

neurotransmitter

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



fall 2019

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he Fall 2019 edition of *Neurotransmitter* focuses on the national epidemic of acute traumatic brain injury (TBI) through the multi-faceted lens of the George Washington University (GW).

GW Hospital's Level 1 Trauma Center cares for these patients in the minutes and hours after injury, often quite literally bringing them back to life. The journey to recovery takes a team of therapists, emergency room physicians, neurosurgeons, nurses, psychiatrists, and rehabilitation specialists to restore their lives, which often are transformed by their experiences.

The most severe TBI cases are categorized as disorders of consciousness, leaving patients with devastating symptoms. Unfortunately, clinical research for these seriously ill patients is limited, in large part due to a lack of assessment tools to measure recovery of consciousness. To address this gap, Trudy Mallinson, PhD, from the GW School of Medicine and Health Sciences (SMHS) Department of Clinical Research and Leadership, has been developing a "Disorders of Consciousness Scale" to enable clinical researchers to measure their work with severe TBI patients. Chronic brain injury is also the focus of Robert W. Turner II, PhD, also in the Department of Clinical Research and Leadership at SMHS. He's exploring the individual social impacts of TBI on a special population: professional football players who suffer TBI as an inherent consequence of the sport.

GW recently received several prestigious awards that reflect the commitment our clinical partnership has toward treating brain injury. GW Hospital was honored by the American Heart Association/American Stroke Association with its highest award for advancing the comprehensive care of stroke patients. Henry J. Kaminski, MD, earned one of only 25 rare disease network grants from the National Institutes of Health (NIH) to provide an infrastructure to study the rare autoimmune disease myasthenia gravis. Sally Moody, PhD, the chair of the Department of Anatomy and Cell Biology at SMHS, received an NIH grant to evaluate the genetic basis of developmental disorders.

The SMHS community recently welcomed Sanjay B. Maggirwar, PhD, as the new chair of the Department of Microbiology, Immunology, and Tropical Medicine. His research addresses how HIV may produce accelerated vascular aging, which would predispose individuals to stroke at an early age.

We believe these and other stories make it evident that GW is at the forefront of the care of traumatic brain injury, as well as many other areas of brain health. We hope you agree and that you enjoy this edition of *Neurotransmitter*. Please feel free to contact us with any questions.

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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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Stroke Treatment Center
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RAPID STROKE CARE

Timing is everything when it comes to stroke care, and thanks to advanced brain imaging software, the George Washington University (GW) Hospital can now make faster care decisions for patients experiencing a stroke.

The hospital's new RAPID CT Perfusion software streamlines treatment decisions for doctors when patients present to the hospital with a stroke more than six hours after the event occurred.

In the past, patients who arrived in the later stages of a stroke would not have been candidates for aggressive stroke treatment because it was difficult for doctors to determine the amount of brain damage, and whether more damage was imminent, said Kathleen Burger, DO, director of the GW Hospital Comprehensive Stroke Center.

Now, in only 90 seconds, the RAPID software can generate information on how much damage has occurred in the brain and what areas have not yet been affected but are still at risk as time goes on. Burger said that data gives doctors information to help them determine the efficacy of certain surgical procedures.



TOP HONOR

GW Hospital received the highest honor awarded for stroke treatment by the American Heart Association/American Stroke Association. The award recognizes GW Hospital's commitment to stroke treatment.

ON THE HONOR ROLL

The George Washington University (GW) Hospital received the American Heart Association/American Stroke Association's (AHA/ASA) Get With The Guidelines® Target: Stroke Honor Roll Elite Plus Gold Plus Quality Achievement Award. The award is the highest stroke recognition possible from the organizations. It recognizes GW Hospital's commitment to providing the most appropriate stroke treatment according to nationally recognized, research-based guidelines.

To qualify for the Target: Stroke Elite Plus Honor Roll, GW Hospital had to meet quality measures developed to reduce the time between the patient's arrival at the hospital and treatment with the clot-buster tissue plasminogen activator.

According to the AHA/ASA, stroke is the fifth-leading cause of death and a leading cause of adult disability in the United States. The award program is the association's hospital-based quality improvement effort that provides hospitals with tools and resources to increase adherence to the latest guidelines.



UNDERSTANDING THE DEVELOPMENT OF STATE DEPENDENCE AND CONTINUITY

A team from the George Washington University School of Medicine and Health Sciences (SMHS) has published a study in the *Journal of Neuroscience* suggesting the thalamus, a tiny nucleus deep in the brain, controls the development of state dependence and continuity.

Previously, it was thought that to be fully functioning, the brain needed to achieve two milestones: continuity, meaning the brain is always active; and state dependence, meaning brain activity is modulated by sleep, waking, and attention. The circuit mechanisms behind the development of continuity and state dependence have been widely assumed to be located in the cerebral cortex.

"Our results indicate that cellular changes in the thalamus relay function may be critical drivers for the maturation of background activity," said Matthew Colonnese, PhD, associate professor of pharmacology and physiology at SMHS. "Humans undergo developmental transitions in brain activity before and near birth."

