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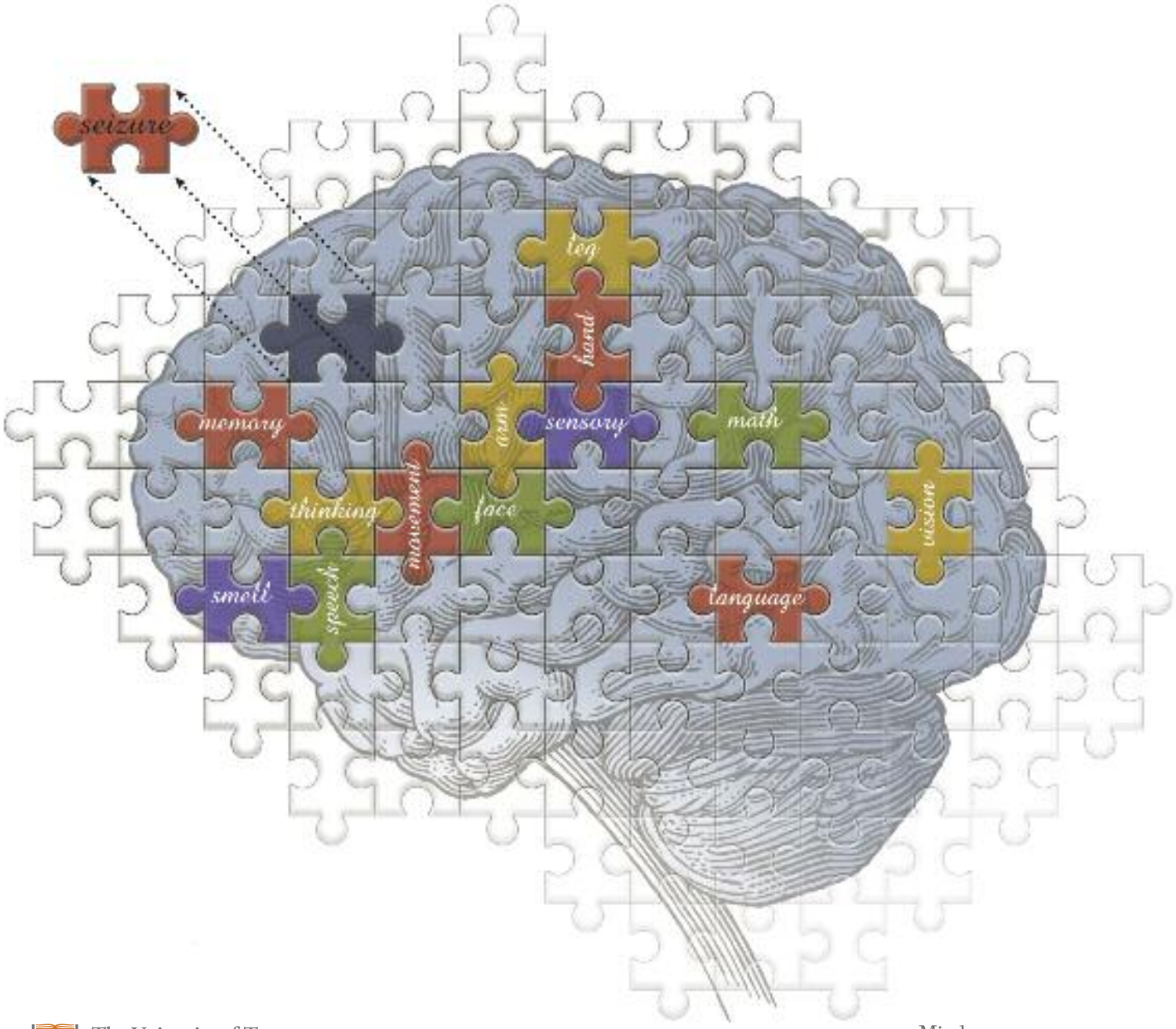

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Mischer Neuroscience Institute

MEMORIAL® HERMANN

In This Issue

Features

News of Note

News of Note (cont.)

In Print

New Lines of Thought

IN MEDICINE, innovation begins with an idea that leads to new ways of thinking about patients, processes and procedures. At the Mischer Neuroscience Institute, we continually push the envelope in neurological and neurosurgical care in ways that are appropriate for the patients we treat.

In this issue we highlight the successes of two patients singled out from among the thousands we treat annually at our centers of excellence: Jonathan Van Pelt and Carrie Tackett. We're grateful to both of them for their willingness to share their stories.

Mr. Van Pelt spent 10 years of his life in standard-of-care treatment for early-onset idiopathic Parkinson's disease before meeting an MNI specialist who considers early intervention with deep brain stimulation the new standard for appropriately selected patients. A little less than 12 years after her first grand mal seizure, Mrs. Tackett benefited from the MNI's impressive suite of diagnostic tools and solid record of success in resective surgery for epilepsy.

A LITTLE LESS THAN 12 YEARS AFTER HER FIRST GRAND MAL SEIZURE, MRS. TACKETT BENEFITED FROM THE MNI'S IMPRESSIVE SUITE OF DIAGNOSTIC TOOLS AND SOLID RECORD OF SUCCESS IN RESECTIVE SURGERY FOR EPILEPSY.

We are also pleased to announce more faculty recruits. In the last two years, we've recruited a large number of neurologists and neurosurgeons to the MNI team, including the five we welcome this winter.

We hope you'll find this issue of the Mischer Neuroscience Institute Journal interesting and informative.

With best wishes,

Dong H. Kim, M.D.

Director, Mischer Neuroscience Institute at Memorial Hermann

Professor and Chair, Department of Neurosurgery, The University of Texas Medical School at Houston

James C. Grotta, M.D.

Co-Director, Mischer Neuroscience Institute at Memorial Hermann

Professor and Chair, Department of Neurology The University of Texas Medical School at Houston

Deep Brain Stimulation Offers a Young Patient a Life-Changing Option for Early-Onset Idiopathic Parkinson's Disease

Based on low complication rates and outstanding outcomes, Mya Schiess, M.D., and her colleagues at Mischer Neuroscience Institute and UT MOVE advocate for early use of deep brain stimulation (DBS) in appropriate patients.

A little more than 10 years ago, when Jonathan Van Pelt was in his late twenties, he developed a twitch in his head and arm that manifested during periods of stress. The twitch led to his first visit to a neurologist and a diagnosis of left temporal lobe epilepsy.

"I was prescribed Lamictal® and Dilantin® but the medications only made matters worse. I became moody and cried at TV commercials," Van Pelt says with a laugh. "About that time the Internet was starting to become a useful tool for information, and there was a lot of talk about Parkinson's disease (PD) when Michael J. Fox announced he had it. I read several magazine articles, stopped taking Lamictal and started seeing other neurologists in search of a diagnosis."

