David O'Connor, Ph.D., professor in the Department of Pathology and Laboratory Medicine at the School of Medicine and Public Health at UW, and his team infected a pregnant rhesus macaque monkey with the Zika virus.

"They're releasing all of the results from her pregnancy, live," says Chiara Manzini, Ph.D., assistant professor of pharmacology and physiology at the GW School of Medicine and Health Sciences (SMHS). "They're planning to do a C-section as soon as she's ready because they want to get the placenta [to analyze it]."

The free flow of data from UW is standard – now – for Zika virus research. While in the past, investigators might have worked in siloed environments, the Zika virus has spurred researchers around the globe to share data as soon as possible.

"This is a race," Manzini says.

In the months since the World Health Organization declared the Zika virus an international public health emergency, researchers have made significant strides; specifically, they've connected the virus to neurological disorders and established public health protocols for those living in, or visiting, the Zika zone.

MAKING STRIDES

In the months since the World Health Organization declared the Zika virus an international public health emergency, researchers have connected the virus to neurological disorders and established public health protocols for those living in, or visiting, the Zika zone.

"Research has not only added to the body of evidence suggesting that Zika virus does cause microcephaly, but there are also additional suggestions that neurological damage in infants born to mothers who have become infected with Zika during pregnancy is worse than we thought," explains Douglas Nixon, M.D., Ph.D., chair of the Department of Microbiology, Immunology, and Tropical Medicine and Walter G. Ross Professor of Basic Science Research at SMHS. "There may be a number of different neurological problems in addition to microcephaly that infants may develop."

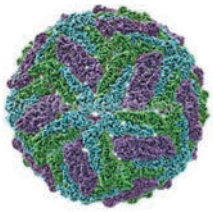
Or, as Manzini phrases it: "Microcephaly is just the tip of the iceberg."

The virus, she explains, infects the brain and kills the proliferating cells, which can cause severe growth defects in the developing fetal brain. Microcephaly, a condition in which a baby is born with an abnormally small head and potential brain damage, is one possible result, as is Guillain-Barré Syndrome, a rare autoimmune disorder of the central nervous system.

It's precisely because the virus has been linked to these disorders that researchers are sharing data as they sprint toward a solution.

"Microcephaly is just the tip of the iceberg."

CHIARA MANZINI, Ph.D.



"Nobody has the general expertise to deal with this; it isn't like other epidemics where it's simply the passing of the virus and it just infects the host," says Jeffrey Bethony, Ph.D., professor of microbiology, immunology, and tropical medicine at SMHS. "[Zika] has long-term effects that you wouldn't even know existed unless you had a multidisciplinary team."

That team includes people like himself, a vaccinologist, and those such as Manzini, who studies brain malformations, as well as neurologists and fetal immunologists. For her part, Manzini is using a zebrafish model to look at "brain development in real time on a very short timeline." Researchers have also looked at other animal models – the rhesus macaque at UW, mice, and fruitflies – and while none are precisely perfect for Zika, all offer some type of information, Manzini says, adding to the communal pool of data.

The National Institutes of Health (NIH) is also working to develop a vaccine as soon as possible, though that comes with certain challenges, according to Nixon and Bethony. The NIH has to ensure the vaccine isn't more harmful than the virus; in other words, it has to be safe. It's a process that requires significant testing despite the urgency.

"Who do you want to vaccinate?" Bethony asks. "You want to vaccinate women of childbearing years, or potential mothers."

Developing a vaccine for such a patient group is particularly difficult, he says, adding "the idea of a physician is 'do no harm,' so they're going to be very cautious."

Right now, according to the NIH, its National Institute of Allergy and Infectious Diseases (NIAID) is focusing on a DNA-based vaccine similar to the West Nile Virus vaccine. Researchers also are exploring a live-attenuated, or weakened, vaccine that's related to the vaccine for dengue virus, which is a member of the Flavivirus genus, like Zika, yellow fever, and chikungunya. NIAID is looking at other potential vaccine approaches as well, including a whole-particle inactivated vaccine similar to that used against dengue and Japanese Encephalitis.

"In terms of physically making a vaccine that could be tested in people, I think we're getting close – quite soon," says Nixon.

Meanwhile, at GW, those interested in Zika-related research are applying for grants, and a Zika interest group, Nixon says, has formed between those at SMHS, the GW Milken Institute School of Public Health, and GW clinical partners, the GW Medical Faculty Associates and Children's National Health System.

"People are becoming excited about Zika research," he says, "and it really is a very exciting opportunity."