Drawing on previous work by Colonnese, his team used advanced techniques to record simultaneously from multiple brain regions to pinpoint the circuit change responsible for the acquisition of continuity and state dependence measured in the sensory cortex. They were surprised to learn that activity changes in the thalamus, which could explain most of these critical developmental milestones.

GW HOSPITAL EXPANDS ACCESS THROUGH HELIPAD



In Spring 2019, District of Columbia Mayor Muriel Bowser signed a bill to allow the George Washington University (GW) Hospital to construct a helipad at its Foggy Bottom facility.

The approval followed unanimous support from the D.C. City Council and its Committee of the Whole. The helipad, which opened in November 2019, expands access to GW Hospital's lifesaving critical care services, including its Level I Trauma Center care and comprehensive stroke care.

"We would like to thank everyone who assisted us through this important pursuit, including our patients, their loved ones, our community part-

ners, and city and federal government representatives, as well as all of our employees and providers," said Kimberly Russo, MBA, MS, CEO of the GW Hospital.



STUDYING GENES LINKED TO BOS

Craniofacial abnormalities are among the most prevalent birth defects, which include branchiootorenal spectrum disorders (BOS). Researchers at the George Washington University (GW) received a \$1.9 million grant from the National Institutes of Health to study the known and unknown genes associated with BOS.

The research will focus on mutations in two genes linked to BOS, *SIX1* and *EYA1*, according to Sally A. Moody, PhD, chair of the Department of Anatomy and Cell Biology at the GW School of Medicine and Health Sciences (SMHS), a principal investigator on the grant.

"We hypothesize that there are other key co-factor proteins that bind to *SIX1* to regulate its activity, and that mutations in these co-factors contribute to the unknown causes," Moody said. "We hope to identify these additional genes, which could lead to more comprehensive screening for infants with suspected hearing impairment."

Other principal investigators include Karen Neilson, PhD, assistant research professor of anatomy and cell biology at SMHS; Dominique Alfandari, PhD, of the University of Massachusetts Amherst; and Francesca Pignoni, PhD, of SUNY Upstate Medical University.

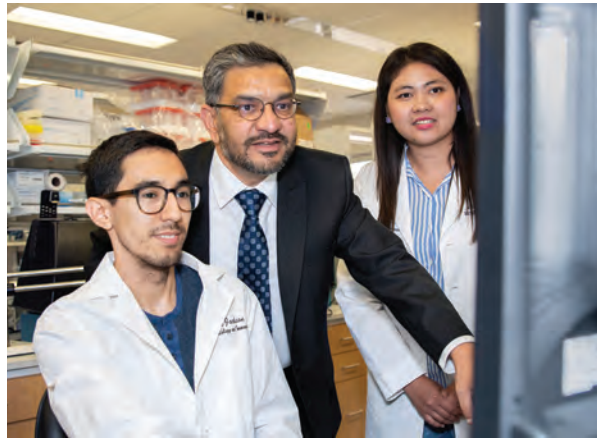
HIV-1 DEMENTIA RESEARCHER SANJAY MAGGIRWAR JOINS SMHS

Sanjay B. Maggirwar, PhD, MBA, who has vast experience researching underlying causes of HIV-associated conditions, recently began his tenure at the George Washington University (GW) School of Medicine and Health Sciences as chair of the Department of Microbiology, Immunology, and Tropical Medicine.

His main research focus is on the inflammatory secondary complications of HIV infection experienced by those living longer with the disease, compared to their aging, uninfected counterparts. Maggirwar is exploring the inflammatory mechanisms associated with HIV-1 dementia. He also leads research projects looking at platelet-mediated neuroinflammatory responses to HIV, accelerated vascular aging in those undergoing combination antiretroviral therapy, and more.

Maggirwar has published nearly 100 research articles in peer-reviewed journals and has been invited to give seminars and present at conferences and symposia around the world. In 2017, he received the "School of Medicine and Dentistry Faculty Academic Mentoring Award" from the University of Rochester Medical Center and, in 2016 he received the "T32 Outstanding Program Director" award. He was also a recipient of the "Distinguished Service Award" from the Society on Neuroimmune Pharmacology.

In addition to providing management and leadership to the department, Maggirwar is responsible for maintaining an active, externally funded research program; overseeing the department's research centers and collaborative research partnership; participating in and coordinating the educational programs in the department; and engaging in service to the school and university.



SANJAY B. MAGGIRWAR, PhD, MBA, (center) has vast experience researching underlying causes of HIV-associated conditions. He recently began his tenure at the GW School of Medicine and Health Sciences as chair of the Department of Microbiology, Immunology, and Tropical Medicine.

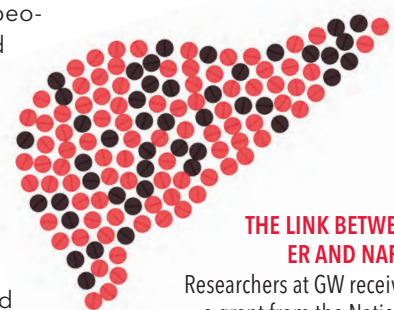
Sanjay Maggirwar has published nearly 100 research articles in peer-reviewed journals and has been invited to give seminars and present at conferences and symposia around the world.

