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Rehab Progress — Winter 2010 Michael C. Munin, MD Senior Editor Kaufmann Medical Building Suite 201 Pittsburgh, PA 15213 muninmc@upmc.edu

From the Director's Desk



Dr. Boninger

Two years ago in my first departmental meeting as the new interim chair, I explained to the faculty that in addition to the university having to decide if they wanted me, I wasn't ready to

decide if I wanted to be the permanent department chair. I needed to try out the position. I equated it to test-driving a new car. As a warning, I explained that when I take a car out on a test drive I like to alternately floor it, step on the brakes, and accelerate into hairpin turns. I asked for the faculty's help and support, explaining that to advance the department's mission, we needed to run like a Porsche. I needed their help steering, and in fact, they were the engine of the car. Near the end of 2009, the test drive ended and I removed the "interim" designation from my title. In reality, the test drive ended a month after it started, when I realized how amazing the car turned out to be.

If you follow this column you know a little about the drive, but let me summarize our past two years on the road:

- We moved our core inpatient units into an amazing new facility that is part of a Level 1 trauma center.
- We merged two great residency programs into one great program, making us one of the largest PM&R residencies in the country.
- We recruited new clinical faculty with specialty training in SCI, TBI and sports medicine.
- We recruited new research faculty investigating spinal cord regeneration and repair, motor plasticity using transcranial magnetic stimulation, and direct brain interfaces for control of robotics, FES, and prosthetics.
- We fulfilled a promise I had made for years, becoming the No. 1 NIH-funded rehabilitation medicine department in the country.

Amazingly, no one threw up along the way.

The car is humming and hairpin turns (health care reform) are clearly on the horizon. But we're all tuned up and ready to go. I'll keep you in the loop.

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Michael L. Boninger, MD

Director, UPMC Institute for Rehabilitation and Research Associate Dean for Medical Student Research University of Pittsburgh School of Medicine Professor and Chairman Department of Physical Medicine and Rehabilitation

Transcranial Magnetic Stimulation at UPMC



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During the last decade, transcranial magnetic stimulation (TMS) has been used as a noninvasive method to investigate motor cortical reorganization and neuroplasticity in humans with and without a central nervous system injury. It has been used most extensively in the corticospinal system, since the output of the primary motor cortex (M1) can be easily assessed in the form of a motor-evoked potential (MEP) by using surface electromyographic (EMG)recording electrodes. The use of TMS during behavioral tests has made it possible to make inferences about cortical function during motor learning and a variety of other motor and cognitive processes. More importantly, these studies have provided some of the basic knowledge for the formulation of interventional strategies to ameliorate motor function after a lesion, an issue of relevance in clinical neurorehabilitation.

How does TMS work?

TMS is based on Faraday's principles of electromagnetic induction. A brief and high-current pulse is produced in a coil of wire, which is called the magnetic coil. A magnetic field is produced with lines of flux passing perpendicular to the plane of the coil. The magnetic field can reach up to about 1.5 to 2 Tesla depending on the specific device, and usually lasts for about 100 µs. While the voltage of the field itself may excite neurons, it induces

currents that run parallel to the plane of the coil. Neuronal elements are activated by the induced electric field via two mechanisms. First, if the electrical field is parallel to the neuronal element, the field will be most effective where the intensity changes and becomes more diffuse with distance below the coil. Second, if the field is not completely parallel, activation will occur at bends of the axons. When the current amplitude, duration, and direction are appropriate, they will depolarize cortical neurons and generate action potentials. Therefore, the magnetic field serves as a vehicle for delivering currents focally in the brain. The induced electrical current is responsible for the excitation of the cortical neurons.

Which neuronal elements are activated by TMS?