Studying Clues to Fetal Mysteries

GW RESEARCHER EXPLORES NEURAL DEVELOPMENT FROM ITS EARLIEST STAGE

BY **THOMAS KOHOUT** AND **ERIC BUTTERMAN**

You see it all the time, couples placing headphones on a pregnant woman's belly to share a little Bach or Beatles with their soon-to-be newborn, reading the stories they imagine one day telling just before bedtime, or stomaching all manner of juice concoctions in an effort to strike that ideal nutritional balance. It's all done in the name of development. In the anxious months leading up to the birth of a child, expectant parents will try just about anything to give their growing baby a little edge.

But what's really going on during pregnancy? How aware is that fetus growing inside? What can science do to ensure the best possible outcome after birth? Despite all that medical professionals have come to know about pregnancy, neural development remains more enigmatic than indubitable. Unravelling the complex wiring processes taking place within the developing brain may allow for early recognition of neurological problems affecting life after birth.

WHAT'S GOING ON?
Knowing how aware a fetus is in the womb may allow for recognition of problems with the fetus earlier, which, combined with treatment, might just alter quality of life concerning issues such as preterm infancy.

With the support of a nearly $2 million grant in 2013 from the National Eye Institute, Matthew Colonnese, Ph.D., assistant professor of pharmacology and physiology at the GW School of Medicine and Health Sciences (SMHS) and a researcher with the George Washington University Institute for Neuroscience, is working to shed more light on the fetal brain developmental period in the hopes of providing those answers.

"My fundamental hypothesis is development in circuits are specialized, and it's a specifically tuned system at work to do something different than the adult brain."

MATTHEW COLONNESE, Ph.D.

Eyeing Development

Colonnese has been exploring the subject of fetal brain development for years, dating back to his days as a graduate student. "At Yale, I was studying how the retina lines up to targets centrally. We knew this required activity in these targets, but had little idea what this activity consisted of." Exploring how the brain constructs the neural circuitry that links the retina to the thalamus and the cerebral cortex, Colonnese says, ultimately led him to the work he delves in today.

Colonnese wanted to understand the timeline in brain development when the various pieces of the brain begin to talk to one another. Before arriving at GW, he collaborated with a team of clinicians in Paris who made brainwave recordings on preterm infants, at ages before they would have been born – in gestational weeks 28–34. The group also studied neural activity in the cortex using baby rats.

"We designed an experiment to give those pre-term infants light flashes and did the same with the rats," explains Colonnese, who heads SMHS's Laboratory of Systems Neural Development. "We could map the activity patterns that were occurring in the babies onto the rat."

The work established a baseline for comparison between the fetal rat brain and the human fetus. By matching brainwave patterns, and understanding what patterns to expect

"What's most interesting to me are spending days sticking electrodes in and having no idea what you will see. It's completely unknown — it feels like exploring the moon."

MATTHEW COLONNESE, Ph.D.

at the equivalent ages, researchers could extrapolate observations in the rat and mouse models onto the fetal brain development timeline.

Measuring the Flow

In his investigations, Colonnese has noted that many of the neural circuits in the fetal brain are specialized and specifically tuned to complete a developmental task that is different than the task they perform in the adult brain. Colonnese wondered whether the specialized properties of the fetal neurocircuitry might prevent the normal flow of information from the eye to the brain.

Using an array of electrodes to simultaneously record the activity of hundreds of neurons across multiple regions of the brain, the team discovered that the thalamus, acting as a way station for signals traveling between the eye and the cortex, contains a "booster" that amplifies the signals before sending them to the rest of the brain. Those observations were published in the October edition of eLife.

Typically in the adult brain, the eye sends information in a specific pattern, explains Colonnese. The eye transmits a refined stream of signals. "In the adult brain, it's graded," he says. "If you see a little bit of light, you get a little response; if you see a lot of light, you get a big response."

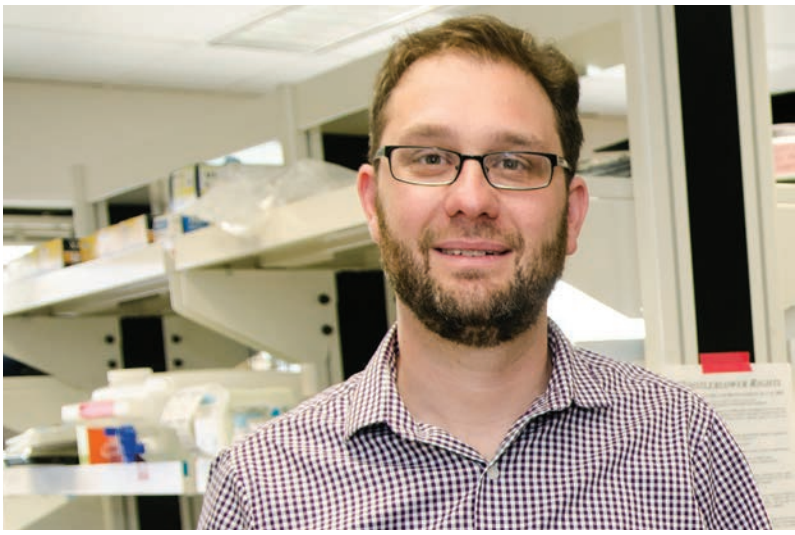
In the fetal brain, on the other hand, the eye doesn't provide that same pattern. Instead, the retina sends a massive burst of activity that Colonnese believes reflects a unique circuitry there to amplify the activity early in fetal development. "In the fetal brain, you get nothing, nothing, nothing, BOOM! You get everything.