It was a difficult time for the Van Pelts. "My wife and I were young and scared, and we didn't know what was happening to me," he says. "We had two young kids and no answers, and I was getting worse. I'd been an athlete in high school and was in good shape, so I didn't understand why I was getting so fatigued."

When he consulted a second neurologist, the doctor told Van Pelt he didn't think he had epilepsy but also said he couldn't diagnose the problem. By the time he saw his third neurologist, Van Pelt's tremor had worsened, his right arm was stiffened toward his body and he was having trouble walking. "I remember the doctor saying, 'I don't know what you've been told but you present like you have Parkinson's disease. It's really unusual for a 30-year-old, although it's not unheard of.' He prescribed carbidopa-levodopa and told me that if I responded to the drug, it was a clear indication that I had Parkinson's. I responded almost immediately. I felt like I was 10 feet tall and bullet proof."

Based on his response to the drug, Van Pelt's neurologist told him he had good news and bad news. "The good news was that I had responded to the Sinemet®. The bad news was that he had to take it away," he says. "Carbidopa-levodopa is the silver bullet for Parkinson's but he wouldn't prescribe it because of my age. Most patients get only 10 good years from the drug."

He also told Van Pelt that he needed a lifelong doctor and gave him the names of two specialists, one of whom was neurologist Mya Schiess, M.D., who is

"MANY NEUROLOGISTS WON'T CONSIDER INTERVENTION WITH DBS UNTIL PARKINSON'S DISEASE IS MORE ADVANCED THAN WE MIGHT LIKE TO SEE AT THE MISCHER NEUROSCIENCE INSTITUTE. BUT WE CONSIDER THE PROCEDURE RIGHT UP FRONT BECAUSE WE KNOW THAT IT DELIVERS. WHEN DONE CORRECTLY WITH APPROPRIATE PATIENTS, IT'S JUST AS GOOD, IF NOT BETTER THAN MEDICAL MANAGEMENT OF PARKINSON'S DISEASE."

Early Intervention with Deep Brain Stimulation

The Food and Drug Administration approved deep brain stimulation (DBS) as a treatment for essential tremor in 1997, for Parkinson's disease in 2002 and for dystonia in 2003. Despite its successful 13-year history, how DBS works to control the motor symptoms associated with these three disorders remains a mystery to physicians and researchers.

"Using PET we can compare images of the brain's frontal lobes and critical structures before DBS surgery – at rest and during motor activity – and after surgery with the stimulator on," says Albert J. Fenoy, M.D., a neurosurgeon on the medical staff at the Mischer Neuroscience Institute and an assistant professor of neurosurgery at The University of Texas Medical School at Houston. "With PET we can see the end result, but we can't visualize the process that produces it. We know that stimulation provides an effective intervention by regulating aberrant circuitry, but worldwide we're lacking the technology to produce images with the fine temporal and spatial resolution we need to really understand how DBS works."

Neurologists have long viewed DBS as a last-resort treatment for patients who have failed medication. As a result, many have not had access to the intervention until they are older and have more advanced disease. "But we're seeing tremendous improvements with early implantation of deep brain stimulators and learning that it's better not to wait until the patient is 60 or 70, particularly with Parkinson's disease, in which later manifestations may not be helped by DBS," Dr. Fenoy says. "Our surgical team is well trained, our complication rate is extremely low and our outcomes are good. There are many good reasons to consider DBS as an early intervention instead of an end treatment, including its specificity, which provides an advantage over medical management. We can place the electrodes precisely and program the stimulators accurately to regulate the motor fluctuations most patients have. As science improves, we'll find newer and better targets in the brain that offer more exquisite control for our patients."

"WE'RE SEEING TREMENDOUS IMPROVEMENTS WITH EARLY IMPLANTATION OF DEEP BRAIN STIMULATORS AND LEARNING THAT IT'S BETTER NOT TO WAIT UNTIL THE PATIENT IS 60 OR 70."

Precisely because of the unknowns, Dr. Fenoy views deep brain stimulation as an exciting field of study. "Studies in animal models have shown that DBS has led to an increase in dopamine in the substantia nigra," he says "The hypothesis that DBS can lead to an increase in dopamine production in humans is among the theories that remain to be clinically tested.

"There are some aspects of Parkinson's disease that aren't very well controlled by stimulation or other therapy," he adds. "Our goal is to look at these issues more closely and further refine the target areas both clinically and in the primate model."

Researchers worldwide are also investigating new applications for DBS, including depression, cluster headache, Tourette syndrome, craniofacial pain and obsessive-compulsive disorder. "We know where different sites of abnormal activation exist in the human brain from the research we're doing both in imaging and by seeing results in clinical trials," Dr. Fenoy says. "We know which areas are hypo- or hyperactive. We can place the stimulator and intervene effectively. Our aim is to be able to refine and reproduce the results in a variety of disorders taking each person's uniqueness into account."

professor and vice chair of the department of Neurology and holds the Adriana Blood Endowed Chair at The University of Texas Medical School at Houston. Dr. Schiess is on the medical staff of the Mischer Neuroscience Institute at Memorial Hermann and is also the director of UT MOVE, a program focused on clinical care, education and basic science research on the neurological conditions of motor systems disruption, including movement disorders, cerebral palsy, spasticity, neurodegenerative diseases and dementias.

Van Pelt made an appointment with the other specialist, and five years would pass before he met Dr. Schiess at a meeting of the Houston Area Parkinson's Society (HAPS). During those years, he sampled the full range of available agonists and participated in a clinical trial that was stopped two years after his enrollment.

"Each time we started a new medication, I was fine but the higher the dosage, the worse I felt," he says. "To sum it up, I was taking medications that helped me somewhat with my symptoms and improved my motor skills but I felt like I had the flu all the time. It started to become a question of whether the side effects outweighed the benefits of the medication. When I met Dr. Schiess, I liked what she said to me about her approach to treating Parkinson's disease, so I made an appointment."

"At the UT MOVE clinic, we had Jonathan maximized and optimized on medical management, but before he got into severe trouble with motor fluctuations, we talked with him about deep brain stimulation (DBS)," Dr. Schiess says. "Many neurologists won't consider intervention with DBS until Parkinson's disease is more advanced than we might like to see at the Mischer Neuroscience Institute. We consider the procedure right up front because we know that it delivers. When done correctly with appropriate patients, it's

just as good, if not better than medical management of Parkinson's disease. We're very comfortable with the procedure and work closely with the neurosurgeons. We have a phenomenally low complication rate and good outcomes. We're also very good DBS programmers. Why wait until a patient is debilitated to offer an option that we know will work?"

In March 2008 at the age of 39, Van Pelt underwent testing to determine whether he was a candidate for DBS. "One of the indications for the potential success of DBS is a sustained and robust effect of levodopa, the biologically active precursor to the neurotransmitter dopamine, which is used to increase brain concentrations in patients with Parkinson's disease," Dr. Schiess says. "The primary transmitter is low in patients with PD. If you take patients off levodopa for 12 hours and evaluate fine motor skills, postural ability, muscle tone and the presence or absence of tremors using the Unified Parkinson's Disease Rating Scale (UPDRS), then reevaluate them while they're on their medication, a high rate of improvement is proof positive that the patient will respond to DBS." Van Pelt showed a 68 percent improvement on the UPDRS between his off- and on-medicine states.

