**Study Finds More is Less for Dystonia Treatment**

A Mount Sinai study has found that patients with dystonia—a neurological disorder characterized by uncontrolled, often painful twisting movements—benefited from deep brain stimulation (DBS) therapy using a lower stimulation frequency than the higher one that is commonly used. Stimulation of the internal globus pallidus (GPI) is usually administered at frequencies greater than 130 cycles per second. This higher stimulation frequency is effective, but it rapidly depletes the batteries of the implanted devices, forcing patients to undergo replacement surgery every two to three years. The Mount Sinai study, which was reported in the August 14 issue of *Neurology*, suggests that stimulation at a lower frequency (just 60 cycles per second) is just as effective as the higher frequency and has the added benefit of extending the battery life of the brain stimulation devices.

The DBS device is comprised of three main parts: the stimulating lead, which is equipped with four electrodes and is implanted into the desired brain structure; a battery powered pacemaker-like pulse generator, which creates the electrical signals that stimulate the brain target and are implanted under the skin on each side of the chest (one for each side of the brain); and an extension cable, which is tunneled from the chest to the head, connecting the stimulating lead to the pulse generator. The DBS system, which is manufactured by Medtronic, Inc., is approved in the United States for the treatment of tremor, Parkinson’s disease, and dystonia.

The Mount Sinai team, led by neurosurgeon Ron Alterman and neurologist Michele Tagliati, studied 15 patients with dystonia who had undergone the standard deep brain stimulation (DBS) procedure. However, instead of stimulating at the standard higher frequency (130 to 180 cycles per second), they used a frequency of only 60 cycles per second. “The thinking behind this study was to determine if we could achieve similar therapeutic responses employing a lower stimulation frequency while also extending the life of the pulse generator,” stated Dr. Alterman. “The answer, we’re pleased to say, is yes.” Drs. Alterman and Tagliati found that over the course of a year, the patients showed steady and consistent improvement. On average, motor function improved by 38 percent after just one month of stimulation and an amazing 89 percent after one year. Seven of the 15 patients did so well with the treatment that they were able to discontinue their medications entirely, while another six patients were able to reduce their medications by 50 percent.

“What’s interesting about this study is that we changed only the frequency, not the voltage or pulse widths, so it is a true savings in energy and a very practical and real benefit for our patients,” Dr. Alterman continued on page 2
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continued from page 1

said. “Our finding also challenges scientific dogma regarding the mechanisms by which DBS works. “No one before has ever evaluated the use of lower frequencies this systematically, so this could open up more questions, but also more treatment opportunities.”

Dr. Tagliati told Reuters Health, “Our overall experience with DBS for dystonia at Mount Sinai is very positive, in particular with patients with primary dystonia. We have implanted some 60 dystonia patients with improvements ranging from 50 to virtually 100 percent, in a disease that frequently benefits very little from pharmacological therapy.”

New Clinical Trials

Dr. Ron Alterman and colleagues at The Mount Sinai Hospital are beginning a study in which patients will receive genes that investigators hope will trigger the production of dopamine. Mount Sinai is one of nine institutions, including Baylor College of Medicine, Cleveland Clinic, Duke University, Oregon Health Sciences University, Rush University Medical Center, University of Alabama at Birmingham, University of California, San Francisco, and University of Pennsylvania, participating in Ceregene’s Phase 2 Clinical Trial for Parkinson’s disease. The trial will evaluate CERE-120, a gene therapy product developed by Ceregene, a biopharmaceutical company, for the treatment of Parkinson’s disease. This trial follows the positive results from a Phase 1 trial of CERE-120 in twelve patients in which preliminary data showed the treatment to be well tolerated and to provide a 35-40 percent (p<0.001) reduction in Parkinson’s symptoms at six through twelve months post treatment. Information from the Phase 1 trial was presented at the American Academy of Neurological Surgeons meeting on April 16, 2007. Fifty-one patients with advanced Parkinson’s symptoms will be enrolled in the second study: the two thirds in the active treatment group will receive CERE-120 through a tiny “burr hole” drilled into their skulls to reach the putamen—a region of the brain affected by the degeneration of neurons in Parkinson’s disease. Patients will be followed for twelve months. The one third of the patients relegated to the control group will have a sham operation and no infusion.

