



REHAB PROGRESS



News from the UPMC Institute for Rehabilitation and Research

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From the Chairman's Desk

As we go to press with this issue of *Rehab Progress*, the University of Pittsburgh Medical Center (UPMC) Institute for Rehabilitation and Research (IRR) continues to exemplify excellence in rehabilitation medicine. Our clinicians provide the highest quality care for today's patients, while our academic excellence supports leading-edge research and training for the next generation of practitioners, scientists, and educators.

In this issue, we focus the spotlight on some of our exciting research initiatives in musculoskeletal disorders. We've recently recruited several young investigators, and initiated interdisciplinary collaborative efforts with others, whose careers show great promise for unlocking the biochemical secrets of conditions such as disc degeneration, muscular dystrophy, and skeletal-muscle trauma such as some injuries sustained in combat or during participation in high-intensity sports. The possibilities being studied include motion-based treatments and gene therapy for intervertebral disc degeneration, stem-cell-based interventions for Duchenne muscular dystrophy, and intramuscular pharmacotherapy for lacerations or contusions of muscle.

These investigations reflect the synergy of scholarship in different schools and diverse departments within the University of Pittsburgh, along with the individual and collective genius of the research teams to which they contribute. Our collaborative efforts rely on researchers from the University of Pittsburgh schools of Engineering, Health and Rehabilitation Sciences, and Medicine, and from the departments of Bioengineering, Rehabilitation Science and Technology, Molecular Genetics and Biochemistry, Neurobiology, Orthopaedic Surgery, and Physical Medicine and Rehabilitation — to name a few.

Our contribution at national and international meetings is a vital component of our academic mission. The IRR's visibility was apparent at the American Academy of Physical Medicine and Rehabilitation Annual Assembly last October in Philadelphia, headlined by Dr. Andrew Schwartz's keynote address, "Useful Signals from the Motor Cortex." A number of IRR faculty members were active participants in the Assembly, and I myself was honored to serve as co-chairman. We report here on recent scholarly publications by IRR researchers (Page 6), along with more presentations by our faculty and faculty awards (Page 8).

Lastly, I would like to invite you to our Department of Physical Medicine and Rehabilitation's grand rounds lecture series, *Panther Rounds*, which we are now web casting monthly at no cost on our Internet site. *Panther Rounds* offers high-quality continuing education — accessible at your fingertips, in the convenience of your home or office and on your own schedule. See and hear the presentations of internationally known guest lecturers, as well as young investigators from our own Department. The program is sponsored by the University of Pittsburgh School of Medicine Center for Continuing Education in the Health Sciences, the Department of Physical Medicine and Rehabilitation, and the Accreditation Council for Graduate Medical Education.

Be sure to visit us at www.rehabmedicine.pitt.edu, where you can access lectures from our archives and see the upcoming schedule. If you will be in Pittsburgh on the day of a scheduled lecture, I warmly invite you to be my guest for a live presentation of *Panther Rounds*. More details are available on Page 7 of this issue of *Rehab Progress*.

Sincerely,

Ross D. Zafonte, DO

Chairman

Department of Physical Medicine and Rehabilitation
University of Pittsburgh



**Best Hospitals
2005**

Mechanical strain on the intervertebral disc: A force for good?

Low back pain is one of the most frequently voiced complaints of adults seeking medical treatment. Clinical evidence and outcome studies document the benefits of motion-based therapy in treating low back pain. However, the mechanisms that effect those benefits are not clear.

The UPMC Institute for Rehabilitation and Research (IRR) recently began enlarging its efforts to tackle the problem of back pain, particularly pain caused by intervertebral disc degeneration.

IRR researcher Gwendolyn Sowa, MD, PhD, assistant professor of physical medicine and rehabilitation, is dissecting the problem at the molecular level. Her work is helping to show that mechanical force exerted on the disc can have beneficial effects, and to help determine the therapeutic window — forces of sufficient intensity to elicit a beneficial response, but not so extreme as to produce damage.