In humans, TMS can evoke responses involving specific muscles through the activation of monosynaptic and non-monosynaptic corticospinal neurons in both arms and legs. Electrophysiological studies support the view that with TMS we can assess monosynaptic corticospinal connections by examining the effect of TMS on (a) the probability of discharge of single motor units voluntarily preactivated (i.e. poststimulus time histograms, PSTHs); and (b) the amplitude of H-reflexes of upper and lower limbs. A suprathreshold TMS stimulus results in multiple descending waves as recorded from epidural electrodes positioned over the

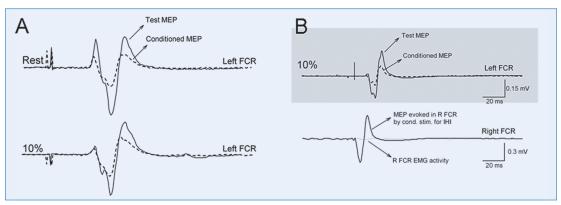


Figure 1: Short-interval intracortical inhibition (SICI) and interhemispheric inhibition (IHI) measurements. (A) SICI measured in the left flexor carpis radialis (FCR) in a representative healthy subject when the right FCR was at rest or performing 10% of maximal right-wrist flexion force. Solid lines are Test MEPs; dashed lines are Conditioned MEPs. The conditioning subthreshold pulse was given 2.5 ms earlier than the Test pulse. Note the well-defined SICI at rest and 10% of maximal right-wrist flexion force. (B) IHI from the left M1 to the right recorded from the left FCR of a representative subject during performance of 10% of maximal right wrist flexion force. Solid lines are Test MEPs; dashed lines are Conditioned MEPs. The conditioning suprathreshold pulse was given 10 ms earlier than the Test pulse. Recordings from the right FCR are shown to demonstrate with solid lines the MEP evoked by the conditioning stimulus (for eliciting IHI) and in solid lines the raw EMG activity in the right FCR at the time of application of the test stimulus alone. Note the well-defined IHI at 10% of maximal right-wrist flexion force. Figure modified with permission from Perez and Cohen 2008.



spinal cord and in a complex configuration of MEP as measured by single motor-unit recordings with needle electrodes. A short latency direct wave (D-wave) is followed by several longer latency indirect waves (I-waves). The D-wave is thought to result from direct depolarization of the initial axon segment of the cortico spinal tract (CST) neuron and is most effectively activated in human subjects by high intensity TMS or by transcranial electrical stimulation. I-waves, which follow the D-wave, occur sequentially with a periodicity of approximately 1.5 ms and reflect the delay required for synaptic discharge.

The reason for the periodicity is not completely understood at this time. It has been proposed that it may depend on reverberating activity of circuits within the cortex or, alternatively, on changes in the membrane properties of corticospinal neurons, which cause it to fire repeatedly after the application of a synchronous depolarizing stimulus. The first I-wave (I1)

is thought to be generated through the depolarization of an axon synapsing directly onto a corticospinal neuron (i.e. monosynaptically), and the following I-waves (I2 and later) may require local polysynaptic circuits.

Electrophysiological measurements acquired by TMS

Several TMS applications have been developed to examine the physiology of the human motor system. These range from simple measurements that are used in clinical practice, such as the assessment of central-motor conduction time, to more complex examples that include the use of pairs of TMS stimuli or pairs of TMS and peripheral nerve stimuli used to assess the excitability of corticospinal neurons, interneurons, and connected structures. Paired pulse TMS protocols have provided insight into the nature of the cortical circuitry that is activated by TMS. Two of the most largely used techniques include short interval intracortical inhibition (SICI) and interhemispheric inhibition (IHI) (Figure 1).

On these protocols two conditions are assessed: (1) a test response is elicited (Test MEP); and (2) in a second condition, the Test MEP is preceded by a conditioning stimulus applied a few milliseconds earlier (Conditioned MEP). The size of the Conditioned MEP is expressed as a percentage of the Test MEP to examine the magnitude of inhibition. For both techniques, direct recordings of the effects on descending volleys have not only confirmed the mechanisms of these effects,



but also revealed some degree of selectivity for different waves (D, I1, I2, etc.) of the response.