Parkinson’s disease is a progressive movement disorder that affects as many as one million people in the United States. It is caused by a reduction in dopamine containing nerve cells of the midbrain. Dopamine is a neurotransmitter involved in controlling movement and coordination, so Parkinson’s patients experiencing a reduction of dopamine-producing nerve cells exhibit the progressive inability to initiate and control physical movements. There is currently no cure for Parkinson’s disease.

Having given financial support for the first trial and encouraged by the positive results, the Michael J. Fox Foundation for Parkinson’s disease chose to contribute funding for the Phase 2 trial as well. Investigators are hopeful that this therapy may provide an opportunity for patients who have begun to run out of effective treatment options because of the advanced stage of their disease. It will take years before all the data is compiled and the results are known, but looking ahead, Dr. Alterman said, “If we get a strong enough response that dopamine levels normalize, then patients probably will not have to take medications.”

The Phase II Trial of EGFRvIII Vaccine in the Treatment of Newly Diagnosed Glioblastoma Multiforme (GBM) has begun at The Mount Sinai Medical Center Comprehensive Brain Tumor Center.

Expression of the EGFRvIII mutation of the EGFR (epidermal growth factor receptor) confers an even worse prognosis in glioblastoma multiforme than usual. The initial clinical study of this vaccine in humans demonstrated a significant survival advantage. Potential patients must not have had any radiation or chemotherapy.

Candidates for the study include:
Patients with a presumed diagnosis of GBM who have not had surgery;
Patients who have had surgery and have insignificant residual tumor after the surgery;
Patients with significant post-operative residual tumor might qualify if they have the potential for a greater than 95% tumor resection by our neurosurgeons.

Candidate patients require pre-operative consent to assay for the presence of the EGFRvIII mutation in the tumor tissue. Unstained or archived paraffin embedded brain tumor tissue may also qualify if the surgery has accomplished or has the potential to accomplish a greater than 95% tumor resection (very strict post-operative MRI criteria must be satisfied). If patients have the EGFRvIII mutation, they are randomized either to receive conformal radiation, chemotherapy, and the experimental vaccine or to join the control group (conformal radiation and chemotherapy only) at a 2:1 ratio to the experimental treatment arm. The experimental vaccine is continued on a monthly basis but will be discontinued if the tumor relapses.

If you have questions, know someone or have a patient who you think might qualify, please call Principal Investigator, Robert Aiken, MD, at 212-241-4503 or e-mail him as soon as possible at robert.aiken@mssm.edu. Entry into the trial is time sensitive.
On May 30, The Jeannette and Bernard S. Post, MD, Endowed Lecture was presented by Kim J. Burchiel, MD, John Raaf Professor and Chairman, Department of Neurological Surgery, Oregon Health and Science University, Portland, Oregon. Dr. Burchiel explained that a project he did as a resident on trigeminal neuralgia and epilepsy defined the direction for the rest of his career: his talk was titled “New Perspectives on Trigeminal Neuralgia.” He quoted a statement made in 1905 by J. Hutchinson, Jr., FRCS: “The surgeon, however, is chiefly concerned with the question: What cases of neuralgia are suited for operative treatment, and what are the best methods to employ? The answer, obviously, should depend upon a scientific classification, based solely upon the causes of neuralgia; at present such a classification is impossible.” One hundred years later, Dr. Burchiel contends that the current terminology still does not work, and thus he has devised a patient-oriented classification scheme, with Type 1, lancinating and episodic, being the most common, and Type 2, aching and constant, being less common. Type 1 can progress to Type 2. There is another group of less common cases. He maintains that patients with trigeminal neuralgia often get inappropriate treatment. To help combat that, he has developed an accurate test which patients can access on the web to learn if they are candidates for treatment for TN: https://neurosurgery.ohsu.edu/tgn.php. Dr. Burchiel also covered the surgical options for trigeminal neuralgia.

Aspects of aging are partially reversible by the response to estradiol... 