In November and December 2008, Van Pelt's two deep brain stimulators, which target the subthalamic nucleus, were implanted by Richard Simpson, M.D., a neurosurgeon affiliated with Memorial Hermann-Texas Medical Center. "He's now more than one year out from the surgery and with his current DBS stimulation settings and very slimmed down medication regimen, he has control over all the motor symptoms of his disease with no fluctuations," Dr. Schiess says. "This is a 40-year-old man with no difficulty with his motor function, who does a full day's work and more and is very involved with his family life. He is functioning 100 percent."

Van Pelt, who is pleased with the outcome, describes Dr. Schiess as "a great doctor who's not afraid to think outside the box. When you have a condition you have to live with, you really have to be your own advocate," he says. "You have to make decisions in life that aren't always easy. Having someone there to play devil's advocate and say, 'Yes, you can do that, but then this will happen' is very important. That's the role Dr. Schiess has played for me. It's a good partnership."

Parkinson's is a very treatable disease, which makes staying positive important, Dr. Schiess says. "We encourage our patients to stay mentally and physically active and have fun. We also emphasize education because people do much better when they understand their disease. We consider the whole person, so we always keep an eye out for anxiety, disrupted sleep, depression, problems with concentration or forgetfulness – and take these things into consideration as we develop and adjust our treatment plans."

"WE HAVE A PHENOMENALLY LOW COMPLICATION RATE AND GOOD OUTCOMES. WE'RE ALSO VERY GOOD DBS PROGRAMMERS. WHY WAIT UNTIL A PATIENT IS DEBILITATED TO OFFER AN OPTION THAT WE KNOW WILL WORK?"

Van Pelt has made a personal commitment to maintaining a positive perspective. "As a parent, I can make a big difference in my kids' experience of my disease," he says. "My kids are so funny, and when I crack jokes on my bad days, they laugh and tell me I'm inappropriate. But if you can't laugh at yourself, who can you laugh at? I used to get upset at work when I was first diagnosed. Now I feel like it's all about keeping things as simple as possible. Life is a gift to enjoy while it's here. I plan on living it to the fullest."

Resective Surgery for Refractory Epilepsy Opens Doors for Carrie Tackett

A young Houston woman benefits from the Texas Comprehensive Epilepsy Program's full suite of diagnostic tools and its track record of successful resective surgery in lesional and non-lesional patients.

When Carrie Tackett was 3 years old, she lived through every mother's nightmare. She fell out of a grocery cart, hit her head and was hospitalized with a severe concussion. "I was in a deep sleep for a couple of days. The doctors told my parents I seemed fine, but they also alerted them that there might be repercussions in the future," Tackett says.

On Easter Sunday in 1996, during her freshman year in college, Tackett had her first grand mal seizure. Testing revealed that the seizure activity was originating from her right frontal lobe, the site of her earlier head injury. She was prescribed anti-seizure medications, which worked initially.

Two years later, during her junior year, she had another grand mal seizure, an isolated event. "By 1999, I was taking carbamazepine and doing well," she says. "My neurologist suggested that we might want to consider trying to wean me off my medication eventually. I took things into my own hands – a crazy idea – and tried decreasing the dose myself and had a seizure. I went back on carbamazepine and things were fine for a few more years."

Tackett married in August 2000 and had her first child, a son, in January 2002. The following year, while she was living in St. Louis and pregnant with her second child, her seizures recurred, manifesting as staring episodes and blanking-out spells. "My neurologist told me that I couldn't drive. Shortly afterwards, we found out our son had trisomy 18. He passed away in December 2004, soon after birth. My staring spells continued, and so my neurologist increased the dosage of my medications. But it didn't have any effect."

In April 2005, the Tacketts moved to Houston. Her new neurologist changed her medications, and after living six months seizure-free, she had permission to drive again. "Then a few months later, I began having complex partial seizures and switched to another neurologist, who started tacking on more medications to my treatment regimen," she says. "By September 2007, I was still having seizures and was fed up and ready to try another neurologist, when my doctor told me she'd like to refer me to the Epilepsy Monitoring Unit (EMU) at Memorial Hermann-Texas Medical Center. She thought I might be a good candidate for resective surgery."

Tackett spent seven days in the EMU undergoing Phase 1 testing conducted by epileptologist Jeremy Slater, M.D., director of the Texas Comprehensive Epilepsy Program and an associate professor of neurology at The University of Texas Medical School at Houston. "On average we like to record at least four or five typical events on video EEG monitoring," Dr. Slater says. "Sometimes we have to make a decision about whether the patient is a good candidate for surgery based on fewer seizures, but we want to feel that we've captured the event they're concerned about. We may also find seizures they haven't described, originating from a different area of the brain."

A 3-Tesla MRI scan of Tackett's brain using imaging protocols specifically designed to localize epileptic foci produced results consistent with her video EEG findings: a focal defect in the right frontal lobe. Magnetoencephalography (MEG), which maps neurological function and localizes epileptic spike discharges by tracking tiny changes in brain magnetic fields, revealed spikes in the cortex around the affected area.

"Research, some of which has been conducted at the Mischer Neuroscience Institute and UT, has shown MEG to be reliable at helping to locate the source of seizures and possibly minimizing operative risk by defining the regions of the brain critical to speech and motor function," Dr. Slater says. "If we can find a focal area with MEG, the odds are good that the seizures are originating there. When video EEG, MRI and MEG all point to the same epileptogenic zone, we've amassed some very strong evidence."

Tackett met with neurosurgeon Nitin Tandon, M.D., a neurosurgeon on the medical staff at the Mischer Neuroscience Institute and an assistant professor of neurosurgery at the UT Medical School, to discuss surgery. "Given all the concordant data from her noninvasive studies, Carrie was an excellent candidate for epilepsy surgery," Dr. Tandon says. "Her MRI suggested an area of gliosis in the basal frontal region. We thought she would do well."

Phase 2 electrocorticographic testing and surgery were scheduled for January 2008. In the interim, Tackett underwent a functional MRI scan to localize eloquent cortex.

"So prior to Phase 2 testing, we already had a great deal of information from MEG and functional MRI about

parts of the brain that are critical for function," Dr. Slater says. "The more information you have, the better off the patient will be following surgery. We don't want to remove any more of the brain than is absolutely necessary. Having all of these diagnostic tools available has contributed to our track record of successful resective surgery in lesional and non-lesional patients."

On January 15, 2008, Tackett was admitted to Memorial Hermann-TMC for surgery. She was less concerned about the surgery than about having her long hair shaved before the procedure. To show their support, her husband Sean and seven-year-old son J. T. also shaved their heads.