"You can't see using that information," he adds. "It's a just massive burst of stuff that is going through telling the other parts of the brain, 'yes something happened.' "

Colonnese believes this booster mechanism has evolved to help maintain signal strength between the various parts of the brain while the circuitry is being established. The amplifier, he says, explains how the fetal brain continues to stay active despite underdeveloped synapses.

The next goal, Colonnese says, will be to generate a kind of EEG "atlas" of neurodevelopment, pinpointing when the fetal brain transitions from a developmental stage to more adult-like patterns of behavior. With that information at their disposal, he says, physicians could identify problems with particular brain regions through disruptions in brain activity.

"This may give neonatologists a sense of what is wrong with a child who has an abnormal EEG," he says, and point to a possible plan to address those problems.



MATTHEW COLONNESE, Ph.D.

The Search is Just Starting

Despite early strides, the major challenge will continue to be understanding the large number of changes during the brain's development. Colonnese explains that trying to link a specific pattern change to a specific circuit can be similar to searching for a needle in a haystack.

"Everything is changing. How do you separate one change among the many we are observing?" he asks. "Our approach is to systematically go through the many potential candidate cells, neurotransmitters, and receptors and remove them, one by one, to see which can modify the timing of development."

Colonnese knows there is a long way to go in his work, but the days with little to go on are worth it for the ones that reveal breakthroughs. "You think about the brainwave patterns in the fetus that have been described for something like 50 years, but their origin has always been mysterious," he says. "What's most interesting to me are spending days sticking electrodes in and having no idea what you will see. It's completely unknown – it feels like exploring the moon – and it's even trying to answer the most basic question: 'Why is the fetus kicking?' You don't have to be a researcher to ask that one. But hopefully this work will be a part of answering it."

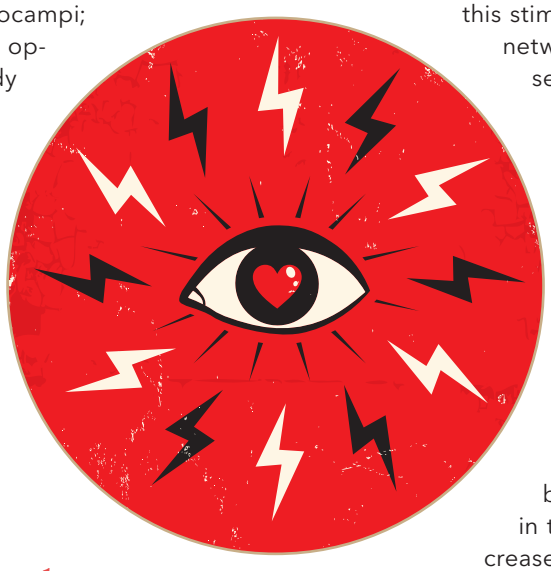
The Stimulation Inspiration

TRACKING THE RESULTS OF LOW-FREQUENCY DEEP BRAIN STIMULATION ON EPILEPSY PATIENTS

BY **C.J. TRENT-GURBUZ**

When the National Geographic cameras began rolling last year, Danette Cunningham was struggling with epilepsy: she had twice suffered from seizures while driving and had experienced constant shakiness. Cunningham's seizures originated from both hippocampi; for her, surgery would not be an option, and medications had already proven ineffective. Mohamad Koubeissi, M.D., director of the Epilepsy Center and associate professor of neurology at the GW School of Medicine and Health Sciences (SMHS), however, had a potential solution.

As documented in the TV show "Breakthroughs," Koubeissi used a pioneering approach to treat Cunningham and a second patient, Yakov Krug, both of whom were diagnosed with temporal lobe epilepsy. Koubeissi, and a GW Hospital surgical team led by Donald Shields, M.D., Ph.D., FACS, assistant professor of neurological surgery, implanted a permanent electrode for Deep Brain Stimulation 5 inches inside the brains of Cunningham and Krug. The stimulator sent out low frequency electrical pulses into the hippocampus.



"In previous deep brain stimulation trials, the results have never been that good."