What research are we doing in our laboratory?

The focus of our research is on understanding how the brain and spinal cord control voluntary movements in healthy humans and in individuals with spinal cord injury. This theme is mainly investigated from a neurophysiological point of view, using a combination of TMS and peripheral nerve stimulation techniques. Single and paired-pulse TMS and spinal cord reflex protocols are used to examine changes in excitatory and inhibitory pathways in humans. Particularly we use TMS-based methods to investigate the physiology of intrinsic cortical connections in the brain, as well as the interactions between them. These protocols open the possibility to estimate excitability in the GABA-ergic circuit in the human cortex. We employ spinal cord reflex protocols to examine changes in presynaptic inhibition and reciprocal inhibition between antagonistic lower- and upper-limb muscles during movement. This work is complemented by studies that focus on understanding the neuronal mechanisms involved in motor-skill acquisition involving the hand and leg representation of the primary motor cortex.

Transcranial magnetic stimulation is supported by a K99/R00 grant from the National Institute of Neurological Disorders and Stroke of the National Institutes of Health. Support also is provided by the Center for Neural Basis of Cognition, a joint venture of the University of Pittsburgh and Carnegie Mellon University, and the Systems Neuroscience Institute, Department of Neurobiology, University of Pittsburgh School of Medicine.

For more information, please contact Monica Perez, PhD, at perezmo@pitt.edu.

NIH Toolbox Assessment of Neurological and Behavioral Function



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The Department of Occupational Therapy in the School of Health and Rehabilitation Sciences is participating in validation studies supporting the development of The National Institutes of Health (NIH) Toolbox (www.nihtoolbox.org/default.aspx). The NIH Toolbox project addresses the need for brief, well-validated neurological and behavioral health assessments that are applicable for both well and unhealthy people of all ages.

The aim of the NIH Toolbox project is to use the information gathered for longitudinal and epidemiologic studies to ultimately predict and prevent disability. Once released, the Toolbox will be widely disseminated and readily available. Over time, the consistent inclusion of these tests in clinical research and practice will enable comparison and integration of data across multiple studies and settings. To achieve this goal, steps have been taken to ensure that the tests cover a full range of normal functions, rather than disease states, and that they are dynamic, adaptable, and easy to administer.

The tests chosen must (1) be performance-based and applicable to ages 3 and older; (2) not infringe upon intellectual property; and (3) have substantial validity and reliability.

In addition, the final battery for each domain cannot take longer than 30 minutes to administer. Each of the domain areas addressed in the Toolbox is essential for successful participation in daily-living activities, and relate to one's ability to carry out tasks independently, safely, and adequately.

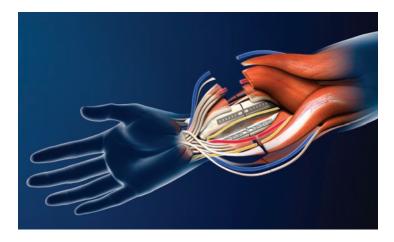
Under the leadership of Margo Holm, PhD, OTR/L, and Joan Rogers, PhD, OTR/L, our Department of Occupational Therapy is assisting in validating somatosensation assessments. Somatosensation is the ability to recognize body sensations, such as light touch, vibration, firm pressure, texture discrimination, pain, and the ability to sense the location and movement of body parts. Research has shown that the ability to perceive these sensations changes over the lifespan and that they can be affected by disease processes. The somatosensation portion of the NIH Toolbox project will ultimately assess 350 individuals between 3 and 85 years of age. Both healthy and chronically ill subjects will be assessed. In Pittsburgh, recruitment includes subjects between the ages of 71 and 85, 80 of whom will be healthy and 40 of whom will have type 2 diabetes with neuropathy.

