Treatment of Sleep Disorders

Improving Outcomes for Cerebrovascular Disease Patients

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stroke and Sleep Disordered Breathing (SDB) are common disorders associated with significant morbidity and mortality. SDB is highly prevalent in patients with strokes. Several epidemiologic studies have shown a strong association between SDB and stroke independent of well-established modifiable risk factors for cerebrovascular disease. SDB encompasses habitual snoring, increased upper airway resistance syndrome, periodic breathing and sleep apnea. The most effective treatment for SDB is positive airway pressure (PAP). Physicians at the UHealth Sleep Center are currently using PAP therapy with the goal of alleviating the burden of patients with SDB.

The UHealth Sleep Medicine Program, accredited by the American Academy of Sleep Medicine and led by Dr. Alberto Ramos, Assistant Professor of Clinical Neurology, and Dr. Alexandre Rocha Abreu, Assistant Professor of Pulmonary Medicine, is a regional leading sleep program offering the latest advances in sleep medicine evaluation, treatment, research and training. Using a multidisciplinary approach, the USleep medical and clinical partnerships actively address a variety of sleep disorders, including SDB. At the same time, the clinician scientists in the program conduct research and education in their respective disciplines related to various sleep conditions. Our physicians and sleep technicians perform PSG sleep studies on an outpatient basis, seven nights/days a week, in our seven-bed diagnostic testing facility at the University of Miami Medical Campus as well as in our four bed sleep lab at the Hotel Indigo located in the Kendall area of Miami-Dade County.

To provide a robust substrate for junior and senior scientists to investigate sleep disorders, The UHealth Sleep Program has created a Sleep Disorders Registry to systematically collect valuable patient data for analysis including demographic, clinical and sleep physiologic information. The cultural diversity of South Florida offers our researchers the unique opportunity to evaluate a multi-ethnic population and examine race/ethnic differences in multiple sleep disorders.

In addition to the collection of data for future studies, our physicians and scientists are conducting NIH funded research on sleep medicine. Dr. Ramos is currently conducting a study on Sleep Related Symptoms, White Matter Hyperintensities and Sub- clinical Infarcts in the Northern Manhattan Study. This study provides the opportunity to evaluate common sleep related complaints and sub-clinical markers of cerebrovascular disease, such as white matter hyperintensities and sub-clinical infarcts.

“Sleep disorders and their surrogates are novel modifiable risk factors for stroke and cardiovascular disease,” said, Alberto R. Ramos, M.D.

“Using standardized NOMAS data collection instruments, we are able to analyze how frequently healthy individuals report snoring, daytime sleepiness, and other common sleep complaints. This study provides the opportunity to evaluate differences in common sleep related complaints and sub-clinical markers of cerebrovascular disease between different race/ethnic backgrounds. There is a particular concern for the growing Hispanic population and African Americans who are at a higher risk of stroke and have a greater prevalence of self reported sleep symptoms when compared with whites,” said Dr. Ramos.

Another member of the team, Dr. William Wohlgemuth, is the site PI for the Sueno-ancillary study to the Hispanic Community Health Study. This study will look at the correlation between abnormal sleep habits and obesity, hypertension, diabetes and cardiovascular disease among other health outcomes. Dr. Shirin Shafazand, Assistant Professor of Pulmonary Medicine, is leading a research study funded by the American Board of Sleep Medicine on Hispanic Sleep Knowledge.

Among other clinical and research efforts, UM physicians are currently using transcranial Doppler ultrasonography (TCD) to evaluate brain hemodynamic changes in patients with newly diagnosed SDB. An early impairment in brain hemodynamics may also be an indicator of increased risk for vascular events in patients with SDB. Following diagnosis, patients are then fitted for CPAP masks and referred to our PAP compliance clinic where sleep technicians closely follow each patient to resolve any equipment use issues that may impede the patient’s treatment, as well as improving patient’s knowledge/compliance with sleep therapies. We are also committed to provide and develop more educational programs to our patients in order to improve treatment outcomes and prevent vascular diseases.

To refer a patient for participation in one of our Sleep Medicine clinical studies, please call 305-243-2905 or to make a referral for a comprehensive sleep evaluation, please call 305-243-5195.

The University of Miami/Jackson Memorial Hospital departments of Neurology and Neurosurgery are ranked #1 in the state of Florida and #29 in the nation by US News & World Report’s Best Hospitals 2010.
Dear Colleagues,

The Departments of Neurology and Neurological Surgery are committed to conducting cutting-edge research and innovative clinical trials to treat neurological diseases and injuries.