MOHAMAD KOUBEISSI, M.D.

"All previous trials used high frequencies in the range of 90 to 130 pulses per second, or hertz; that's very high," Koubeissi explains. "In the current trial, what we're using is 1 to 5 hertz, so it's low frequencies, which explains why the patient doesn't feel anything. Over time, this stimulation tends to alter the seizure network or create changes within the seizure network that paves the road to fewer seizures and maintains or even improves cognitive function."

A month after healing, Cunningham and Krug each showed a massive reduction in their seizures.

"In previous deep brain stimulation trials, the results have never been that good," Koubeissi says. "There are numerous other targets in the brain that have been tried, and, in the best of subjects, seizures decrease by 30 percent or 40 percent, and some patients do not seem to benefit at all. Despite the small sample in our study, the benefit is more than 90 percent."

A year has since passed, and the results, though limited to two patients, "continue to be unique and promise to be a real game changer." The next step, Koubeissi says, is identifying more patients who fit the criteria for the procedure and designing an extensive clinical trial. He'd also like to apply for funding and, depending on the efficacy and tolerability of the intervention in a larger sample, seek FDA approval.

Koubeissi is encouraging any patients who might qualify for the treatment to reach out to the SMHS Department of Neurology's research office at **raly@mfa.gwu.edu**.

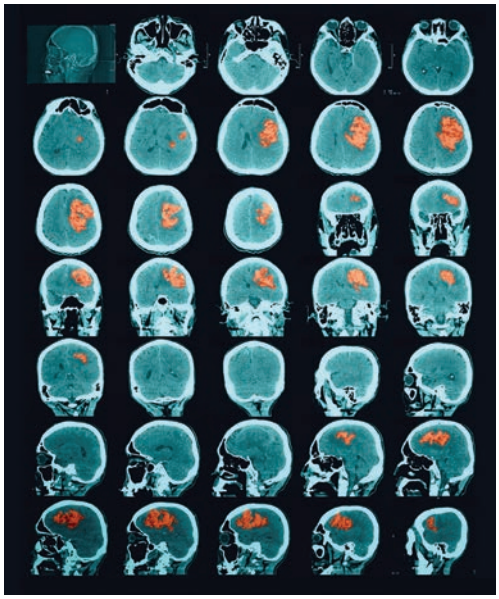
Turn Back Time by Acting Fast

GW HOSPITAL'S STROKE TEAM IS AMONG THE NATION'S LEADERS IN ACUTE CARE

BY **STEVE GOLDSTEIN**

Last autumn, an ambulance rushed into the emergency entrance of George Washington University Hospital (GW Hospital) bearing a middle-aged woman who had developed an acute left-sided weakness that morning. Fearing a stroke, her family called 911. Upon examination, doctors assessed her as an 11 on the National INstitutes of Health (NIH) Stroke Scale, evidenced by dysarthria (slurred speech), left facial droop, and severe left arm and leg weakness. An X-ray computed tomography scan (CT) of her head ruled out bleeding in the brain.

The patient was given IV tPa (intravenous clot-busting medication) less than an hour after symptom onset. A CT angiogram of the head showed a blood clot in the right middle cerebral artery. She was taken to the angio suite where neurointerventionalist Wayne Olan, M.D., assistant professor of neurological surgery, and colleague Dimitri Sigounas, M.D., assistant professor of neurological surgery, used a stent-retriever device to successfully remove the clot. After the procedure she had only mild left facial weakness and mild left hand incoordination. The woman was recently seen in the GW Medical Faculty Associates clinic and has subtle left facial droop but is otherwise back to normal. She is working, performing all of her activities of daily living, walking independently, and driving.



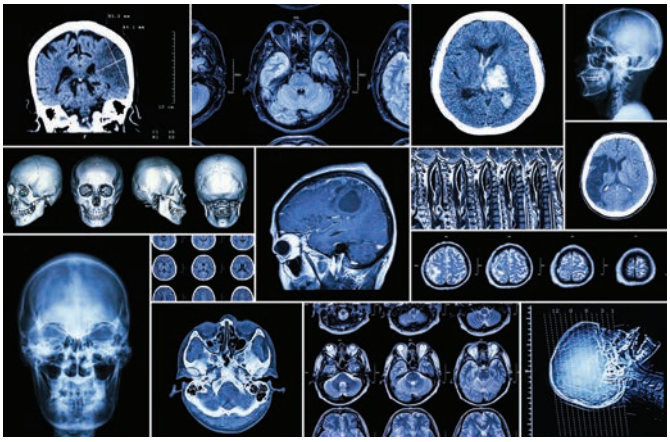
TIME IS BRAIN

In the event of a stroke, rapid response is crucial; quick recognition and treatment can save lives or minimize the long-term effects of a stroke. GW Hospital is certified as a Comprehensive Stroke Center, which is a designation that recognizes the specific capabilities of hospitals that can treat the most complex stroke cases. Less than 2 percent of U.S. hospitals – less than 100 – have that certification.