LINKING NERVOUS SYSTEM STRESS TO FATTY LIVER DISEASE

Non-alcoholic fatty liver disease (NAFLD), the accumulation of fat in the liver of people who drink little or no alcohol, is believed to be generated and maintained by endoplasmic reticulum (ER) stress, a protein folding process in the brain. Researchers at the George Washington University (GW) received more than \$2.4 million from the National Institutes of Health to investigate ER stress.

NAFLD is a significant risk factor for Type 2 diabetes, insulin resistance, and hepatic carcinoma, and incidence of the disease is increasing with the obesity epidemic in the United States. The researchers, led by Colin Young, PhD, assistant professor of pharmacology and physiology at the GW School of Medicine and Health Sciences, aim to better understand the role of forebrain and hypothalamic ER stress in obesity induced hepatic sympathetic overactivity and NAFLD development.

Young and his team will examine the role of ER stress in the activation of activator protein-1 (AP-1) – a transcription factor that regulates gene expression in response to a variety of stimuli – in hypothalamic neurons during the development of NAFLD.



THE LINK BETWEEN ER AND NAFLD
Researchers at GW received a grant from the National Institutes of Health to investigate endoplasmic reticulum stress, which is believed to cause non-alcoholic fatty liver disease.



Better Living through Measurement

BY **THOMAS KOHOUT**

Each year, close to 3 million Traumatic Brain Injury (TBI)-related emergencies arrive at hospitals and ambulatory care centers across the country, according to the Centers for Disease Control. While many of those are relatively minor, stemming from a fall or a bump on the head, more serious cases can result in a disruption of normal brain function, bringing on an extended period of unconsciousness.

The more severe instances are categorized as Disorders of Consciousness, with symptoms ranging from a lack of concentration to chronic coma to brain death. Considering the number of people experiencing some type of serious brain injury annually, you might think there would be a wealth of clinical trials to address rehabilitation for these patients. Unfortunately, there aren't.

"There really hasn't been a successful clinical trial for severe TBI patients. They generally get stopped early, or they don't appear to be effective," explains Trudy Mallinson, PhD, OTR/L, FAOTA, FACRM, associate dean for research in health sciences and associate professor of clinical research and leadership and of health, human function, and rehabilitation sciences at the George Washington University School of Medicine and Health Sciences.

A key criticism of these trials, Mallinson explains, is there aren't good assessment tools to measure recovery of consciousness.

To address that gap, Mallinson and Theresa Bender Pape, DrPH, clinical neuroscientist with the

Edward Hines Jr. Veterans Administration (VA) Research and Development Service and a research associate professor at Northwestern University's Feinberg School of Medicine, have collaborated on a series of studies, largely funded by the VA Health Services Research and Development Service and the Department of Defense, to establish and develop the Disorders of Consciousness Scale, or DOCS-25: a tool enabling clinical researchers to measure their work with severe TBI patients.

The tool uses a rating system consisting of 25 stimuli contained in four sensory domains to evaluate patients based on their responses. The four neurobehavioral domains assess specific capabilities: Auditory/Language, response to a voice or a command; Somatosensory, dealing with touch such as light touch or heavy pressure, hot or cold; Visual, a patient's ability to focus on and track an object or face; and Gustation/Olfactory, relating to taste or smell, such as sweet or sour.

Responses are scored based on the patient's best overall observable response to a sensory stimuli. Using a psychometric approach called Rasch analysis, these researchers have ordered the sensory items from low to high in terms of their relative difficulty to respond to.

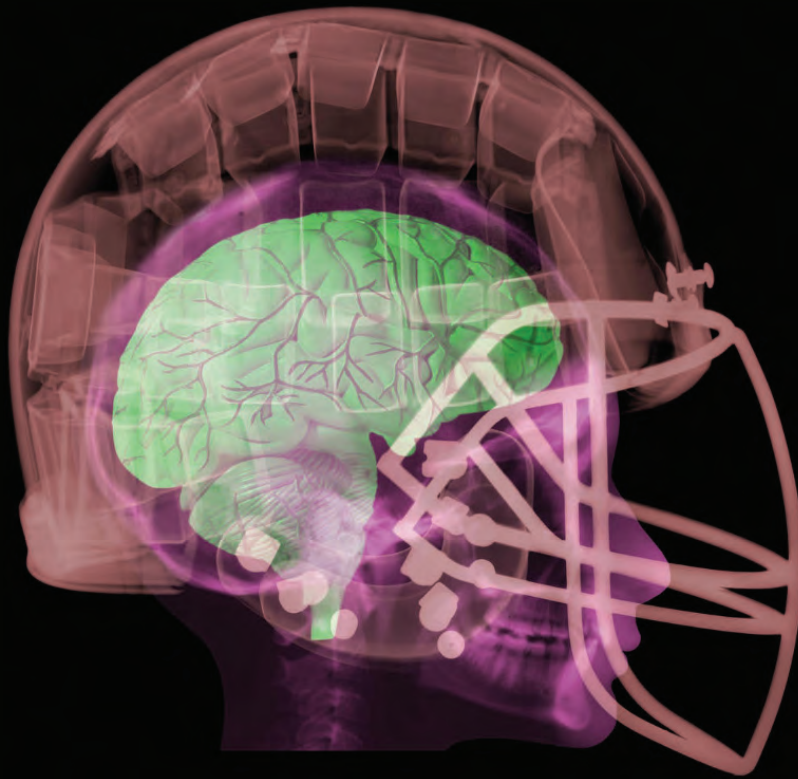
"Our data show the items form a really nice hierarchy," Mallinson says. "We are pretty convinced about the validity of DOCS-25. We know it's reliable."