Alzheimer’s disease. He concluded that aspects of aging are partially reversible by the response to estradiol, but cautioned that there may be a window of opportunity when the neurons are still healthy for the estradiol to be administered in order to keep them healthy. He compared his hypotheses to the findings in the much-published Women’s Health Initiative Report which concluded that HT regimen did not improve cognitive function and, in fact, increased the risk for probable dementia in postmenopausal women aged 65 or older. According to Dr. Morrison, in that study, however, because estrogen was given to women 65 and older, “the window of opportunity” was probably lost. Dr. Morrison currently directs a large NIH-funded program on estrogen and the aging brain as well as one on the neurobiological basis of cognitive aging.


The first author, Paul Saphier, MD, won the newly established Kalmon D. Post Neurosurgery Resident Publication Award for this paper. The award of $2000 was presented at Research Day in May.
Malis Lecture

Peter W. Carmel, MD, Professor and Chairman of the Department of Neurological Surgery at UMDNJ, delivered the first Dr. Leonard I. Malis, MD, Endowed Lectureship on September 26. Originally titled, “Dr. Leonard I. Malis: Life, Legend and More,” the final title became “Remembering Lenny.”

Dr. Carmel, whose close ties with Dr. Malis began in 1959 when he worked in Dr. Malis’s laboratory, traced Dr. Malis’s life and career from Lenny’s time in high school in Atlantic City fixing slot machines, to university and medical school at the University of Virginia, army service, residency at Mount Sinai, fellowship at Yale, research at Marineland in Florida and the Brookhaven National Laboratory, faculty and chairmanship at Mount Sinai. The audience was introduced to Malis’s mentors and collaborators as well as to his family. Dr. Carmel emphasized Dr. Malis’s genius at improving instruments already in use as well as inventing many of his own. In Dr. Carmel’s opinion, one shared by many, Dr. Malis “is the neurosurgeon of his century:” his technical innovations, especially his contributions to microneurosurgery, improved all of Neurosurgery; he also raised the bar for the treatment of acoustic neuromas with hearing preservation; his surgical skills set new standards. Dr. Malis liked fast boats and big cars, the latter of which, according to Dr. Carmel, he drove fast with hands off the wheel, guiding the car with his knees: “it was terrifying.” Combining Dr. Malis’s great and lasting influence on Neurosurgery with allusions to his love of boats and cars, Dr. Carmel ended his talk: “He’s still at the helm. He’s still cruising.”

Hollin Lecture

What should be the core curriculum of a residency? How long should the training be? Should fellowships be enfolded into the residency? What will encourage more women to become neurosurgeons? Nicholas Barbaro, MD, Professor, Vice-Chairman, and Residency Director of the Department of Neurosurgery at UCSF, raised these and other provocative questions in his talk on October 3. He was the 17th Sidney A. Hollin Lecturer and the first to speak about the education of residents. The title of his talk, “Pain and the Training of Neurosurgeons: 20 Years Experience,” was influenced by the book, Pain and the Neurosurgeon: a 40 Year Experience, written when resident education was approached differently from that advocated by Dr. Barbaro. First, Dr. Barbaro outlined the seven years of the program at UCSF which has an academic mandate that requires strong faculty support. Residents write three peer-reviewed papers a year and also learn to write grants because they try to obtain funding for their own research. If they have a grant, they have a “protected research year” with no call. Dr. Barbaro recommends that each resident be assigned a faculty mentor who should encourage the resident to develop relationships and outside interests. He advocates that residents take a “disease-based approach” in an area they love (learn all the ways to treat that particular condition). Some of the challenges he mentioned are conflicting time demands of clinical and academic work, the maintenance of a normal lifestyle and the high risk of malpractice. He wants all residents to take away from residency a life long love of learning. The field is changing so fast, he said, that neurosurgeons must continue to learn new things even when they are long out of residency.

Moving In...

Yakov (Jake) Gologorsky, MD
Harvard University, BA
University of Pittsburgh SOM, MD

Soriaya Motivala, MD
McGill University, BS
Indiana University SOM, MD

Fedor (Ted) Panov, MD
Schreyers Honors College, (Penn State), BS
Jefferson Medical College, MD
Charity Softball

Eleven teams gathered on the Great Lawn of Central Park on Saturday, June 9, to participate in the Fourth Annual 2007 Charity Softball Tournament Sponsored by George Steinbrenner and The New York Yankees. Proceeds were to benefit pediatric brain tumor research. Participants came from as far as Atlanta: when a computer glitch cancelled air traffic from Atlanta, the team from Emory rented a van to drive to the tournament. Some of those players arrived in Manhattan as late as 5 AM but were pleased to have had a chance to compete.