Currently, the NIH is sampling 300 to 600 subjects for each of the 48 assessments being considered for inclusion in the NIH Toolbox. It is expected that a minimum of 5,800 individuals, both children and adults, Spanish- and/or English-speaking subjects, will be included in the normative data. The NIH Toolbox project addresses the long-identified need for a broadly applicable clinical kit of well-researched neurobehavioral assessments applied across the lifespan. Our Department of Occupational Therapy was invited to participate in this endeavor to provide expertise from a rehabilitation perspective.

For more information, contact Dr. Rogers at jcr@pitt.edu or Dr. Holm at mbholm@pitt.edu.

Bilateral Hand and Forearm Transplants Performed

In May, a UPMC transplant team performed bilateral hand and forearm transplants on a quadruple amputee. Ten years ago, the patient required bilateral transradial and bilateral transtibial amputations due to streptococcal sepsis.



Hand transplants fall into the transplant category of composite tissue allotransplantation (CTA). Donor bone, muscle, circulatory components, and tendons are surgically fixed, attached, or repaired to the recipient bone, muscle, circulatory components, and tendons. The only donor tissue not used during the hand transplant is nerve tissue. The recipient's nerves grow into the transplanted tissue. Nerve growth and regeneration is carefully tracked as motion and sensitivity return to transplanted tissue.

Rejection of the new hand and future health of the recipient are major concerns for the transplant team. The Pittsburgh Protocol is being used to reduce the incidence of transplant rejection and decrease the possibility of drug side effects, such as diabetes and high blood pressure. The protocol uses antibodies on the day of surgery followed by donor bone marrow infusion a few days later. The

Pittsburgh Protocol has been successful in reducing both rejection and the number and doses of immunosuppressant drugs in solid organ transplants, and is proving successful in hand transplants.

Double-hand transplant recovery with inpatient rehabilitation

Recovery after the bilateral hand/forearm transplants required six weeks of postoperative bed rest for wound healing. As a result, upon admittance to the UPMC Institute for Rehabilitation and Research Inpatient Unit the patient was profoundly deconditioned and nonambulatory. He also experienced limited weight-bearing capacity at the transplant sites, an open skin graft site, and femoral nerve neurapraxia.

Prosthetic rehabilitation initially utilized a body-weight support apparatus due to the patient's limited weight-bearing ability from leg weakness and his inability to take substantial weight through his forearm grafts. In addition, due to the right-thigh donor skin graft, his right lower limb transtibial prosthesis was switched from a suction suspension to pin locking system. His transplants were stringently monitored for evidence of rejection indicated by a spotty or blotchy rash.

Outcome

At discharge the patient had progressed from nonambulatory status to walking with a platform walker more than 600 feet. He could climb four stairs with minimal assistance. He also was able to toss a small football with his right hand, indicating improved flexor function. With improved ambulatory and medical function following his inpatient rehabilitation admission, the patient was able to focus exclusively on motor relearning for his bilateral arm transplants. Six months after surgery the patient has movement in his wrists and is able to grasp small objects with his right hand. He also can differentiate between hot and cold on his palms, indicating sensory nerve growth into the transplanted hands.



Mark Your Calendar for IRRDay 2010

The 2010 Institute for Rehabilitation and Research annual research day (IRRDay 2010) will be held Wednesday, June 2, at the University of Pittsburgh's William Pitt Student Union. Guest faculty members will be Deirdre Dawson, PhD, OT, associate professor in the Department of Occupational Science and Occupational Therapy, University of Toronto, and Joel Press, MD, associate professor in the Department of Physical Medicine and Rehabilitation, Feinberg School of Medicine, Northwestern University.

Recent Contributions by IRR Faculty

The following is a sampling of recent presentations by IRR faculty members.

American Psychological Association 118th Annual Meeting Toronto, Aug. 8

Joseph Ricker, PhD, associate professor and director of the Division of Neuropsychology and Rehabilitation Psychology, Department of PM&R, was invited to present "Functional Neuroimaging after Traumatic Brain Injury." Valerie D. Weisser, MA, Department of Psychology, Drexel University, Philadelphia, was co-author.