Stroke is a killer. Thanks to new procedures and proactive stroke prevention measures, stroke has, in the last decade, dropped to fifth from the third leading cause of death in the United States. Rapid response is crucial; quick recognition and treatment can save lives or minimize the long-term effects of a stroke. "Time is brain" is a key mantra of stroke neurology. Not long before the incident described above, GW Hospital was certified as a Comprehensive Stroke Center, a designation which may have saved the woman's life.

"We have the clinical expertise to take care of complicated stroke cases. In addition to providing the routine care that Primary Stroke Centers can deliver, we can provide endovascular procedures on a 24/7 basis, and we're actively engaged in research trials. It also means we have more vigorous metrics and measures that must be collected."

CHRISTOPHER LEON-GUERRERO, M.D.



TAKING THE CARE FURTHER

In addition to the routine care that GW delivers as a Comprehensive Stroke Center, the hospital is also actively engaged in research trials. It is constantly examining data and re-evaluating its service to patients.

What is a Comprehensive Stroke Center (CSC)? The designation recognizes the specific capabilities of hospitals that can treat the most complex stroke cases. Less than 2 percent of U.S. hospitals – less than 100 – have that certification. "It means that we have the clinical expertise to take care of complicated stroke cases," says Christopher Leon-Guerrero, M.D., assistant professor of neurology at the GW School of Medicine and Health Sciences, who attends the stroke and general inpatient service at GW Hospital. "In addition to providing the routine care that Primary Stroke Centers can deliver, we can provide endovascular procedures on a 24/7 basis, and we're actively engaged in research trials. It also means we have more vigorous metrics and measures that must be collected, so we're constantly examining data and re-evaluating service to patients."

The Joint Commission and American Heart Association/American Stroke Association instituted a new level of certification in September 2012 to identify the medical facilities with the resources, staff, and training, such as advanced imaging capabilities and specialized treatments, necessary for the care of complex stroke cases. "This designation demonstrates not only the unique expertise of our physicians, but also the exacting collaborative procedures that GW Hospital has developed involving everyone from the transport staff, technologists, nurses, and physicians to the CEO and hospital leadership," says Henry Kaminski, M.D., chair of the Department of Neurology and Meta Amalia Neumann Professor of Neurology at SMHS.

GW's CSC certification is good news for a region that sits at the northern end of the so-called "stroke belt," a swath of mostly southern states stretching west to Texas with a high incidence of stroke. "The treatments that we now have," says Leon-Guerrero, "have been proven to lower the amount of damage people suffer from strokes." The evolution of advances in stroke treatment can be described in three categories:

- **Primary stroke prevention:** Preventive measures, such as diet, blood pressure control, and exercise, can lower the risk of stroke.
- **Acute treatment:** IV tPA (intravenous tissue plasminogen activator) clot-busting medication can be given in the first 4 1/2 hours to dissolve the clot and results in better clinical outcomes for patients.
- **Endovascular procedures:** These are designed to restore perfusion to the brain in areas that are blocked off. For example, a stent-retriever or "stent-triever," can be used to deploy a stent to pull the clot out of an artery. "We offer this to patients up to six hours from symptom onset," says Leon-Guerrero. "The clot has to be in a blood vessel that's reachable by catheter, a proximal large vessel occlusion. Some clots are so small that they are not amenable to this procedure."

SPOTTING SIGNS OF STROKE

- **Sudden numbness or weakness of the face, arm, or leg, especially on one side of the body**
- **Sudden confusion, trouble speaking, or understanding**
- **Sudden trouble seeing or blurred vision in one or both eyes**
- **Sudden trouble walking, dizziness, loss of balance or coordination**
- **Sudden severe headache with no known cause**

"This designation demonstrates not only the unique expertise of our physicians, but also the exacting collaborative procedures that GW Hospital has developed involving everyone from the transport staff, technologists, nurses, and physicians to the CEO and hospital leadership."

HENRY KAMINSKI, M.D.

Leon-Guerrero says elapsed time is of the essence. "The earlier you treat, the more likely the patient will benefit," he says. "These devices are also all time dependent." Disagreement among practitioners remains over treating patients beyond the six hour mark. Another contentious issue is figuring out when to start the clock when a person wakes up with stroke symptoms. As of yet, no biomarkers in the blood have been discovered that could put a "time stamp" on onset.

Damage to the core of the brain is inevitable in virtually all strokes. The part of the brain not getting enough blood, but which is salvageable, is the penumbra (the cells surrounding a blockage where blood flow and oxygen levels are reduced). "The sooner we can restore profusion, the more of the penumbra we can save," Leon-Guerrero explains.