The next big hurdle is establishing a minimally clinically important difference (MCID); basically finding out how much change in the measurement matters to patients, researchers, and clinicians. While developing DOCS-25, Mallinson and Pape realized none of the assessment tools, including DOCS, had a well-established MCID.

"If you have a 2-point change, does that matter?" asks Mallinson. "How much change is enough that researchers can say, 'yes, that's a real change?' The reason that's important is because that's what you power clinical trials on. If you believe your clinical trial is going to produce a 6-point clinical change, plus or minus the standard deviation, that's the information you use to power your clinical investigation."

Mallinson says their focus now is on tying the kinds of meaningful change that clinicians and caregivers want to see to the recovery ruler. If they can do that, clinicians could then have the tools to show families and caregivers where things are in terms of recovery and help families and clinicians make better treatment decisions together.

"That's really what drives us," says Mallinson. "If we can measure things better, we can understand what we're doing and how to treat patients better." ■



TACKLING TRAUMATIC BRAIN INJURY

GW RESEARCHER ROBERT W. TURNER II, PhD, DEVELOPS A BASELINE FOR THE PSYCHOSOCIAL AND NEUROCOGNITIVE FACTORS ASSOCIATED WITH LONG-TERM EXPOSURE TO MILD TRAUMATIC BRAIN INJURY

BY **STEVE GOLDSTEIN**

Robert W. Turner II has a doctorate in sociology from the City University of New York, but his most significant degree was earned at the School of Hard Knocks – more familiarly known as professional football. Turner, assistant professor of clinical research and leadership at the George Washington University School of Medicine and Health Sciences, is uniquely qualified to explore mild Traumatic Brain Injury (mTBI) and its relationship to cognitive decline and dementia.

“What I’m trying to do,” says Turner, who was an offensive lineman in the Canadian Football League and the NFL, “is understand the psychosocial and neurocognitive factors as they are associated with accelerated cognitive decline, mTBI, and potential links to Alzheimer’s disease and related dementia.” The NIH-funded study will collect data using a mixed-method design that consists of a survey, focus groups, and in-depth interviews. At some point, brain imaging may also be

SCHOOL OF HARD KNOCKS

Robert Turner’s background as an offensive lineman makes him uniquely qualified to explore mild Traumatic Brain Injury and its relationship to cognitive decline and dementia.



employed, Turner says. His cohort will consist of two groups of former college and NFL players, one group with members 30–49 years old, and the other age 50 and above. Two similarly aged groups of people who have not played any contact sports will serve as controls.

The three research aims will enable Turner to integrate and apply knowledge gained through the proposed training activities by creating a more robust portrait of psychosocial protective and risk factors that may impact the long-term consequences of mTBI among men than previously possible. “What we hypothesize is that those who’ve had a higher degree of exposure to cognitive events will be impaired,” he says, “and we should see a correlation between cognitive impairment and white matter degradation over time.”

A major goal of the research is to reveal both the risk factors and the protective measures attending to mTBIs. “Are there things that these men can do that will guard against traumatic effects or brain injury over time?” Turner asks. “Do we see a link from injury to cognition and is that decline different from persons who do not sustain such an injury?”

The study is titled “An Analysis of Psychosocial Risk and Protective Factors: Accelerated Cognitive Aging and Mild Traumatic Brain Injury (MTBI) Among Retired NFL & Former NCAA Football Players.” The five-year grant from the National Institute of Aging concludes in 2022. ■

Turning Heads

GW'S SYSTEMIC APPROACH TO TREATING
CONCUSSION AND TRAUMATIC BRAIN INJURY

BY **STEVE GOLDSTEIN**

In early 2018, a woman in her 30s, we'll call her Sue although that's not her real name, decided that she'd like to try one of those hip electric scooters she'd seen whizzing around town. Bad decision. Unprepared for sharp turns and close encounters with cars and pedestrians, Sue lost control and crashed, suffering a cervical vertebra injury. Rushed to the hospital, she was checked out by the George Washington University (GW) Hospital's Department of Emergency Medicine (ED) staff and referred to the Department of Neurosurgery. There she had a CT scan to see whether there was any internal bleeding or a skull fracture. The scan came back negative, so attention shifted to the spinal injury. Ultimately, Sue underwent successful surgery.