IEEE Engineering in Medicine and Biology Society 31st Annual International Conference Minneapolis, Sept. 2 to Sept. 6

Wei Wang, MD, PhD, assistant professor and associate director of PM&R's Human Rehab Neural Engineering Lab, presented "Human Motor Cortical Activity Recorded with Micro-ECoG Electrodes during Individual Finger Movements." Additional authors of the abstract were Alan Degenhart, University of Pittsburgh School of Engineering; Jennifer Collinger, PhD, Human Engineering Research Laboratories; Ramana Vinjamuri, PhD, and Gustavo Sudre, PM&R, research associates under Dr.Wei's direction; P. David Adelson, MD, Donald Crammond, PhD, and Elizabeth Tyler-Kabara, MD, PhD, of the Department of Neurosurgery; Deborah Holder, MD, Department of Pediatric Neurology; Michael Boninger, MD, professor and chair, Department of PM&R; Andrew Schwartz, PhD, McGowan Institute for Regenerative Medicine; Eric Leuthardt, MD; Daniel Moran, PhD, Washington University, St. Louis; and Douglas Weber, Department of PM&R.

Ramana Vinjamuri, PhD, lead author and PM&R post-doctoral associate, presented "A Fuzzy Logic Model for Hand Posture Control Using Human Cortical Activity Recorded by Micro-ECoG Electrodes." Co-authors were Douglas Weber, PhD, PM&R assistant professor; Alan Degenhart, graduate student researcher, School of Engineering; Jennifer Collinger, PhD, Human Engineering Research Laboratories; Gustavo Sudre, PM&R graduate student researcher; Donald Crammond, PhD; P. David Adelson, MD, Department of Neurosurgery; Deborah Holder, MD, Department of Pediatric Neurology; Michael Boninger, Department of PM&R; Andrew Schwartz, PhD, McGowan Institute for Regenerative Medicine; Elizabeth Tyler-Kabara, Department of Neurological Surgery; and Wei Wang, assistant professor, Department of PM&R.

Congress on Spinal Cord Medicine and Rehabilitation Dallas, Sept. 23 to Sept. 24

Michael Boninger, MD, professor and chair, Department of PM&R, moderated "The Latest Research and Developments in Assistive

Technology for Mobility in SCI and Implication for Clinical Practice." Joining Dr. Boninger were Rosemarie Cooper, MPT, ATP, assistant professor, Department of Rehabilitation Science and Technology; Greg Nemunaitis, MD; and Jennifer Nagy, MPT, Northeast Ohio Regional Spinal Cord Injury Model System.

Biomedical Engineering Society Annual Meeting Pittsburgh, Oct. 7 to Oct. 10

Podium Sessions

Wei Wang, MD, PhD, assistant professor, Department of PM&R, presented "Human Micro-Electrocorticographic Signals Recorded During Action Execution and Observation." Co-authors were Ramana Vinjamuri, PhD, post-doctoral associate; Michael Boninger, MD, professor and chair, Department of PM&R; Gustav Sudre, graduate student researcher; Douglas Weber, PhD, assistant professor, Department of PM&R; Andrew Schwartz, PhD, Department of Neurobiology; Donald Crammond, PhD; Elizabeth Tyler-Kabara, MD, PhD, Department of Neurosurgery; Alan Degenhart, Department of Bioengineering; Jennifer Collinger, PhD, Human Rehab Neural Engineering Lab; Eric Leuthardt, MD; and Daniel Moran, PhD, University of Washington, St. Louis.