Neurosurgery departments from Columbia, Cornell, Duke, Einstein, Emory, Harvard, Hopkins, NYU, Penn, Mount Sinai, Thomas Jefferson and Yale fielded teams. Sinai had a bye in the first round because of their third place finish last year. They defeated NYU in the second round, but were defeated by the eventual winner, Penn, in the third round. Cornell forfeited the consolation game which again put Sinai in third place. All the teams were invited to an “after party” in the evening with food, drinks and music at the Hudson Beach Café. Such a good time was had by all that four more teams have signed up for next year!

Philanthropy Corner

The Department of Neurosurgery is pleased to report that it has received a large gift from George and Mary Lou Strong which will enable us to extend and expand our research in the area of skull base and cerebrovascular scientific investigations. We greatly appreciate this generous contribution.

As you may know, the current level of research funding from the National Institutes of Health (NIH) has been reduced to a point where only 10% of grants are approved, placing many promising, novel research projects at risk. The need for private philanthropy has become critical to achieving the scientific advances and discoveries that will improve tomorrow’s patient care. In today’s healthcare environment of rising costs and shrinking reimbursements, new and improved treatments require support from individuals as well as industry and government funding.

Mount Sinai’s Department of Neurosurgery is fully engaged in a robust program of clinical and basic science research. Our neurosurgeons, using the latest in diagnostic and surgical techniques, bring a wide-array of expertise to treating patients. Also, our faculty is proud to be training those who will become leaders in the field. Whether your interests lie in research, patient care, or education, there are opportunities for you to play a role and make a difference.

We would like to express our sincere thanks to the Strongs and all our thoughtful donors for their commitment to our efforts. If you or someone you know would like information about supporting our work, please contact Kim Woodward of Mount Sinai’s Development Office at (212) 659-1594 or at kim.woodward@mountsinai.org.

Moving On...

The annual dinner to honor the chief residents was held at Tavern on the Green on June 13. In an evening packed with levity and seriousness, the residents, from PGY1 to PGY4, spoke of the influence and impact that both Brian Snyder and Paul Saphier had on their education and careers. Faculty members reminisced about their experiences with the two graduates, and Dr. Post gave parting advice to the two before he sent them on their way. Paul is spending a year in Los Angeles at UCLA doing an Endovascular Fellowship, and Brian has headed to Canada for a Functional/Restorative Fellowship at the University of Toronto.

Dr. Post, graduates Brian Snyder and Paul Saphier, Dr. Bederson
Dr. Eliza Geer joined the Mount Sinai faculty in July, 2006, with an appointment in the Division of Endocrinology, and a secondary appointment in the Department of Neurosurgery. She is the principal investigator of a study investigating body composition and appetite in Cushing’s disease. This prospective study, which is supported by a CREFF award, evaluates patients with newly diagnosed Cushing’s disease before and again six and twelve months after transsphenoidal surgery by Dr. Kalmon D. Post. Each study visit includes measurements of adipokines, including leptin and adiponectin, and a whole-body MRI to evaluate body composition, particularly the proportions of visceral and subcutaneous fat. Additionally, each patient is given a standard test meal in the GCRC; and fasting and post-meal appetite hormones, including insulin, total and active ghrelin and PYY are measured. Hunger is measured pre- and post meal with a visual analogue scale questionnaire. Currently 15 Cushing’s patients have been enrolled in the study, and preliminary data was presented at the June 2007 Endocrine Society Conference. Data including the six-month post-operative visit of five patients showed significant decreases in weight, BMI, and waist circumference. Additionally, whole-body MRI showed significant decreases in total and subcutaneous fat and a trend towards a decrease in intramuscular fat. There was also a significant decrease in fasting leptin values six months post transsphenoidal surgery and a trend toward decreased hunger and normalization of post-meal ghrelin suppression. Additional studies are underway to further understand the relationship between appetite hormones and body composition changes in Cushing’s disease.