Months later, still wearing a brace, Sue visited the Concussion and Traumatic Brain Injury (TBI) Program Clinic at GW Hospital, complaining of headaches and dizziness. Marilyn F. Kraus, MD, director of the clinic, determined Sue had been concussed. "She was on pain meds, and in this case, it was hard for her to realize she had a concussion because of the lingering pain from the spinal injury, which may have masked the concussion effects," says Kraus, who also serves as associate professor of psychiatry and behavioral sciences in the GW School of Medicine and Health Sciences. "Almost all these c-spine injuries have a concussion component."

After Sue completed her rehabilitation from the surgery and shed the brace, Kraus referred her to the GW Hospital's spe-

cialized physical therapy unit, where Senior Out-patient Physical Therapist Kirsten Quinn, DPT, put her on a therapy program to address the vestibular (or balance) issues. Specialized physical therapy for concussion and traumatic brain injury is relatively recent and is a key component of the continuum of care at the hospital. Following six weeks of therapy, Sue was free of dizziness and her headaches had subsided. She decided to stick to Capital Bikeshare and wearing helmets when getting around town.

Good decision.

Sue's case is illustrative of GW Hospital's seamless, multidisciplinary approach to head injuries. Concussion and TBI are increasingly common and GW has responded by developing a systemic continuum of care for treating insults to the brain. Like a point-to-point medical map, the continuum of care

A SEAMLESS APPROACH

GW Hospital takes a seamless, multidisciplinary approach to head injuries.

Concussion and TBI are increasingly common and GW has responded by developing a systemic continuum of care for treating insults to the brain.

When I first started handling care for brain injuries more than 20 years ago, it was like having a compass and a flare gun – you did the best you could. Now we have specialists every step of the way and there's a continuity at GW.

– Marilyn F. Kraus, MD



links any necessary medical services along the route to wellness. The map ensures each medical service stop along the way is close enough in proximity to allow immediate communication. Patients steadily move on the road to recovery. Seems logical, right? Yet the idea was decades in the making, as concussion and TBI swelled to become significant public health issues.

“When I first started handling care for brain injuries more than 20 years ago, it was like having a compass and a flare gun – you did the best you could,” says Kraus. “Now we have specialists every step of the way and there’s a continuity at GW.”

The challenge is massive. According to the Centers for Disease Control and Prevention, approximately 1.5 million Americans suffer a brain injury each year, 85,000 people suffer long-term disabilities, and 50,000 people die as a result of TBI each year. In the United States, more than 5.3 million people live with disabilities resulting from TBI. The top three causes of TBI are: car accidents, firearms, and falls. Young adults and the elderly are at highest risk for TBI, and both groups are particularly susceptible to spinal cord injuries – another type of traumatic injury that can result from those same top three causes.



DRAWING ON 20 YEARS OF EXPERIENCE IN TREATING BRAIN INJURIES

Marilyn F. Kraus, MD, is the director of the Concussion and Traumatic Brain Injury Program Clinic at GW Hospital. She also serves as associate professor of psychiatry and behavioral sciences in the GW School of Medicine and Health Sciences.

PHYSICAL THERAPY FOR BRAIN INJURIES

Senior Outpatient Physical Therapist Kirsten Quinn, DPT, works in GW Hospital’s specialized physical therapy unit. Specialized physical therapy for concussion and traumatic brain injury is relatively recent and is a key component of the continuum of care at the hospital.



The list of common symptoms of a brain injury is long, but it includes dizziness, headache, fatigue, nausea or vomiting, double or blurry vision, and difficulty concentrating or remembering. Many people who suffer a concussion feel better within a few days or weeks. Others, however, may have a lengthier or more complicated rehab, perhaps lasting months. Appropriate evaluation, management, and understanding can help promote a faster, more complete recovery.

With heightened public awareness of concussion and TBI, the volume of cases has risen dramatically. According to GW’s medical records, 861 individuals visited the concussion clinic during fiscal year 2018. Over a period of 18 months, from the beginning of January 2017 through the end of June 2018, the GW Hospital trauma center treated 626 patients – 328 injuries from falls, 97 from assaults, 81 from motor vehicle accidents, 55 pedestrian mishaps, 37 from bicycle accidents, and eight from self-harm. There are always outliers, of course. Kraus has treated patients who have sustained head injuries from a host of unique activities, including one from roller derby, and another who had to be treated after repeatedly head-butting her dog. Some people will do anything for fun.

According to the Centers for Disease Control and Prevention, approximately 1.5 million Americans suffer a brain injury each year. Each year, 85,000 people suffer long-term disabilities, and 50,000 people die as a result of a traumatic brain injury.

Assuming those playful head butts lead to something more serious, there are a number of things patients can expect.