Later that morning, Dr. Tandon placed subdural grid electrodes over the right hemisphere of Tackett's brain to record electrical activity from the cortex. A week later, she was back in the operating room to have the electrodes removed and undergo resection of the epileptic focus in her right orbital-frontal cortex.

"This region of the brain sometimes masquerades as the temporal lobe, producing the same kind of seizure," says Dr. Tandon, who is engaged in research on orbital-frontal epilepsy and has seen more patients whose seizures originate in this area of the brain than many contemporary neurosurgeons.

Tackett was discharged from the hospital three days later. "My recuperation went quickly," she says. "The doctors did a good job of preparing me for what to expect, and the nurses were great. We have nothing but the utmost respect for Dr. Slater and Dr. Tandon. I bombarded both of them with questions and they took the time to answer all of them. We really appreciated that. It made the decision to go forward with the surgery so easy for us."

"At the end of the day it's miraculous to me that patients undergo a procedure in which we remove a portion of their brain, and they come out of anesthesia and are fine," Dr. Slater says. "Carrie is a very gratifying success. She had a more complicated type of epilepsy that required testing with implanted electrodes. Since the surgery, she's been seizure-free on a single medication. We feel we achieved our target outcome."

"The challenge in all epilepsy surgery is to eliminate the epilepsy without affecting normal function," Dr. Tandon says. "We work to optimize our outcomes for all our patients through precise functional localization and functional preservation. Carrie is an excellent example of the success of our approach to resective surgery."

When Tackett saw Dr. Slater for her annual follow-up in July 2009, she was 13 weeks pregnant. Her simplified medical regimen and freedom from seizures improved the likelihood that her pregnancy would be normal.

"I just had my baby in January, and we are both doing fine," says Tackett, who is now 33. "I can't say enough about the people at Memorial Hermann and UT. There would be no way we'd have considered trying to get pregnant again had my seizures continued. So I can say that my surgery has been life altering. We feel very, very grateful."

Neurocore: An Innovative IT Application Aids in Research, Education and Practice Management

USING a specially designed clinical documentation and communication program called Neurocore, researchers at the Mischer Neuroscience Institute are gathering patient data that will improve knowledge of neurological illness and ultimately change the way care is delivered.

Developed in Boston by William Gormley, M.D., and Dong H. Kim, M.D., in conjunction with Clearpath Solutions, the Neurocore system is a complete information system environment that runs the clinical services in the ICU. Neurocore is used to digitally document patients' history, examination findings, plan of treatment and outcomes. Neurocore also interfaces with the hospital information system, automatically downloading patients' laboratory values as well as their vital signs. Upon discharge, Neurocore de-identifies patient data to become a research database including patient imaging data. This capability to collect patient data in a standardized manner enables researchers to search for patterns in medical histories and track outcomes. "In addition to its research platform, Neurocore functions as an acute care and practice management system that includes clinical documentation, billing support and workflow enhancement at the point of care," says Justin Smith, president of Clearpath Solutions. "It has the capability to analyze information with a narrow and deep focus, making it particularly useful in specialties like neuroscience."

The system also offers clinical decision support through imbedded protocols for the treatment of specific conditions. "Neurocore facilitates research and evidence-based medicine and also supports our mission as a medical school and teaching hospital to educate future leaders in neuroscience," says Dr. Kim. "The system helps our residents advance their knowledge and practice and offers us the opportunity to monitor adherence to and departure from protocols, as well as change existing protocols and introduce new ones."

Neurocore is being put to use in the development of the Neuroscience Research Repository (NRR), which will collect samples from patients who consent to be included in the study for clinical, genomic and proteomic analysis. Over the next five years, approximately 5,000 patients will become part of the prospective database and tissue sample bank, a joint project of the Memorial Hermann Healthcare System and The University of Texas Medical School. Data gathered through Neurocore will be electronically transferred to the NRR database for analysis. To protect patient privacy and ensure HIPAA compliance, the data will be de-identified.

NEUROCORE IS BEING PUT TO USE IN THE DEVELOPMENT OF THE NEUROSCIENCE RESEARCH REPOSITORY, WHICH WILL COLLECT SAMPLES FROM PATIENTS WHO CONSENT TO BE INCLUDED IN THE STUDY FOR CLINICAL, GENOMIC AND PROTEOMIC ANALYSIS.

Researchers began enrolling patients at Memorial Hermann-Texas Medical Center in the spring of 2009. Eventually, data will be gathered from patients at all 11 Memorial Hermann hospitals. "When patients consent, we will collect samples of

residual tissue – tumor, blood, saliva and other available samples," says Gigi Hergenroeder, R.N., director of the NRR and an assistant professor in the department of Neurosurgery at the UT Medical School. "By examining tissue on the molecular level and comparing treatments provided to various patients, we hope to gain knowledge that will allow us to predict and improve outcomes by offering patients earlier interventions." Development of the NRR is being funded by the Vivian L. Smith Center for Neurological Research; Memorial Hermann funded the development of Neurocore at the hospital.

"Neurocore builds on the existing clinical electronic record of the hospital by bringing us closer to a larger and more integrated data warehouse," Dr. Kim says. "That datamart, along with other technology improvements on the horizon, will help us create an environment that promotes the best delivery of care."

Imoigele Aisiku, M.D., and the Neuro ICU staff at the Mischer Neuroscience Institute chart patients' medical treatments during rounds using Neurocore.

Mischer Neuroscience Institute and UT Welcome New Recruits

A neurologist and four neurosurgeons have joined the staff of the Mischer Neuroscience Institute (MNI) and the faculty of The University of Texas Medical School at Houston.

Vascular neurologist and neurointensivist **George A. Lopez, M.D., Ph.D.**, joins the UT Medical School as an associate professor in the department of Neurology and director of systemwide neurocritical care and the medical staff at the MNI. He comes from Baylor College of Medicine, where he was director of neurologic critical care, assistant professor of neurology and assistant professor of neurosurgery and radiology. He received both his medical degree and doctorate in physiology at the University of California, San Francisco, in 1995, followed by an internship in internal medicine and a residency in neurology at the same institution. In 2001, he completed a fellowship in neurological critical care at the University of Virginia Medical Center division of Critical Care in Charlottesville. He is board certified in neurology, neurocritical care and vascular neurology.

Dr. Lopez is principal investigator for Minimally Invasive Surgery Plus rtPA for ICH Evacuation (MISTIE) and co-investigator for the Albumin in Acute Stroke (ALIAS) Trial and Clear IVH: Evaluating Accelerated Resolution of Intraventricular Hemorrhage. He has co-authored research published in *Nature, Neuron, Biochemistry, Archives of Ophthalmology* and *Neurosurgical Focus.* His clinical and research interests include hypothermia following cardiac arrest and stroke, acute stroke therapy, neuroprotection, intracerebral and subarachnoid hemorrhage, interventional treatments for stroke and intracranial atherosclerosis and critical care management of acute brain injury.