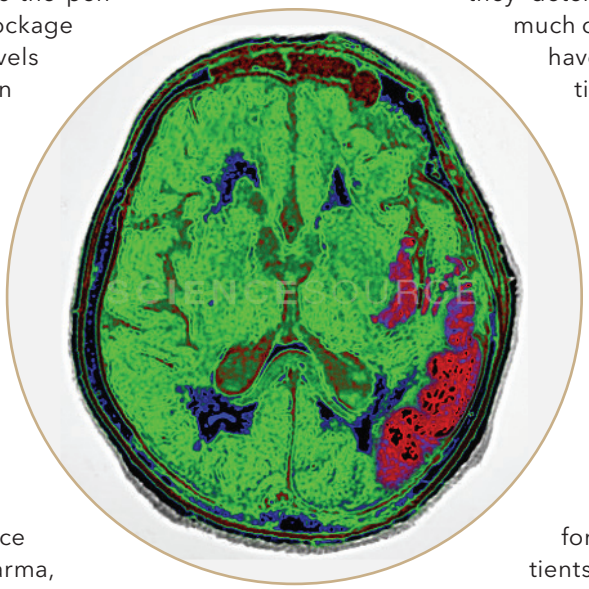
When a person suffers a stroke, the treatment protocol shifts to secondary stroke prevention, aimed at reducing the risk of reoccurrence. GW Hospital has a 16-bed inpatient rehabilitation unit. "We use an evaluation system called the Functional Independent Measure, an ordinal scale from one to seven that determines the level of assistance the patient needs," says Annu Sharma, D.O., instructor of neurology, who works in the rehab department at GW Hospital. The evaluation covers ambulation, transportation, mobility, and self-care, and it is scaled from total independence to maximum assistance needed.

Following the CSC certification, the unit has been receiving more referrals from stroke. Along with Ty Lai, M.D., instructor of neurology at SMHS, Sharma manages the unit and they determine, with the neurologist, how much daily therapy can be tolerated. "We have to be alert to changes in cognition during evaluation; whether a stroke might be getting bigger, or a new stroke is occurring," she adds.

The benefits of aggressive therapy are substantial and relatively rapid. "We can see recovery in three to four weeks, sometimes in two weeks," she says. "We see patients go from being significantly weak on one side to being able to have fully restored function."

Among the basic requirements for a CSC is to treat 20 or more patients per year with a diagnosis of subarachnoid hemorrhage caused by an aneurysm and to administer IV tPA 25 or more times per year for eligible patients with acute ischemic stroke.

Leon-Guerrero says GW Hospital is expecting 600 to 700 stroke patients in 2016 and welcomes the new status the hospital has for serving the community. "I enjoy acute decision-making," he explains. "I like to deal with patients who are faced with these unfortunate life-changing events, and neurology is filled with life-changing events. There's a chance you can make a huge and lasting impact on someone's life."



LIMITING THE DAMAGE

Damage to the core of the brain is inevitable in virtually all strokes. The part of the brain not getting enough blood, but which is salvageable, is the penumbra. The sooner profusion is restored, the more of the penumbra can be saved. The benefits of aggressive therapy are substantial and relatively rapid. Recovery can be seen in three to four weeks, sometimes in two weeks.

ACT FAST

F ace: Facial drooping

A rm: Arm weakness

S peech: Difficulty or slurred speech

T ime: Call 911 immediately

Addressing Global Mental Health Issues Across Town and Around the World

GLOBAL MENTAL HEALTH PROGRAM PROVIDES UNIQUE TRAINING OPPORTUNITIES FOR RESIDENTS

BY **THOMAS KOHOUT** AND **SANDEEP RAVINDRAN**

Since 2011, according to the United Nations High Commissioner for Refugees, 4.8 million men, women, and children have fled Syria, a nation devastated by five years of warfare. Nearly 7 million more are internally displaced within the country.

Many of those fleeing the destruction take an arduous route out of Syria, traveling hundreds of miles on foot across Turkey to the Aegean Sea. From the Turkish coast, the refugees board overcrowded boats for a risky water-crossing to reach Greek islands Chios and Lesbos, and then it's on to the Greek mainland and into Europe. Along the way, teams of nongovernmental organization (NGO) aid workers triage the incoming refugees, spotting the sick from among the weary and offering what help they can. Amidst the flow of refugees, volunteers, global media, and border patrols during a peak in the exodus last November 2015 stood Catherine May, M.D., associate clinical professor of psychiatry and behavioral sciences at the GW School of Medicine and Health Sciences (SMHS), assessing the mental health landscape on behalf of medical NGO Remote Area Medical (RAM).