When arriving in the emergency department, the first triage determines whether patients can be treated as an outpatient or if they need to be admitted. One objective measure is nystagmus, sometimes known as “dancing eyes.” Out of approximately 200 patients daily, one-third have been injured (as opposed to a medical complaint) and, of that number, an average of two patients a day have a serious trauma, according to Robert Shesser, MD, MPH, professor and chair of the Department of Emergency Medicine. If the concussion sustained is believed to be mild, the patient is given basic care guidelines and sent home.

If the head injury is more severe, on the other hand, the patient will go to the trauma bay of the ED. In 2013, GW Hospital first earned a Level 1 Trauma Center designation. There the self-described “maestro” is Babak Sarani, MD ‘97, RESD ‘04, the director of Trauma and Acute Care Surgery at GW Hospital. Sarani actually functions like an orchestra conductor as much as a physician.

“We start with a physical exam, including assessing the patient’s level of consciousness, then we lean very heavily on getting a CT scan,” Sarani explains. “We look at all injuries not just brain injuries. Then we may initiate the consults to neurology and neurosurgery. We do the coordination of the care. Throughout the patient’s stay in the hospital, we’re the coordinating body. We’re the ones making sure the departments are talking to each other, that the patient is getting adequate nutrition and so on.”

Should surgical intervention be necessary, patients are directed to GW’s Department of Neurological Surgery led by Anthony Caputy, MD, chair of the Department of Neurological Surgery and Hugo V. Rizzoli Professor of Neurological Surgery

SYMPTOMS OF A CONCUSSION

A traumatic brain injury (TBI) is a type of brain injury caused by a blow to, or penetration of, the head. A TBI can occur during a car accident, a serious fall, an explosion, or an assault, among other reasons. After a TBI, nerve cells in the brain may be damaged. The neurons may have trouble doing their job of carrying signals to different parts of the brain. A concussion is a minor form of brain injury, though some concussions can be severe.

Typically, concussion symptoms appear soon after an injury occurs, according to the Centers for Disease Control and Prevention, but they can sometimes take longer to manifest.

- > Headache
- > Dizziness or vertigo
- > Lack of awareness
- > Loss of consciousness
- > Nausea and vomiting
- > Poor attention and concentration
- > Fatigue
- > Double or blurred vision
- > Irritability and/or bothered by light or noise
- > Memory problems
- > Sleep disturbances

A traumatic brain injury is a type of brain injury caused by a blow to, or penetration of, the head. A TBI can occur during a car accident, a serious fall, an explosion, or an assault among other reasons.



TREATING TRAUMA

Robert Shesser, MD, MPH, professor and chair of the Department of Emergency Medicine, (left), said two patients a day, on average, have a serious trauma. In those cases, the patient goes to the trauma bay of the ED, where Babak Sarani, MD '97, RESD '04, is the director of Trauma and Acute Care Surgery.

at SMHS. The department is staffed by a team of experts trained in all aspects of the treatment and management of neurological disorders. As a discipline, neurosurgery covers a large number of procedures from minimally invasive techniques for the brain and spine – deep brain stimulation to treat movement and mood disorders, craniotomy techniques for mapping brain function, radiosurgery, carotid artery stenting, and minimally invasive treatment of brain aneurysm (coiling) – to more traditional open surgeries to relieve cranial pressure, treat traumatic brain injury, or correct malformations of blood vessels.

“Neurosurgery is the acute part of the continuum of care, and, along with the trauma team, we are the initial evaluators,” says Michael Rosner, MD, professor of neurological surgery, and a key member of Caputy’s surgical team. Rosner brings vast experience with TBI cases. Before coming to GW, Rosner was a staff neurosurgeon at Walter Reed, and he also served with the 86th Combat Support Hospital in Baghdad, Iraq, in support of Operation Iraqi Freedom. As soon as the trauma team identifies any kind of neurological concern, “we are there within seconds,” Rosner says, adding the neurosurgeons do

their own imaging and a neurological exam, paying particular attention to whether there is inter-cranial bleeding.

As Caputy notes: “We get more patients because we are a Level 1 Trauma Center. The beauty of the system here is that there isn’t any [discussion] of who takes the patient at the next stage of recovery.

“At GW,” he adds, “the system is among the best in the country at ensuring patients are taken care of appropriately by the next expert at every level of care.”

Last in the line of GW’s continuum of care is the Concussion/TBI Clinic, but in many ways it’s the step that takes patients from better to back to normal. Located in the neurology department, the clinic follows patients and organizes care soon after injury. Patients receive treatment across the full range of their recovery, from post-operative to the weeks, months, or even years after the precipitating event. Treatment can range from the subacute phase, when the injury is just starting to heal, into the chronic phase, typically six months after an injury and continuing throughout the patient’s life, as needed.

“We see athletes, as well as any other types of head injury, including motor vehicle and work-

... [N]eurosurgery covers a large number of procedures from minimally invasive techniques for the brain and spine ... to more traditional open surgeries

related incidents," says Kraus, adding that each case requires a complete evaluation in order to develop a comprehensive treatment plan. No two brain injuries are alike and the consequence of two similar injuries may be very different.