Juan Ortega-Barnett, M.D., an assistant professor in the department of Neurosurgery at the UT Medical School, has expertise in brain tumor management, image-guided brain surgery, neuro-oncological brain surgery, minimally invasive spine surgery, peripheral nerve disorders, hydrocephalus and the management of cranial nerve disorders. A native of Texas, Dr. Ortega received his undergraduate training and medical degree at La Salle University in Mexico City. Following his training, he spent a year performing public service and then returned to Mexico City to complete residencies in general surgery and neurosurgery.

Dr. Ortega completed a four-year general surgery residency at West Virginia University in Morgantown prior to completing a neurosurgery residency, including one year as chief resident, at Pittsburgh Allegheny General Hospital. He completed a neurosurgery fellowship at Brigham and Women's Hospital in Boston before joining South Shore NeuroSpine Group, LLC in South Weymouth, Mass., in 2007. He held medical staff appointments at South Shore Hospital and Brigham and Women's Hospital prior to joining the medical staff at the MNI. Dr. Ortega has co-authored studies published in *West Virginia Medical Journal* and *Neuromodulation.*

Hanh Truong, M.D., assistant professor in the department of Neurosurgery, joins the UT Medical School and the medical staff at the MNI following completion of a one-year trauma/surgical critical care fellowship at the Shock Trauma Center in Baltimore, where she was involved in the development of an extracorporeal preservation resuscitation protocol. She received her medical degree at Southwestern Medical School in Dallas in 2004, followed by an internal medicine internship at the UT Medical School and a three-year emergency medicine residency at Mount Sinai School of Medicine in New York City.

Dr. Truong has made presentations at the Society of Critical Care Medicine on safe extubation in the emergency department and the Surgical Critical Care Lecture. Her clinical and research interests include shock and resuscitation.

Karl Schmitt, M.D., has joined the UT Medical School as an assistant professor in the department of Neurosurgery and the medical staff at

the MNI. A 1978 graduate of The University of Texas Medical Branch at Galveston, Dr. Schmitt completed a five-year neurosurgery residency at the same institution. In 2005, he completed the Yale Comprehensive Spinal Fellowship at Yale University School of Medicine in New Haven, Conn.

Dr. Schmitt served as an assistant professor of neurosurgery at the University of Maryland at Baltimore before joining the MNI team. From 1995 until 2004, prior to completing his spinal fellowship, he was a member of Spinal and Neurological Surgery Associates, PLLC in Bryan, Texas, with a faculty appointment as adjunct assistant professor at the Texas A&M School of Medicine. He was in private practice in Bryan from 1984 to 1995.

Dr. Schmitt is board certified by the American Association of Neurological Surgery. His clinical and research interests include traumatic brain injury and complex spine disorders.

Asma Zakaria, M.D., an assistant professor of neurology and neurosurgery, received her medical degree from Aga Khan University in Karachi, Pakistan. She joins the UT Medical School and the medical staff at the MNI, following completion of her residency in neurology at Baylor College of Medicine in Houston in 2007 and her fellowship in neurocritical care at Cleveland Clinic in 2009.

Dr. Zakaria has co-authored articles that have appeared in *Neurology, Pediatric Neurology, Epileptic Disorders, Neuro-Imaging* and the *Journal of Pakistan Medical Association*. She is board certified by the American Board of Psychiatry and Neurology and board eligible in neurocritical care by the United Council for Neurologic Subspecialties. Her clinical and research interests include hypothermia, cerebral vasospasm and neuro-humeral responses to brain injury.

Accolades

NICOLE GONZALES, M.D., RECEIVES YOUNG INVESTIGATOR'S AWARD

Nicole R. Gonzales, M.D., was honored at the 5th Annual Young Investigator's Appreciation Luncheon held in October to recognize the research achievements of junior faculty at The University of Texas Medical School at Houston. Her work was recognized by

Larry R. Kaiser, M.D., F.A.C.S, president and Alkek-Williams chair at The University of Texas Health Science Center at Houston.

Dr. Gonzales is principal investigator of "The Safety of Pioglitazone for Hematoma Resolution in Intracerebral Hemorrhage (SHRINC) and MRI Evaluation of Hematoma Resolution as a Surrogate Marker of Clinical Outcome in Intracerebral Hemorrhage." The study compares the safety of pioglitazone with standard of care for patients with spontaneous intracerebral hemorrhage. The hope is that the drug can stimulate the body's own cells to absorb the hematoma faster and, as a result, lead to more rapid recovery.

ANDREW BARRETO, M.D., GRADUATES FROM PHYSICIAN QUALITY & SAFETY LEADERSHIP ACADEMY

Andrew Barreto, M.D., assistant professor of neurology at The University of Texas Medical School at Houston, was among seven graduates in the second class of the Physician Quality & Safety Leadership Academy, a collaborative

effort of Memorial Hermann-Texas Medical Center and the UT Medical School. The Academy was developed in 2008 to build a core group of physician leaders considered experts in this arena.

Dr. Barreto was nominated for the Academy by Neurology department chair James C. Grotta, M.D., co-director of the Mischer Neuroscience Institute. Highlights of the nine-month course included immersion in Six Sigma methodology and LEAN process, and the opportunity to interact with nationally renowned physician quality advocates, including Brent James, M.D., and Jim Reinertsen, M.D.

Projects were selected in conjunction with Academy leaders, and the results of the physicians' work were presented at the graduation ceremony on November 18, 2009. Dr. Barreto's project was entitled "Time to Intra-arterial Therapies for Stroke Patients."

NEUROSURGERY CHIEF RESIDENT RECOGNIZED BY THE GOLD FOUNDATION

Neurosurgery chief resident **Bart MacDonald, M.D.**, is among six residents at The University of Texas Medical School at Houston to receive the Arnold P. Gold Foundation's Humanism and Excellence in Teaching Award. Nominated by fourth-year

medical students, he was recognized for his compassion and empathy in the delivery of care to patients and for illustrating professional behavior.

Dr. MacDonald received his medical degree from the Medical College of Georgia in Augusta in 2000, followed by an internship in general surgery at the University of Florida in Gainesville. He completed his first year of neurosurgical residency at the University of North Carolina in Chapel Hill in 2001, followed by four years at Brigham and Women's Hospital and Children's Hospital in Boston, where he also conducted research in hydrocephalus. His clinical and research interests include complex spine and vascular neurosurgery.

The Arnold P. Gold Foundation advances humanism in medicine, perpetuating the tradition of the caring doctor.

RESEARCH UPDATE

Since September 2008, researchers at the Mischer Neuroscience Institute and The University of Texas Medical School at Houston have received more than $8.7 million in grants for clinical trials and laboratory research in neurology and more than $4 million in grants for studies related to neurosurgery. Following are brief descriptions of the awards.