American Association of Neuromuscular & Electrodiagnostic Medicine San Diego, Oct. 7 to Oct. 10

Posters

Steven Brose, DO, Spinal Cord Injury Medicine fellow, Department of PM&R; Michael Munin, MD, associate professor, Department of PM&R; David Stone, MD, assistant professor, Department of Orthopaedic Surgery; Robert Goitz, MD, associate professor, Department of Orthopaedic Surgery; David Fischer, DPT: "An Unusual Case of Chronic Exertional Compartment Syndrome Presenting as Diffuse Muscle Pain."

Melissa Statham, MD, Department of Otolaryngology; Michael Munin, MD, associate professor, Department of PM&R; Clark Rosen, MD, associate professor, Department of Otolaryngology: "Electromyographic Laryngeal Synkinesis Alters Prognosis in Vocal Fold Paralysis."

American Association of Physical Medicine and Rehabilitation Austin, Oct. 22 to Oct. 25

Instruction

Leonard Cabacungan, MD, assistant professor, Department of PM&R; Eric Lenze, MD, associate professor, Department of Psychiatry; and Michael Munin, MD, associate professor, Department of PM&R: "Comprehensive Rehabilitation Approach to Improve Outcomes After Hip Fracture." This course originated as the second issue of the Department of PM&R's UPMC Rehab Grand Rounds. A PDF version of this and other issues in the series is available at: www.rehabmedicine.pitt.edu/content.asp?id=1937

Nadler Research Presentation

Gwendolyn Sowa, MD, PhD, assistant professor, Department of PM&R, recipient of the 2008 research grant, presented research results, followed by critique and discussion: "Investigation into the Utility of Serum Biomarkers to Assess Intervertebral Disc Degeneration."

Brad Dicianno, MD, assistant professor; Angela Garcia, MD, resident; and Mary Louise Russell, MD, assistant professor, Department of PM&R: "Lymphedema and Other Co-Morbid Medical Conditions in Adult Spina Bifida." This course was a review of current and new topics in the management of patients with adult spina bifida.

Michael Munin, MD, associate professor, Department of PM&R: "Advanced Assessment and Management Skills for Spasticity, Dystonia, and Related Motor Disorders: An Interactive, Hands-On Workshop." Dr. Munin was one of the experts in the field providing hands-on skills training in injection techniques for botulinum toxins and neurolytic agents such as anesthetics and phenol.

Michael Boninger, MD, professor and chair, and Gary Chimes, MD, PhD, assistant professor, Department of PM&R: "Hands-On Diagnostic Musculoskeletal Ultrasound: Where We've Been and Where We Are Headed." Drs. Boninger and Chimes were among the expert faculty of this preconference course highlighting the diagnostic benefits of ultrasound.

Posters

Gary Chimes, MD, PhD, and Megan Cortazzo, MD, assistant professors in the Department of PM&R; Lynne Huber, BS, OTR/L, UPMC Rehab Services; Cheryl Bernstein, MD, Department of Anesthesiology Division of Pain Medicine: "Mirror Therapy for Persistent Upper Limb Pain Following Spinal Cord Tumor Resection: A Case Report."

Feguens Bataille, MD, resident, Michael Munin, MD, associate professor, and Steven Brose, DO, SCI fellow, Department of PM&R: "Reversible Encephalopathy Following Prolonged Course of Metronidazole: A Case Report."

Gwendolyn Sowa, MD, PhD, assistant professor, Department of PM&R; Ho Lee, MD, PhD, assistant professor, Department of Orthopaedic Surgery; Stephen O'Connell, DO, PM&R resident; Nam Vo, PhD, assistant professor, Department of Orthopaedic Surgery; Gianluca Vadala, MD, Department of Orthopaedic and Trauma Surgery, Campus Bio-Medico University of Rome; Rebecca Studer, PhD, and James Kang, MD, Department of Orthopaedic Surgery: "Toxicity of Bupivacaine on Intervertebral Disc Cells."