"We address all the potential abnormal conditions relating to TBI/concussion, including headache, neck pain, vestibular disorders, oculomotor disorders, sleep disorders, cognitive and mood changes," she adds. "Symptoms may appear right away or may not be present for days or weeks after the injury. One of the consequences of brain injury is that the person often does not realize that a brain injury has occurred."

When Kraus evaluates a patient who is complaining of cognitive difficulty that is interfering with daily life, she frequently refers them to neuropsychiatrist Antonio Puente, PhD, who performs a detailed neuropsychological exam designed to produce cognitive measures through memory, problem solving, and attention exercises. "This will provide cognitive measures but also tells us how the patient is doing emotionally and helps inform treatment," Puente explains. "More often than not, our findings are used to change their physical routine."

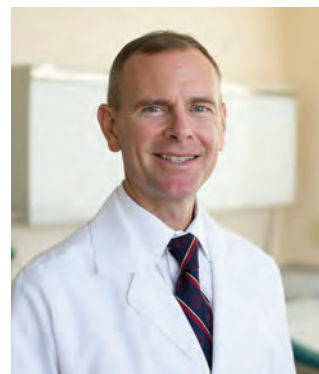


IN NEED OF SURGICAL INTERVENTION

Should surgical intervention be necessary as a result of a traumatic brain injury, patients are directed to GW's Department of Neurological Surgery led by Anthony Caputy, MD, chair of the Department of Neurological Surgery and Hugo V. Rizzoli Professor of Neurological Surgery at SMHS.

FIELD EXPERIENCE

Michael Rosner, MD, professor of neurological surgery, is a key member of GW's neurosurgery team. Before coming to GW, Rosner was a staff neurosurgeon at Walter Reed, and he also served with the 86th Combat Support Hospital in Baghdad, Iraq, in support of Operation Iraqi Freedom.



Ultimately, patients are referred for physical therapy (PT). Senior Outpatient Physical Therapist Kirsten Quinn is a trained therapist specializing in concussion and TBI. Her department receives between 10 and 20 new patients each week suffering from TBI/concussion. They are scheduled for all three therapy disciplines: speech, physical, and occupational "to make sure we're not missing anything," Quinn explains. Sessions are scheduled in the hospital but the patient is also expected to do his/her exercises at home. Vestibular, or balance, dysfunction is a common reason patients are referred for PT. "It's in the patients' best interest to have this close-knit relationship among all our [medical] teams," she adds, "because we can better manage the patient and ensure all their needs are handled."

For patients such as Sue, GW offers an important blend of both the immediacy of treatment and the availability of follow-up care. "The system in place is designed to handle all comers, at all stages, no matter the cause of the head injury," says Kraus. Even someone concussed by banging heads with the family pet. "I never did get a clear answer why she was playing chicken with her dog." ■

GW offers an important blend of both the immediacy of treatment and the availability of follow-up care. The system is designed to handle all comers, at all stages, no matter the cause of the head injury.



Turning to Biomarkers to Put TBI Symptoms in the Past

Researchers Look to Prevent Post-Traumatic Stress Disorder Among Patients Suffering Brain Injuries

BY **STEVE GOLDSTEIN**



ould the brain provide biological clues following a traumatic injury that would improve the outcome for the patient?

The George Washington University (GW) Hospital is partnering in a new study to determine whether biomarkers in a patient who has suffered a traumatic brain injury

(TBI) can help reduce the risk of post-TBI symptoms such as post-traumatic stress disorder. TBIs account

REDUCING THE RISK OF PTSD

GW University Hospital is partnering in a new study to determine whether biomarkers in a patient who has suffered a traumatic brain injury can help reduce the risk of post-TBI symptoms.

for the onset of PTSD in approximately 700,000 Americans each year. Depression and post-concussive syndrome (PCS) are also common in patients who develop

PTSD. Research suggests, however, that if the determinants of risk are better analyzed and understood there is a better chance of successful preventive interventions.

Along with Walter Reed National Military Medical Center (Walter Reed) and the National Institutes of Health, GW's School of Medicine and Health Sciences (SMHS) Department of Neurological Surgery is collaborating in a study funded by the Henry M. Jackson Foundation for the Advancement of Military Medicine. Jessica Gill, PhD, of the National Institute of Nursing Research, is serving as principal investigator. Gill has been exploring the mechanisms underlying neurological symptoms and deficits in military personnel with TBIs, as well as athletes with concussions. This line of inquiry employs a cutting-edge type of biomarker harvesting technology using a nanoparticle capture platform in a prospective sample of patients immediately following a trauma. Findings from her research will identify the clinical and biological risks

Traumatic brain injuries account for the onset of PTSD in approximately 700,000 Americans each year.

Depression and post-concussive syndrome are common in patients who develop PTSD. Research suggests that if the determinants of risk are better understood there is a better chance of successful preventive interventions.

that predict PTSD onset and neurological compromise following a traumatic injury.