Dr. Geer is also mentoring two second year Endocrine fellows, Dr. Dima Yeshou and Dr. Maria Skamagas, in clinical pituitary research. With Dr. Yeshou and Dr. Zaidi, she is investigating the role of ACTH on bone remodeling, specifically looking at the bone loss seen in Cushing’s disease, and the time course of recovery of bone markers after transsphenoidal surgery. With Dr. Skamagas, she is investigating the prevalence of cardiac valvulopathies in hyperprolactinemic patients treated with chronic cabergoline. Echocardiograms of hyperprolactinemic patients who have been on cabergoline for at least two years will be reviewed to assess the prevalence of valvulopathies in this population.
**News Briefs**

*Isabelle M. Germano, MD, FACS,* served as moderator for the “International Brain Tumor Symposium” during the 7th Biennial Joint Section on Tumor meeting in Washington, DC, in April. She was also co-director of the practical clinic, “Pre-operative and Intraoperative Brain Mapping, Including Surgery for Epilepsy” at the American Association of Neurological Surgeons in April. During the same meeting she was invited to serve as moderator for the symposium, “Controversies in Neurosurgery: Vestibular Schwannomas: Radiosurgery versus Surgery” and the breakfast seminar, “Update on Tumor Surgery.” In June, Dr. Germano was an invited speaker at the 56th Italian Neurosurgery Society Meeting and Joint Congress of Neurological Surgeons Meeting in Rome, Italy, and moderator and discussant at the 2nd International Meeting, Updates in Neuro-oncology, also in June in Cortona, Italy.

**Dr. Germano** is the recipient of the Goldhirsh Foundation Brain Tumor Grant for her project entitled “Transgenic embryonic stem cell delivery of mda-7/IL-24 for malignant glioma therapy.” Seeking the most promising, innovative, and novel research strategies that will translate into improved outcomes for brain tumor patients, the Foundation devotes a significant portion of its annual grantmaking support for brain tumor research, through competitive, peer-reviewed application processes. Dr. Germano is also the recipient of the National Brain Tumor Foundation Patient Help Fund. This fund is devoted to patients who will have their primary or metastatic brain tumor treated at Mount Sinai and might need financial help to cover expenses not fully supported by their health insurance.

Several faculty were interviewed by media. **Aman Patel, MD,** was quoted in the *New York Post* on May 8 in an article about treating aneurysms with coil embolization rather than open surgery. On CW 11 News at 10 on May 28, **Dr. Ron Alterman** described the struggles of some of his patients to get their insurance company to cover their surgery for Deep Brain Stimulation. CW 11 and Mount Sinai did convince an insurance company to pay for the procedure for one patient, and some of the staff from CE11 watched while Dr. Alterman performed “the extraordinary procedure that will hopefully change a young man’s life.” Both **Drs. Isabelle Germano** and **Ron Alterman** were interviewed by news stations about the long term treatment of Chief Justice John Roberts after his seizure on Monday, July 29. **Dr. Germano** was also interviewed by *Huliq.com* about new treatment for spinal cancer patients at Mount Sinai. “Hope is being given to patients with malignant and ultimately fatal spinal tumors where hope was never before available. All it takes is one thirty-minute out-patient treatment of pinpointed radiation and the tumor shrinks along with the pain from the cancer. Now cancer spreading to the spine doesn’t mean a lifetime of pain or a wheelchair for a patient anymore.” “The future of radiation oncology and stopping cancer in its track is now at Mount Sinai. This is the best treatment available for tumors that have spread to the spine with the least risk of damage to surrounding healthy tissue,” said Dr. Sheryl Green, Co-Director of The Radiosurgery Program and Assistant Professor of Radiation Oncology at Mount Sinai. **Nirit Weiss, MD,** was quoted in a *Forbes Magazine* article highlighting 15 people who have changed the world. She discussed how the MRI, invented by Paul Lauterbur and Peter Mansfield, has totally transformed neurosurgery: “MRI has allowed us to visualize the brain’s structures so we have a map in our head of where to go and where to avoid.” **Dr. Ron Alterman** contributed to an article on the front page of the Health and Fitness section of the *Chicago Herald* of September 7. The article focused on 17 year old Elisse Lorenc whose life was dramatically and positively changed by her deep brain stimulation surgery to treat her dystonia.