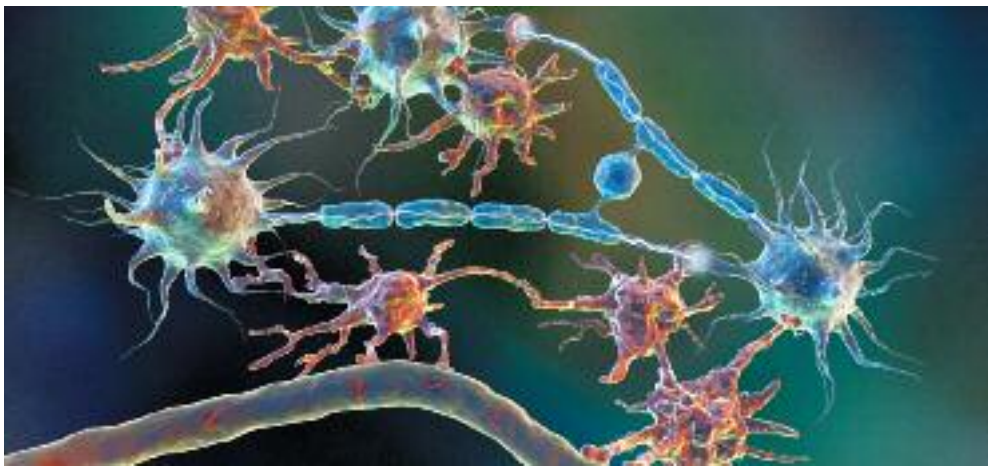
DEPARTMENT OF NEUROLOGY

AHA Clinical Research Program Award
Principal Investigator:
Nicole Gonzales, M.D.
This study explores MRI evaluation of hematoma resolution as a surrogate marker of clinical outcome in intracerebral hemorrhage.

Automated MR Image Analysis in MS: Identification of a Surrogate
Principal Investigator:
Jerry Wolinsky, M.D.
Researchers are developing a general, PC-based automated image analysis system and applying it to determine those MRI metrics that best predict near-term clinical change in multiple sclerosis.

Center for Clinical and Translational Sciences K-Award
Principal Investigator:
Frank Arnett, M.D.
This program supports translational clinical research. As part of a K12 award, our Stroke Center is studying a novel treatment for intracerebral hemorrhage.

Clinical Conversation of Female MZ Twins Discordant for CIS/MS
Principal Investigator:
Staley A. Brod, M.D.
This study is determining if the presence of characteristic MS-like lesions on baseline MRI predisposes to CIS/MS in female MZ twins discordant for CIS/MS.



Combination Therapy in Multiple Sclerosis
Principal Investigator:
Jerry Wolinsky, M.D.
This study is determining if the combination of interferon beta-1a and glatiramer acetate is superior to either drug as monotherapy in relapsing-remitting multiple sclerosis.

Cyclic Amplification of Prion Protein Misfolding
Principal Investigator:
Claudio Soto, Ph.D.
The major goals of this project are to understand the mechanism of prion replication and the nature of the infectious agent, and to develop novel strategies for diagnosis of prion diseases.

Evaluation of Oral Administration of ACTH (Corticotropin) in Normal Volunteers: A Pilot Study
Principal Investigator:
Staley A. Brod, M.D.
This study is designed as a prospective cohort study to determine whether oral administration of ACTH has immunological and endocrinological effects.

GBS/CIDP Foundation Grant
Principal Investigator:
Kazim A. Sheikh, M.D.
Researchers are engineering chimeric proteins to enhance nerve repair in antibody-mediated preclinical models of autoimmune neuropathy.

Improving Ambulation Post Stroke with Robotic Training
Principal Investigator:
Elizabeth Noser, M.D.
This study compares robotic-assisted rehabilitation therapy using the Lokomat® with standard physical therapy to improve ambulation after stroke.

Lacosamide Double-Blind Study
Principal Investigator:
Jeremy Slater, M.D.
The purpose of this historical-controlled, multi-center, randomized trial is to demonstrate the efficacy and safety of conversion to lacosamide for subjects with partial onset seizures who are withdrawn from one to two antiepileptic drugs. Lacosamide (LCM) is an investigational anti-convulsant drug.

Merci® Registry
Principal Investigator:
Andrew Barreto, M.D.
This prospective, multi-center, multi-national registry is evaluating the safety and efficacy of mechanical embolectomy in the cerebral vasculature.

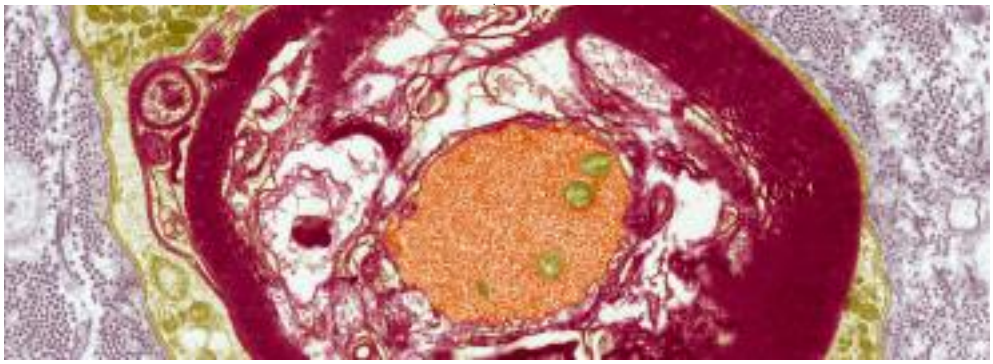
MR and Recanalization of Stroke Clots Using Embolectomy (MR RESCUE)
Principal Investigator:
James Grotta, M.D.
Researchers are determining if diffusion-perfusion MRI can identify patients who might benefit from mechanical embolectomy with a balloon catheter and retriever.

Neurodegeneration in Prion Diseases
Principal Investigator:
Claudio Soto, Ph.D.
This study is investigating the mechanism of brain degeneration in prion diseases and in particular, the role of the endoplasmic reticulum chaperon protein Grp58.

New Target for Stroke: Peroxisome Proliferator Activated Receptor-Gamma
Principal Investigator:
Jaroslaw Aronowski, Ph.D.
This study examines the role of PPARγ in neurons and microglia as a factor protecting these cells from insult produced by ischemic stroke.

Oxygen-enhanced MRI in Epilepsy
Principal Investigator:
Giridhar Kalamangalam, M.D.
Researchers are developing a novel MRI technique for better visualization of abnormal brain areas in epilepsy patients.

Pathogenesis, Transmission and Detection of Zoonotic Prion Diseases
Principal Investigator:
Claudio Soto, Ph.D.
Researchers are studying the pathogenesis and routes of propagation of bovine spongiform encephalopathy and chronic wasting disease and developing novel strategies for the detection of infected animals.