SMHS serves as a site for sample collection from civilian patients. Gill is joined on the Jackson grant by Anthony Caputy, MD, chair of the Department of Neurological Surgery and Hugo V. Rizzoli Professor of Neurological Surgery at SMHS, and Babak Sarani, MD '97, RESD '04, director of the Center for Trauma and Critical Care at GW Hospital and associate professor of

surgery and of emergency medicine at SMHS. The subjects are individuals who have had a severe closed (non-penetrating) head injury resulting from a fall, a car accident, or an assault, to name some examples. Researchers are collecting specimens from these patients, specifically blood and cerebrospinal fluid, in order to search for these biomarkers that could predict an outcome. By examining the proteins and lipids in the serum of the cerebrospinal fluid they hope to determine if the level of consciousness changed.

Current scanning technologies – CT, MRI, and other techniques – do not necessarily reveal what's happening at the molecular level in the brain. According to the researchers, some small evidence of head injury can be observed in these scans, but it's not that good and not very predictive of the patient's long-term outcome. The goal of the project is to identify a molecular marker to correlate with clinical examinations and imaging findings to better predict patient outcomes and improve their care.

Gill's research suggests that DNA methylation may be a putative biomarker of psychiatric risk, as it reflects long-term changes in the function of the gene and may shape the recovery ability of the TBI patient through changes in cell function. Moreover, the neuroendocrine system appears to have a determine role. Prior research has shown that both PTSD and depression are associated with endocrine alterations, "leading us to question if this biological change may underlie vulnerability for the onset of PTSD as well as depression and post-concussive syndrome following a TBI," according to Gill's hypothesis. "In support of the idea of shared vulnerability, patients with a TBI also often display endocrine function alterations."

Samples are still being collected at GW, from approximately 50 individuals, ages 18 to 65, and data continues to be tabulated and analyzed at the NIH. ■

PTSD SIGNS AND SYMPTOMS

For some people, frightening memories of a terrible event can come back months or even years after the event, making daily life difficult to handle. Mental health experts call this post-traumatic stress disorder (PTSD).

One myth about PTSD is that it most often affects war veterans or survivors of violent assaults, but those who have experienced bad accidents, fires, or natural disasters, and emergency response workers, such as police, firefighters, and medical providers, can also experience the disorder.

People with PTSD may feel anxious or hyper-alert. Other signs of PTSD include:

- > Having frequent nightmares, flashbacks, or other vivid memories of the event
- > Being unable to recall parts of the event
- > Staying away from any reminders of the event, including people, places, thoughts, or activities
- > Feeling always on guard or on edge
- > Having trouble sleeping



GW Researchers Receive \$7.8 Million to Establish Rare Disease Network for Myasthenia Gravis

A George Washington University (GW) research team led by Henry Kaminski, MD, chair of the Department of Neurology and Meta Amalia Neumann Professor of Neurology at the GW School of Medicine and Health Sciences (SMHS), recently received a \$7.8 million award from the National Institutes of Health (NIH) to establish a rare disease network for myasthenia gravis. The network, which will join 24 existing NIH Rare Diseases Clinical Research Networks, will include basic and clinical investigators, patient advocacy groups, and biotechnology and pharmaceutical companies working together to enhance therapeutic development for this rare disease.

A \$7.8 million grant from the National Institutes of Health will fund research into the underlying pathophysiology of myasthenia gravis. The different subtypes of myasthenia gravis are not well understood, and few research labs are studying the disease.

Kaminski, a renowned expert in myasthenia gravis who has devoted decades of study to the disease, is joined on the team by fellow investigators Linda Kusner, PhD, associate research professor of pharmacology and physiology at SMHS, and Alison Hall, PhD, associate dean for research workforce development at SMHS.

"Myasthenia gravis is a chronic autoimmune disease that affects how well the nerves and muscles communicate with each other. Often patients experience extreme weakness, struggle with their vision, and are even hospitalized because of difficulty breathing," says Kaminski. "This grant will give the researcher community the needed infrastructure to study this rare disease in order to develop new therapies."

The grant will fund research into the underlying pathophysiology of the disease. The different subtypes of myasthenia gravis are not well understood, there are no known biomarkers, and few research labs are studying the disease. Upward of 30% of patients are treatment resistant, and all suffer from undesirable or dangerous adverse treatment side effects. The research team will focus on the differences between ocular myasthenia and general myasthenia – subtypes that produce different antibodies that begin attacking nerve and muscle communication – and individualized treatments for the 10% of myasthenia gravis patients who develop tumors triggered by the disease. Additionally, the researchers will identify and collect biospecimens for future study and follow myasthenia gravis patients in order to identify biomarkers.

To increase the research into myasthenia gravis, the grant also will support a career enhancement component featuring training and education opportunities for scientists, physicians, and the lay public. These opportunities will not only increase the pool of young investigators focusing their careers on rare diseases, specifically myasthenia gravis, but improve awareness of the unique needs of myasthenia gravis patients.

"The grant is not just a single project, but the establishment of a resource that will drive research for many years," says Kaminski. "Other rare disease networks funded in the last 10 years have advanced treatments for these disorders that otherwise would have been impossible." ■

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