Understanding how mechanical forces translate into biochemical signals that regulate cell metabolism is important because traumatic force initiates a cascade of inflammatory mediators that activate catabolic processes and inhibit production of matrix structural molecules. Evidence suggests that inflammatory mediators play a key role in both breakdown of the matrix and generation of pain in patients with degenerative disc disease. For instance, inflammatory cytokines such as tumor necrosis factor alpha (TNF- α) are increased in degenerative disc tissue, as are the catabolic matrix metalloproteases, which are regulated by inflammatory cytokines.

However, there is also evidence suggesting that mechanical force exerts a beneficial effect. Compressive forces can produce anabolic effects within the disc by activating production of matrix structural proteins, and physiologic levels of hydrostatic pressure can stimulate production of proteoglycans and the metalloprotease inhibitors that slow degradation of the disc matrix.

Knowledge of the biochemical pathways — and the threshold for anabolic and catabolic responses — will be useful in designing appropriate motion-based strategies to manage discogenic pain and prevent injury.

Dr. Sowa sought to describe the pathways by which mechanical force affects expression of these early inflammatory mediators. She reported on her study, “Motion exerts a protective effect on intervertebral discs,” in an article that was awarded The Electrode Store’s “Best Presentation Paper” at the March 2006 annual meeting of the Association for Academic Physiatrists in Daytona Beach, Fla.

Dr. Sowa and co-investigator Sudha Agarwal, PhD, of Ohio State University compared the response to mechanical force of cells in a healthy environment to that of cells in an inflammatory environment mimicking disc disease. They assessed expression of marker genes that represent early mediators of the interleukin-1 β -induced inflammatory response (TNF- α and inducible nitric oxide synthase — iNOS), early mediators of matrix degradation (matrix metalloproteases MMP-3 and MMP-13), and structural genes (collagen I, collagen II, and aggrecan), in order to examine both anabolic and catabolic effects of mechanical forces. They hypothesized that these forces act on healthy and inflamed disc cells to produce molecular signals that regulate the early determinants of cell metabolism.

The researchers cultured fibrochondrocytes from the annulus fibrosis of rat intervertebral discs in monolayers on a flexible membrane in either: (1) a healthy environment (F12 medium with 10% fetal bovine serum) or (2) an inflammatory environment — supplemented with 1 ng/mL interleukin-1 β (IL-1 β). Cells were then exposed for four hours to cyclic (0.05 Hz) 6% tensile strain (by stretching the membrane) and compared to unstrained cells (See Diagram).

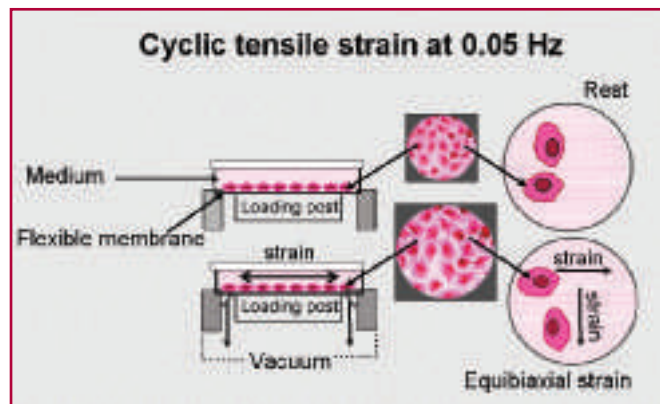
The investigators measured mRNA expression of iNOS, TNF- α , MMP-3, MMP-13, and structural genes collagen I, collagen II, and aggrecan. They found that cells in the inflammatory environment showed a large increase in expression of the catabolic and pro-inflammatory mediator genes iNOS, TNF- α , MMP-3, and MMP-13. But these levels dropped by approximately 50% when the cells were subjected to tensile strain for four hours. When cells in the healthy environment underwent the same tensile strain, there was no significant change in iNOS, TNF- α , or MMP-3 — although expression of MMP-13 was reduced by about 50%. Expression of the structural genes showed no significant change under any of the conditions tested.

Dr. Sowa’s work demonstrates that 6% tensile strain is not sufficient to stimulate an inflammatory response *in vitro*. Quite the opposite, in fact: Under conditions of inflammation, such as would accompany early disc degeneration or acute injury, the data demonstrate that physiologic levels of tensile strain actually act as a potent anti-inflammatory signal by decreasing the expression of pro-inflammatory mediators and degenerative proteases.