Pathogenic Mechanism of Prion Disease
Principal Investigator:
Claudio Soto, Ph.D.
This Program Project grant involves several groups. Our major goal is to understand the molecular basis of human prion replication and to develop novel strategies for diagnosis.

Peripheral and Central Protein Biomarkers of Brain MR Activity in Demyelinating Disease
Principal Investigator:
Staley A. Brod, M.D.
Researchers are determining whether specific protein biomarkers (proteins) in the CSF synchronize with peripheral (blood) and brain MR lesion changes.

Phenotypic Differences in Motor and Sensory Neuron Regeneration in Inbred Mice
Principal Investigator:
Kazim A. Sheikh, M.D.
This study is determining the genetic drivers of phenotypic differences in nerve regeneration in inbred mice.

Pleiotropic Transcription Factors as a Target for Intracerebral Hemorrhage Treatment
Principal Investigator:
Jaroslaw Aronowski, Ph.D.
Researchers are evaluating the role of transcription factor Nrf2 in regulating cytoprotection, antioxidative defense and detoxification of brains injured by intracerebral hemorrhage.

Prion Transport Across the Blood-Brain Barrier
Principal Investigator:
Claudio Soto, Ph.D.
This project's major goal is to evaluate the mechanism by which prions enter the brain, and in particular the contribution of the blood-brain barrier.

Rufinamide Double-Blind Study
Principal Investigator:
Jeremy Slater, M.D.
The primary purpose of this placebo-controlled, parallel-group study is to evaluate the efficacy, safety and tolerability of the investigational drug rufinamide at 3,200mg/day compared with a placebo in refractory epilepsy patients with partial onset seizures who are receiving one, two or three established antiepileptic drugs.

Rufinamide Open-Label, Double-Blind Study
Principal Investigator:
Jeremy Slater, M.D.
This open-label extension study is evaluating the safety and efficacy of long-term administration of rufinamide for the control of epileptic seizures in adolescent and adult patients between 12 and 80 years of age. Subjects have been diagnosed with refractory partial onset seizures and are being maintained on a maximum of three approved antiepileptic drugs.

Small-Molecule Beta-sheet Breaker Peptidemimetics for Alzheimer's Therapy
Principal Investigator:
Claudio Soto, Ph.D.
This project seeks to identify small chemical molecules mimicking the structure and activity of ß-sheet breaker peptides previously demonstrated to be active in inhibiting and disassembling amyloid fibrils.

University of Texas Specialized Program in Acute Stroke (SPOTRIAS)
Principal Investigator:
James Grotta, M.D.
A renewal of The University of Texas Health Science Center at Houston Specialized Program in Translational Research in Acute Stroke, this study includes two clinical trials in stroke patients. The program also includes clinical, data and tissue cores to support these clinical and translational studies, as well as a career development program to train new investigators to carry out future translational studies.

Viral Mimicry and Multiple Sclerosis
Principal Investigator:
Jerry Wolinsky, M.D.
This study investigates immunopathogenic mechanisms relevant to the pathogenesis of multiple sclerosis in animal models of the human demyelinating disease.

DEPARTMENT OF NEUROSURGERY

A Cross-model Synthetic Approach to Eloquent Cortical Regions
Principal Investigator:
Nitin Tandon, M.D.
An integrated application of functional MRI, diffusion tensor imaging tractography and intracranial electrophysiology to understand the mechanisms of language production.

Biomarkers for Pain in Spinal Cord Injury Patients
Principal Investigator:
Georgene Hergenroeder, R.N., C.C.R.C.
Researchers are comparing plasma protein profiles for SCI patients with/without chronic neuropathic pain in order to identify biomarkers associated with this medical condition. They are also identifying a temporal relationship to initial SCI at which these biomarkers manifest.

Bugher Foundation Center for Stroke Prevention
Principal Investigator:
Dong H. Kim, M.D.
This project is focused on identifying gene mutations associated with cerebral aneurysm formation and understanding molecular mechanisms that lead to disease.

Clinical Interventions to Increase Organ Procurement, Nutritional Status and Enteral Absorption Capability After Brain Death
Principal Investigator:
Georgene Hergenroeder, R.N., C.C.R.C.
This project is focused on determining if enteral feeding with a commercially available nutriceutical can result in improved condition of organs and an increased number of organs procured and/or transplanted.

Combinatory Strategies to Functional Remyelination After Spinal Cord Injury
Principal Investigator: Qi Lin Cao, Ph.D.
Researchers are identifying optimal strategies to genetically modify oligodendrocyte precursor cells prior to transportation to promote remyelination and functional recovery after spinal cord injury.

Defining Genetic and Environmental Modifiers of Vascular Disease
Principal Investigator:
Hariyadarshi Pannu, Ph.D.
This research focuses on defining molecular differences between vascular beds, the role these differences play in conferring differential susceptibility to vascular diseases and the identification of factors that lead to variable gender-specific vascular disease susceptibility.

Diffusion Imaging for Seizure Focus Localization
Principal Investigator:
Timothy Ellmore, Ph.D.
This project is evaluating the feasibility of using diffusion-weighted MRI (DW-MRI) to localize the seizure onset zone in epilepsy patients.

Fronto-Basal-Ganglia Circuits for Selective Stopping and Braking
Principal Investigator:
Nitin Tandon, M.D.
This project uses intracranial brain recordings and fMRI to understand the dynamics of the brain substrates involved in cognitive control.

Genetic Analysis of Cerebral Aneurysms
Principal Investigator:
Teresa Santiago-Sim, Ph.D.
Researchers are identifying genetic alterations that predispose individuals to cerebral aneurysms as well as potential cerebral aneurysm biomarkers that can aid in diagnosis of individuals at increased risk of developing disease.

Nano-Engineered, Multi-Channel Scaffolds for Axon Regeneration
Principal Investigator: Qi Lin Cao, Ph.D.
Researchers are identifying the optimal nano-scaffolds for axonal growth in vitro.

The Neural Substrates of Common and Proper Naming
Principal Investigator:
Nitin Tandon, M.D.
This project uses intracranial brain recordings to understand the location and interaction between the substrates involved in fluent generation of nouns and verbs, and in their failure to do so, so-called "tip-of-tongue" phenomena.

Neuroimaging of Cerebrovascular Function
Principal Investigator:
Timothy Ellmore, Ph.D.
Researchers in this study are 1) using high resolution structural and functional neuroimaging to measure aspects of brain anatomy and function in humans at risk for cerebrovascular disease and 2) studying patients who have had hemorrhagic strokes in order to assess the extent of damage, impact on cognitive function, and risk for additional cerebrovascular incidents.

Norepinephrine and TBI-Associated Prefrontal Dysfunction – Research Supplement to Promote Diversity in Health-Related Research
Principal Investigator:
Nobuhide Kobori, M.D.
The overall goal of the grant is to identify the biochemical and cellular mechanisms underlying prefrontal cortex (PFC) dysfunction following traumatic brain injury.