It was an emergency mission made possible by Allen Dyer, M.D., Ph.D., professor of psychiatry and behavioral sciences at SMHS, who leads the department's Global Mental Health residency track program. RAM was organizing a medical response mission to Greece, which is serving as a primary stop-over location for Syrian refugees. The group turned to Dyer for a recommendation based on previous associations as well as his reputation as a global mental health expert. He assembled a team led by May that included GW resident alumni Nicole Nguyen Perras, M.D., RESD '16, and Sandeep Denduluri, M.D., RESD '14. May's mission was organized in fairly short order, in part because the department's second-year residents were already engaged in a simulation exercise where they were preparing to respond to a yet-to-occur global disaster.

At the height of the refugee influx, Greece was receiving as many as 6,000 refugees a day. They were in "migration" mode, eager to reach northern Europe, focused on physical, not emotional, needs.

"That situation rapidly changed in March 2016, with the European Union-Turkey accord," explains Dyer. "With refugees unable to move forward, local resources became strained and the humanitarian workers soon became overwhelmed."

The United States Embassy in Athens, in conjunction with Greek NGO METAdrasi, again turned to Dyer and May to lead a program, "Building Resilience in Humanitarian Workers," which took place in Athens in June 2016. The program also provided an opportunity for Fatima Noorani, M.D., RESD '16, who participated in the workshop while still a resident.

PRIORITIZING MENTAL HEALTH CARE
Whether health care professionals are working in a post-conflict setting, in low-income countries with limited resources, or with refugees and torture survivors in the United States, mental health is a crucial aspect of care. Often underfunded, mental health care is vital to a long, healthy life.

Specializing in Global Mental Health

The department has been involved with Global Mental Health for nearly two decades. Five years ago, James Griffith, M.D., chair of the Department of Psychiatry and Behavioral Sciences and Leon M. Yochelson Professor of Psychiatry at SMHS, parlayed the department's clinical expertise into the nationally recognized Global Mental Health (GMH) residency training program. While all of GW's psychiatry residents participate in GMH training, and second-year residents participate in a variety of seminar series, typically a quarter of GW's 24 residents seek more specialized training.

As the head of the GMH program, Dyer prepares psychiatry residents to respond. Residents in the GMH track participate in up to a year's worth of international training experiences, while fourth-year residents can spend as much as eight months of their final year of training on international missions. During the past two years, GMH track residents participated in projects in Bangalore, India; West Bank, Palestine; Nigeria; Cambodia; Natal, South Africa; and Greece.

These projects serve as unique learning opportunities, says Griffith. "Most of the time, you're working with a very high-need population that has very few resources, little funding, and very few mental health professionals," he explains, "so there's a lot of improvisation, learning how to use the strengths of a culture, strengths of families, to promote mental health."

In the early years of the program, residents bore their costs of travel for international projects, while GW maintained continued salary support. Fortunately, the Charles and Sonia Akman Professorship in Global Psychiatry, established in 2012, now offsets the travel expenses for many of those international projects. Together with travel funds from the Department of Psychiatry and Behavioral Sciences and the SMHS Office of International Medicine Programs, personal expenses for residents on international rotations have been substantially reduced.

Around the world, mental health is the number one priority in terms of Disease Adjusted Life Years, the measure of the impact of health problems.

Global Mental Health Begins at Home

Around the world, mental health is the number one priority in terms of Disease Adjusted Life Years, the measure of the impact of health problems. Whether health care professionals are working in a post-conflict setting, in low-income countries with limited resources, or with refugees and torture survivors in the United States, mental health is a crucial aspect of care. "These are all different populations of people, but they share in common abusive circumstances or settings where there are very few resources for mental health," says Griffith.

To that end, the department's GMH track has become an important feature of the school's residency program. "This is a big drawing card, and one of the reasons that residents come across the country to train here rather than somewhere else," he says. In recognition of its innovative curriculum, the American College of Psychiatrists awarded the global mental health program the 2016 Award for Creativity in Psychiatric Education.

The program was a good fit for the multi-ethnic Washington, D.C. area, which, according to Griffith, is estimated to have more than 40,000 political torture-survivors in addition to other refugees from more than 50 countries. Residents in the GMH track rotate at the Northern Virginia Family Service, which provides community mental health services to immigrant and refugee populations. It's "a perfect example of the global mental health work that we do locally," says Eindra Khin Khin, M.D., RESD '08, B.S. '01, assistant professor of psychiatry and behavioral sciences at SMHS.