The Department of Neurology is currently pioneering new methods for the use of stem cells to treat ischemic stroke under the direction of Dileep R. Yavagal, M.D. Alberto Ramos, M.D., is conducting clinical trials to draw pivotal conclusions between the relationship of Sleep Disordered Breathing (SDB) and the increased risk of stroke.

The Miami Project to Cure Paralysis is conducting Schwann cell transplantation research that after two extremely productive years resulted in a pre-IND discussion with the FDA in July of this year, making significant progress in fast-tracking this basic science discovery toward clinical application.

We are continuing to offer exceptional care that is revolutionizing the lives of patients like Jose Garcia, a Miami resident who had been living in pain for 20 years until he visited Howard B. Levene, M.D., Ph.D. Mr. Garcia learned that his pain was derived from cervical stenosis, but Dr. Levene also found a tumor above his kidney, a discovery that saved Mr. Garcia’s life.

Through our groundbreaking research and exceptional patient care we continue to strive to provide excellence at the University of Miami.

Barth A. Green, MD, FACS, Professor and Chairman of Neurological Surgery

Ralph L. Sacco, MS, MD, FAAN, FAHA, Professor and Chairman of Neurology

Jose Garcia, a local Miami resident, visited Howard B. Levene, M.D., Ph.D. in September of 2009 to receive a consultation on his back and hip pain and the numbness in his legs that was severely inhibiting his ability to walk. His pain, originally derived from the impact experienced from a second story fall in 1986, had been intensifying for over 20 years.

Since his injury, Mr. Garcia attempted to seek treatment at multiple clinics however he only received temporary relief through electric stimulation and therapeutic massages. After years of these failed treatments, a local physician referred Mr. Garcia to Dr. Levene. Mr. Garcia was sent to Dr. Levene with MRI images of his Thoracic and Lumbar spine. Dr. Levene suspected myelopathy from cervical stenosis, and ordered a Cervical MRI as well as repeat Thoracic and Lumbar MRIs to compensate for the limited quality of the original films.

Dr. Levene, after speaking to a radiologist regarding Mr. Garcia’s MRIs, confirmed that he was correct in his preliminary diagnosis. Mr. Garcia did have cervical myelopathy, but there was an additional finding, he also had a tumor above his kidney. Dr. Levene immediately referred Mr. Garcia to Murugesan Manoharan, M.D., University of Miami Urologist, for a further workup.

“I was very concerned to find this tumor,” stated Dr. Levene. “I wanted to help Mr. Garcia, and I didn’t want it to go untreated. I contacted Dr. Manoharan, and we began to coordinate Mr. Garcia’s care.”

Dr. Manoharan further examined Mr. Garcia, conducting a second MRI and confirming the existence of a large tumor above Mr. Garcia’s kidney.

It was determined that two surgeries were necessary. Dr. Levene would first decompress the cervical spine. This would help prevent iatrogenic spine injury from positioning or blood loss for the next portion of his care. The cervical decompression occurred on November 9, 2009. On November 16, 2009 he was transferred to Dr. Manoharan who then removed his tumor.

After recovering from two successful surgeries, Dr. Levene discussed the possibility of a third surgery for Mr. Garcia. In addition to having a narrow cervical spinal canal, Mr. Garcia had a narrow lumbar spine canal. After a detailed discussion, Dr. Levene and Mr. Garcia decided that surgery on the lumbar spine would be necessary to maximize Mr. Garcia’s recovery. On April 8, 2010, Mr. Garcia received his third successful surgery.

“I am over 80% better than I was before. I am so thankful for Dr. Levene. He has a very skillful hand,” said Mr. Garcia.

Follow up tests reveal no signs of cancer and healing from the spinal surgeries is progressing normally. Mr. Garcia is still under the care of Dr. Levene and is receiving physical therapy.

“I am learning to walk through physical therapy. Before the surgeries I had numbness in my legs, and now I feel my legs and I am walking. I am doing things that I could not even imagine before. I will forever be indebted to Dr. Levene because he discovered everything and gave me a new life.”