Novel Neuroprotection Therapeutic Approaches for Spinal Cord Injury
Principal Investigator: Qi Lin Cao, Ph.D.
The goal of this grant is to study the molecular mechanism to regulate the blood-brain barrier of normal adult CNS or after SCI, and to identify new therapeutic targets for SCI and other neurological diseases by protecting the blood-brain barrier.

Novel Restorative Therapy for Spinal Injury
Principal Investigator: Qi Lin Cao, Ph.D.
This study is examining the therapeutic potential of ApoE peptides for spinal cord injury.

Project 2 – Effects of Erythropoietin on Anemia and Need for Transfusion (a component of the Program Project "Vascular Mechanisms of Secondary Injury after Traumatic Brain Injury")
Principal Investigator:
Imoigele Aisiku, M.D.
This study examines the effects of TBI on cerebral blood flood (CBF) and the effect of erythropoietin in CBF.

Targets and Functional Consequences of Altered MicroRNAs Following Stroke
Principal Investigator:
Meredith L. Moore, Ph.D.
The goals of this project are to 1) characterize altered microRNA expression profiles and elucidate the molecular pathways targeted and 2) confirm direct microRNA regulation of potential targets.

Targets and Functional Consequences of Altered MicroRNAs in Models of Acute and Chronic SCI
Principal Investigator:
Meredith L. Moore, Ph.D.
The goals of this project are to 1) characterize altered microRNA expression profiles and elucidate the molecular pathways targeted, 2) confirm direct microRNA regulation of potential targets and 3) identify longitudinal expression patterns of miRNAs.

Vascular Mechanisms of Secondary Injury after TBI
Principal Investigator:
Imoigele Aisiku, M.D.
The goals of the study are to determine if early treatment with erythropoietin will improve outcome and cerebral hemodynamics after TBI, and to determine the optimal hemoglobin concentration to maintain in a TBI patient.

MISCHER NEUROSURGICAL ASSOCIATES MOVE TO NEW OFFICES

Mischer Neurosurgical Associates (MNA) have relocated their Texas Medical Center practice to Suite 2800 in the new 30-story Memorial Hermann Medical Plaza, the tallest building in the Texas Medical Center. The new location offers increased space, convenient parking and easy access to outpatient imaging and laboratory services.

MNA physicians housed in the new building include Dong H. Kim, M.D.; William W. Ashley Jr., M.D., Ph.D.; P. Roc Chen, M.D.; Albert J. Fenoy, M.D.; Michele Johnson, M.D.; Brian C. Oh, M.D.; Karl Schmitt, M.D.; Scott Shepard, M.D.; and Nitin Tandon, M.D.

To refer a patient, call 713.704.7100.

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THROMBOLYTIC THERAPY FOR PATIENTS WHO WAKE UP WITH STROKE

Andrew D. Barreto, M.D., Sheryl Martin-Schild, M.D., Ph.D., Hen Hallevi, M.D., Miriam M. Morales, B.S., Anitha T. Abraham, M.D., Nicole R. Gonzales, M.D., Kachi Illoh, M.D., James C. Grotta, M.D., and Sean I. Savitz, M.D .

From the Stroke division, department of Neurology, The University of Texas Medical School at Houston

ABSTRACT

BACKGROUND AND PURPOSE. Approximately 25 percent of ischemic stroke patients awaken with their deficits. The last-seen-normal time is defined as the time the patient went to sleep, which places these patients outside the window for thrombolysis. The purpose of this study was to describe our center's experience with off-label, compassionate thrombolysis for wake-up stroke (WUS) patients.

METHODS. A retrospective review of our database identified three groups of ischemic stroke patients: (1) WUS treated with thrombolysis; (2) nontreated WUS; and (3) zero- to three-hour intravenous tissue plasminogen activator-treated patients. Safety and clinical outcome measures were symptomatic intracerebral hemorrhage, excellent outcome (discharge modified Rankin score, 0 –1), favorable outcome (modified Rankin score, 0 –2) and mortality. Outcome measures were controlled for baseline NIHSS using logistic regression.

RESULTS. Forty-six thrombolysed and 34 nonthrombolysed WUS patients were identified. Sixty-one percent (28/46) of the treated WUS patients underwent intravenous thrombolysis alone whereas 30 percent (14/46) were given only intra-arterial thrombolysis. Four patients received both intravenous and intra-arterial thrombolysis (9 percent). Two symptomatic intracerebral hemorrhages occurred in treated WUS (4.3 percent). Controlling for NIHSS imbalance, treated WUS had higher rates of excellent (14 percent versus 6 percent; P0.06) and favorable outcome (28 percent versus 13 percent; P0.006), but higher mortality (15 percent versus 0 percent) compared to nontreated WUS. A second comparison controlling for baseline NIHSS between treated WUS and 174 intravenous tissue plasminogen activator patients treated within three hours of symptoms showed no significant differences in safety and clinical outcomes.

CONCLUSIONS. Thrombolysis may be safe in WUS patients. Our center's experience supports considering a prospective, randomized trial to assess the safety and outcome of thrombolysis for this specific patient population.

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RELATIONSHIPS BETWEEN ESSENTIAL CORTICAL LANGUAGE SITES AND SUBCORTICAL PATHWAYS

Timothy M. Ellmore, Ph.D., Michael S. Beauchamp, Ph.D., Thomas J. O'Neill, B.S., Stephen Dreyer, B.S., and Nitin Tandon, M.D.

From the department of Neurosurgery and department of Neurobiology and Anatomy, The University of Texas Medical School at Houston

ABSTRACT

OBJECT. Maps produced using either electrical stimulation or functional imaging have demonstrated a distributed network of cortical regions involved in expressive and receptive language tasks. The pattern of connectivity among components of this network has begun to be explored with diffusion tensor (DT) imaging, but has yet to be completely characterized. In this study the authors used DT imaging–based tractography to examine the interrelationship between cortical areas found to be essential for language by intra-operative electrical stimulation.

METHODS. The authors localized the arcuate fasciculus (AF), a white matter fiber system connecting frontal and parietotemporal areas in ten patients, nine of whom subsequently underwent left hemispheric language mapping.

RESULTS. The authors found that 81 (79 percent) of 102 essential language sites (ELSs) were closely related to the AF. Of all ELSs, 59 percent were located within 7.5 mm of AF fiber pathway terminations, and another 20 percent contained pathways terminating closer to the AF than would be expected by chance ($p < 0.05$). Additionally, direct subcortical stimulation of the AF following focal cerebral resections produced transient language deficits. The close spatial relationship found between ELSs and the AF suggests that tractography data alone may be used for localization of ELSs.

CONCLUSIONS. The deficits evoked by subcortical stimulation validate and demonstrate the utility of this AF localization technique, and provide further evidence that the AF is an important pathway for fluent language. Taken together, these results demonstrate that DT imaging of the AF may be used to predict the location of brain areas that will be eloquent by the standards of stimulation mapping.

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