Khin Khin leads the department's Human Rights Clinic, which works in close collaboration with Physicians for Human Rights to assess asylum seekers. Most individuals have suffered political oppression and have been tortured by their governments or "under color of the law" in their home countries. Their asylum petitions are based upon the threat of harm were they to return to their home countries. Others seek asylum protection as victims of human trafficking or other crimes under the Victims of Trafficking and Violence Protection Act.

"In this day and age of globalization, you really don't have to leave wherever you are to do global mental health projects," says Khin Khin, who has worked with many immigrant and refugee populations, and supervises pro bono psychiatric evaluations for people seeking asylum status in the United States.

She isn't alone in her commitment to global mental health. For Michael D. Morse, M.D., RESD '16, clinical instructor of psychiatry and behavioral sciences at SMHS, practicing medicine – specifically the diagnosis and treatment of patients with mental disorders – was always part of his plan. It wasn't until he journeyed to Jerusalem between college and medical school, however, that he witnessed how his passion for psychiatry and global health could have a real impact on physicians and patients in the Middle East.

"With courage, humility, and dogged persistence, Michael has opened doors in the West Bank and Gaza, and showed how building mental health services can further the cause of peace," says Griffith.

In 2008, Morse, while still a student at the Harvard Medical School, created the Palestinian Medical Education Initiative (PMED), an international NGO based in the West Bank and in the United States. By 2015, the group earned international recognition, receiving funding from the German Regional Fund for the Middle East and North Africa to integrate mental health services into primary care settings in Gaza and the West Bank, and for parenting classes and other mental health initiatives in Ramallah.

"Cross-cultural competency is an essential part of any residency training," says Amir Afkhami, M.D. '03, Ph.D., associate professor of psychiatry and behavioral sciences, and of global health at SMHS, highlighting a strength of GW's program. "Integrating global mental health in that training is a great vehicle to teach that to residents."

He adds that "there's much to learn from the global health setting in terms of engaging with the community, and it's more important than ever. Most places don't have the kind of faculty that we have at George Washington University, with the kind of experience that we have, where this can be taught in the way we can."

The Refugee Mind

CROSS-CULTURAL AWARENESS AND SUICIDE PREVENTION

BY **LAURA OTTO**

"How can we improve suicide prevention services for refugees in the United States, as well as create feasible solutions in settings within the United States where refugees are commonly resettled but there is almost no psychiatric care?" asked Brandon Kohrt, M.D., Ph.D., RESD '13, assistant professor of psychiatry, global health, and cultural anthropology at the Duke Global Health Institute at Duke University.

PREVENTING SUICIDE IN REFUGEES

In his presentation, "Suicide Prevention: Cross-Cultural Perspectives for Refugees and Global Mental Health," Brandon Kohrt, M.D., Ph.D., RESD '13, assistant professor of psychiatry, global health, and cultural anthrology at Duke University, addressed how people think about suicide from a global perspective and how that can inform how we better treat refugees in the United States. Disaster, war, conflict; trauma and abuse; discrimination; stresses of acculturation and dislocations; and isolation and lack of social support are all important risk factors for suicide.

Kohrt returned to the GW School of Medicine and Health Sciences (SMHS) to deliver the 22nd Annual Seymour Perlin, M.D., Lecture on Suicidology. Perlin, Professor Emeritus of Psychiatry and Behavioral Sciences at SMHS, led the school's psychiatry residency program from 1977 to 1993. The Seymour Perlin, M.D., endowment fund was established in 1987 to honor the renowned leader and mentor who specialized in the field of suicidology and to support an annual grand rounds lecture series focusing on suicide.

In his presentation, "Suicide Prevention: Cross-Cultural Perspectives for Refugees and Global Mental Health," Kohrt addressed how people think about suicide from a global perspective and how that can inform how we better treat refugees in the United States.

"The United States is the largest recipient of Bhutanese refugees, about 800,000 have settled here," says Kohrt. "If you look at refugees in the United States, Bhutanese have a suicide rate of 24.4 per 100,000. This is a higher suicide rate than when the Bhutanese were living in refugee camps in Nepal, or for Bhutanese resettled in other countries."

Disaster, war, conflict; trauma and abuse; discrimination; stresses of acculturation and dislocations; and isolation and lack of social support are all important risk factors, according to Kohrt, and part of refugees' experiences, making them a highly vulnerable group. However, refugee resettlement policies in the United States often resettle refugees in rural areas where mental health services are difficult to access. They also separate members of extended families that had lived together for decades in refugee camps, sending them to different regions of the United States where they can no longer maintain their connectedness.

"The take-home message here is the concept of ethnopsychology, the idea that every cultural group has their own way of understanding emotions, feeling, senses, suffering," he says. There are two key pieces to this for the Bhutanese refugees. "One is the idea of the heart-mind, the location of emotions and memories; the other is the idea of the brain-mind, where logic and social control and expectations are all modulated."

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