For more information on Neurology clinical trials please call 1-877-977-7724

For more information on Neurological Surgery Clinical trials please call 1-800-996-3783
In his laboratory, Dileep R. Yavagal, M.D., Director of Interventional Neurology and a member of the Interdisciplinary Stem Cell Institute faculty, is pioneering new methods for the use of stem cells to treat ischemic stroke. As an interventional neurologist, Dr. Yavagal routinely performs cutting-edge emergency clot removal procedures on acute stroke patients at Jackson Memorial Hospital, a comprehensive stroke center serving Miami and the surrounding area. Although these procedures are able to restore blood flow in most cases, he believes that stem cell therapy will be the next breakthrough treatment for ischemic stroke.

“Only restoring blood flow may not be enough to improve outcomes in acute ischemic stroke because a substantial amount of tissue may be irreversibly injured by the time the patient reaches us,” notes Dr. Yavagal. “Treatment with mesenchymal stem cells, derived from adult bone marrow, holds great promise for these patients and for those who have had a stroke in the past.”

Research in the field of stem cell therapy for stroke has focused on transplanting the cells to the brain using direct needle delivery requiring surgical access to the brain. In recent years, however, investigators have been studying intravenous delivery of stem cells for stroke patients although this route may be limited because only a small percentage of the stem cells administered actually reach the damaged brain areas. Dr. Yavagal’s study team has focused on translational studies of catheter based intra-arterial delivery of mesenchymal stem cells in acute and subacute stroke. As increasing numbers of catheter-based interventions are done for patients with acute stroke, intra-arterial delivery of stem cells via this route of delivery has significant clinical potential.

A recent milestone for Dr. Yavagal was establishing a maximum safe dose of intra-arterial stem cells in an experimental stroke model. Although evidence for a therapeutic effect of stem cell treatment for stroke exists, no dose-ranging studies have been performed to identify the optimal stem cell dose. In a platform presentation at the American Academy of Neurology 2010 Annual Meeting, Dr. Yavagal showed that delivering stem cells intra-arterially, directly into the recanalized vessel, was feasible in a rodent stroke model.

He also showed that there is a maximum stem cell dose that should not be exceeded. Above this dose, the stem cells block the cerebral microvasculature. Dr. Yavagal is currently extending his findings to large animals in order to show that the intra-arterial technique is safe and feasible using existing endovascular devices in human-like vasculature. He hypothesizes that the intra-arterial approach will result in more stem cells reaching the brain resulting in a more powerful therapeutic effect and improved functional outcomes. Using the results of his animal studies, he plans to apply for a Phase I clinical trial of stem cell therapy for stroke.

“Once we have the data from a Phase I safety trial, we can begin to test the effect of stem cell therapy on stroke patients who currently have no other options,” said Dr. Yavagal.

Clinical Trial Phase 1
Schwann Cell Transplantation

The Miami Project to Cure Paralysis, under the direction of W. Dalton Dietrich Ph.D., Scientific Director, and Barth A. Green, M.D., Co-Founder, has been making incredible strides in evaluating the safety of Schwann cell transplantation.

In August 2008, The Miami Project initially met with the FDA to discuss the possibility of translating successful discovery research into a clinical trial. The FDA requested specific safety data in animals as a next step; a requirement for all proposed therapies regardless of being a drug, device, or cell.

To fulfill the FDA request, The Miami Project has conducted a series of cellular-based therapies. The benchmark of success for the test is to keep the animals alive for at least 6 months after transplantation and then follow up by very thoroughly evaluating each animal for toxicity, biodistribution and tumorigenicity.

The human Schwann cells for the FDA requirement were prepared using official cell manufacturing protocol and then injected into immune compromised rats. While conducting these experiments it was discovered that the immune compromised rats have a larger injury response than normal rats, making a more hostile transplantation environment; this negatively impacts the Schwann cell survival and produces inconsistent graft results.

An alternative approach was to inject rat Schwann cells with non-immune compromised rats. Prior to beginning this round of experiments, there was an interim discovery made with a pig model. To proportionally deliver the same number of Schwann cells to the pig or human that had been delivered to the rat, a much larger volume would need to be injected. When the larger volume was delivered it actually caused additional damage to the spinal cord. This demonstrates how critical these safety experiments are in order to properly translate Schwann cell research to humans.

As a consequence of this discovery, a short-term experiment is currently being conducted to identify the lowest efficacious dose in rats. Once this is determined, the experiment will then resume with the additional investigation; the pivotal 6-month toxicity, biodistribution, and tumorigenicity experiments.