Accepting an invitation from Nagoya University and financed by a “visiting professor grant,” **Fatima Sehba, PhD,** spent three months in Japan where she was involved in collaborative studies in the Research Institute of Environmental Research (RIEM) at Nagoya University. The study worked on developing new strategies for understanding ischemic cerebral injury after acute subarachnoid hemorrhage.

**Shimon Aronhime,** a second year student at Mount Sinai, was a proud recipient of a 2007 AANS Medical Student Summer Research Fellowship (MSSRF). The AANS awarded ten of these fellowships this year. Shimon spent ten weeks working in **Dr. H. Richard Winn’s** laboratory studying the effects of adenosine on cerebral blood flow. Shimon also received a Glorney-Raisbeck Medical Student Grant in Cardiovascular Research from The New York Academy of Medicine for his work in the lab. On September 25, Shimon and the other student grantees presented their research findings at the Academy’s annual Medical Student Forum to an audience of Academy Fellows, faculty mentors, research colleagues and fellow student grant awardees. A previous winner of the Glorney-Raisbeck Award, medical student **Adam Sandler,** also working in Dr. Winn’s laboratory, won a twelve month fellowship from the American Heart Association.

After four years of service as Chairman of the FPA (Faculty Practice Associates) Board of Governors, **Dr. Kalmon D. Post** stepped down from that position in July. Prior to his Chairmanship, he contributed to the FPA for many years as a member of the Board, Chair of the Finance Committee, and member of the Executive Committee. At the FPA’s meeting in June, Louis S. Russo, MD, CEO of the FPA, remarked that, at a time of significant challenge for the FPA and for Mount Sinai, “the FPA, with Kal as Chair, has met all the challenges and has been a leader in the clinical resurgence and improved financial performance of the School and Hospital.”

**Arthur Jenkins, III, MD,** has joined the Medical Advisory Board of the Alan T. Brown Foundation (ATBF). Since its inception in 1988, the Foundation has targeted a single goal—finding a cure for spinal paralysis. Since that time, the ATBF has been a major supporter of scientific and medical research initiatives worldwide.

continued on page 8
The Alan T Brown Foundation to Cure Paralysis is a certified not-for-profit organization.

In September, Dr. Kalmon D. Post, participated in and spoke at the International Pituitary Surgeons Society meeting in Vienna celebrating the 100th anniversary of the first transsphenoidal pituitary operation performed by Schloffer in Vienna. His topic was comparison of results in Cushing’s disease surgery in patients with and without Inferior Petrosal Sinus Sampling. Dr. H. Richard Winn was the Distinguished Neurosurgeon Lecturer at the Department of Neurosurgery at Hartford Hospital in Connecticut. His lecture was entitled “Is there still a role for surgery in the treatment of cerebral aneurysms?” Coincidentally, the same month, Dr. Aman Patel spoke at the Jacksonville, Florida, Mayo Clinic, about “Endovascular treatment of aneurysms with self-expanding stents and detachable coils.”

The newest member of the Post clan arrived at 1:54 AM on June 3. Hayden Michael Post, 6 pounds 1 ounce, 19 1/4 inches, arrived just at the end of his mother Lauren’s residency in Emergency Medicine. Dad Alex is in his last year of Neurosurgery Residency. At a very young age, Hayden accompanied his parents at a belated but significant combined birthday celebration for his grandfather, Dr. Kalmon D. Post, and Dr. H. Richard Winn on June 10, and also helped cheer the neurosurgery team at the softball tournament the next day.

Dr. Jamie Ullman and husband Mark Nearenberg welcomed Sara Tess Nearenberg on August 23 at 3:13 PM. Dr. Ullman said that she and Mark are “in seventh heaven” over their new little bundle of joy, who weighed 6 pounds and was 19 inches long.

Soon after his graduation from the residency program and her graduation from NYU School of Medicine, Brian and Carly Snyder welcomed Zachary Dylan, weighing 7 lbs 2 oz, at 7:23 AM on July 20th.