Publications

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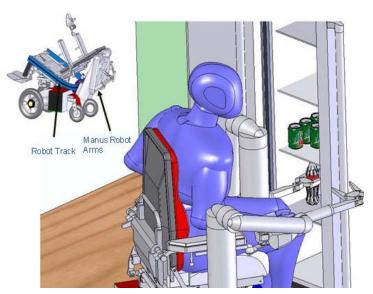
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Technology Showcased at the G-20

The G-20, formally known as The Group of Twenty Finance Ministers and Central Bank Governors, met in Pittsburgh on Sept. 24 and Sept. 25. Many Pittsburgh universities and associated laboratories hosted events that showcased advances in medical and technological areas. The Quality of Life Technology Center (QoLT) used the opportunity to demonstrate the PerMMA project (Personal Mobility and Manipulation Appliance) to Australian Prime Minister Kevin Rudd and first lady Therese Rein, and Chinese Minister of Commerce Chen Deming.

PerMMA is an electric-powered wheelchair with attached robotic arms and web cams. The device is being developed to aid wheelchair users with limited hand function in performing activities of daily living. By combining assistive technology and real time video/web technology, PerMMA's robotic arms can be manipulated by the wheelchair user or via remote control by a technician or caregiver at another location. The wheelchair-mounted webcams relay video to the remote technician when assistance is needed. Control of the arms is transferred to the remote site, and webcams provide visuals for task assistance by the technician/care giver. Some of the tasks successfully completed by PerMMA include picking up objects and bringing them within the wheelchair user's reach, placing food in a microwave, and opening and retrieving food from a refrigerator.

- See PerMMA in action on You Tube at www.youtube.com/watch?v=_bXv9pA-OvM.
- Read more about PerMMA at www.cmu.edu/qolt/Research/projects/permma.html.



Presented by the Quality of Life Technology Center, a collaboration of Carnegie Mellon University and the University of Pittsburgh, PerMMA combines manipulation, mobility assistance, perception, and decision making to help users to become more independent, and reduce or eliminate the need for caregiver assistance.

The PerMMA project is supported by the National Science Foundation and the Human Engineering Research Laboratories, a Veterans Affairs Rehabilitation Research and Development Service Center of Excellence. The research project also receives support from the U.S. Department of Veterans Affairs, the National Institutes of Health, and the Paralyzed Veterans of America. QoLT is a collaboration of Carnegie Mellon University and the University of Pittsburgh.

To learn more about this unique partnership visit www.cmu.edu/qolt/index.html.

AFFILIATE LINKS

UPMC Institute for Rehabilitation and Research http://irr.upmc.com

School of Medicine, Department of Physical Medicine and Rehabilitation http://www.rehabmedicine.pitt.edu

School of Health and Rehabilitation Sciences, Department of Rehabilitation Science & Technology

http://www.shrs.pitt.edu/rst

UPMC Center for Assistive Technology http://www.com/Services/IRR/aboutus/cat

Human Engineering Research Laboratories http://www.herlpitt.org

UPMC

UPMC is an \$8 billion integrated global health enterprise headquartered in Pittsburgh, Pennsylvania, and is one of the leading nonprofit health systems in the United States. As western Pennsylvania's largest employer, with 50,000 employees, UPMC is transforming the economy of the region into one based on medicine, research, and technology. By integrating 20 hospitals, 400 doctors' offices and outpatient sites, long-term care facilities, and a major health insurance services division, and in collaboration with its academic partner, the University of Pittsburgh Schools of the Health Sciences, UPMC has advanced the quality and efficiency of health care and developed internationally renowned programs in transplantation, cancer, neurosurgery, psychiatry, orthopaedics, and sports medicine, among others. UPMC is commercializing its medical and technological expertise by nurturing new companies, developing strategic business relationships with some of the world's leading multinational corporations, and expanding into international markets, including Italy, Ireland, the United Kingdom, Cyprus, and Qatar. For more information about UPMC, visit our website at www.upmc.com.

For more information about our clinical services or for assistance with patient referrals, please call UPMC MedCall at 412-647-7000 or 1-800-544-2500.