In July of 2010, The Miami Project had an official pre-IND discussion with the FDA. The FDA was supportive of the proposed phase I clinical protocol; however, they strongly suggested to consider a dose escalation in the trial.

The first proposed clinical trial would be to transplant autologous human Schwann cells 3-5 weeks post-injury in 6 participants with a complete, thoracic SCI to establish safety. Depending on the safety outcome, subsequent trials would be opened up to include incomplete injuries, chronic injuries, and cervical injuries.

The Miami Project is well positioned with expertise, knowledge and drive to continue to navigate through the FDA process and initiate new human clinical trials involving Schwann cell transplantation. In just 2 short years The Miami Project research team has made significant progress in fast-tracking this basic science discovery toward the clinical application. The guiding principle is to successfully translate therapies to the clinic.

The principal investigators of the study are Allan B. Levi, M.D., Ph.D, and James D. Guest, M.D., Ph.D, (clinical); and Mary Bartlett Bunge, Ph.D., and Damien Pearse, Ph.D., (basic science).
In The News

University of Miami Health System Hosts Healthcare Summit

CurrentMedicine.TV and The University of Miami Health System hosted a summit to discuss reduction in healthcare spending without hurting quality of care. The passage of the new healthcare reform law will expand insurance coverage at a significant cost. To offset that, $500 Billion in cuts must be made for the program to be “budget neutral”. Ralph Sacco, M.D., Chairman, Department of Neurology, was on the panel of experts along with Dr. Donna Shalala, President of the University of Miami.


Barth A. Green, M.D., Receives FANO Award

Barth A. Green, M.D., professor and chair of neurological surgery, received the Florida Association of Nonprofit Organization’s prestigious Lawton’s Heart Humanitarian Award on August 18 for his lifetime devotion to humanitarian causes during an award ceremony at the organization’s annual conference in Fort Lauderdale, Florida. Founded 20 years ago, FANO represents Florida’s non-profits.

He was honored for leading the massive medical relief effort in Haiti after the devastating January 12 earthquake and for co-founding Project Medishare, The Miami Project to Cure Paralysis, and Shake-A-Leg Miami.

What’s Next

8th International Workshop, International Stroke Genetics Consortium

January 13-14, 2011 Miami, Florida

Ralph Sacco M.D., Chairman, Department of Neurology; Tatjana Rundek M.D., Ph.D., Associate Professor of Neurology in collaboration with the Hussman Institute for Human Genomics will be hosting the 8th International Stroke Genetics Consortium. The assembly of international stroke genetics leaders will include discussions of new advancements in the genetics of stroke, results of current studies and collaborative international work. The leaders will also plan future collaborations, large meta-analyses and validation of the findings in different cohorts of stroke patients around the world. For more information call 305-243-1699.

M. Ross Bullock, M.D., President Elect of National Neurotrauma Society, to Host Society Symposiums

July 10-13, 2011 Fort Lauderdale, Florida

M. Ross Bullock, M.D., Ph.D., professor of neurological surgery and director of clinical neurotrauma, is the new president-elect of the National Neurotrauma Society and will organize the 2011 national meeting to be held in South Florida. The three day symposium, which draws expertise from medical and scientific communities, is especially designed for scientists, physicians, postdoctoral fellows, residents and graduate students. The scientific program will include clinical pathophysiology, treatment strategies, basic research models and molecular approaches involved in CNS neurotrauma.

http://www.neurotraumasymposium.com

Resident Spotlight

New Class Profile

The departments of Neurology and Neurosurgery welcomed a new class of residents in July with an incredible array of backgrounds and experiences. They come from a variety of locations including China, India, Puerto Rico and all over the United States. Their experience and interests range from research of post-traumatic epilepsy and traumatic brain injury (TBI), to providing medical care to the homeless. Several of this year’s residents have also served in the U.S. Navy and the U.S. Peace Corps.

The members of this year’s class are medical alumni of NYU, Penn State College of Medicine, University of Miami Miller School of Medicine, University of Illinois, Rush Medical College, Jefferson University in Philadelphia, Loyola College in Chicago, Universidad Central del Caribe in Puerto Rico, Indiana University School of Medicine, University of Hawaii, and the Ponce School of Medicine in Puerto Rico.

The Department of Neurology’s residents are slated to graduate June 2014 and the Department of Neurosurgery’s residents will graduate June 2017.