Drs. Sowa and Agarwal are the first to report the favorable effect of tensile force on intervertebral discs, and to demonstrate biochemical evidence for the beneficial effects of motion on the spine. The results of this work and future studies are expected to supply essential components for the rational design of therapeutic exercise, and to facilitate prediction of movements that might initiate degeneration and pain.

Dr. Sowa currently works closely with Lars G. Gilbertson, PhD, and James D. Kang, MD, of the University of Pittsburgh’s Ferguson Laboratory of Orthopaedic Research (see article on Page 3) to develop a model for investigation of the effects of compressive forces on the intervertebral disc, and to examine the mechanical thresholds of genetically altered disc cells.

Fibrochondrocytes grown in monolayer culture on a flexible membrane are subjected to cyclic tensile strain, 6% at 0.05Hz, via equibiaxial stretching of the membrane.



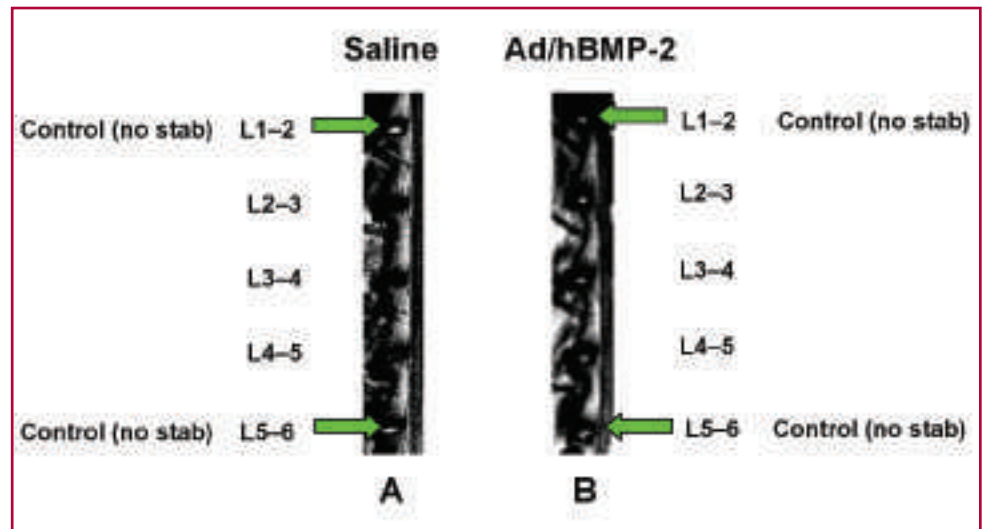
Transfer of growth factor gene mitigates disc degeneration in rabbit model

Although often asymptomatic, intervertebral disc degeneration can bring a patient to the physician with complaints of discogenic back pain, radiculopathy, or other disabling symptoms. For more than a decade, the Spine Research Group in the University of Pittsburgh Fergusson Laboratory for Orthopaedic Research has been studying the mechanics and biochemistry of the intervertebral disc. Evidence from recent studies — in the Fergusson Laboratory and elsewhere — suggests that gene-transfer strategies could be developed into a viable treatment option.

The pathophysiology of disc degeneration is only incompletely understood. Although multiple factors may contribute, depletion of proteoglycans in the nucleus pulposus of the disc seems to be a common pathway in degeneration. Disruption of the balance between anabolic and catabolic processes has been strongly implicated in reduction of disc proteoglycan content. Fergusson Laboratory director James D. Kang, MD, and co-director Lars G. Gilbertson, PhD, in collaboration with Paul D. Robbins, PhD, Department of Molecular Genetics and Biochemistry, are spearheading research of gene therapy to correct the metabolic imbalance. Gene therapy seeks to increase proteoglycan content by promoting pro-anabolic or anti-catabolic effects, or by a combination approach. Whereas direct intradiscal injection of exogenous growth factors has resulted in only transient effects, the Spine Research Group's research has demonstrated sustained, endogenous, transgene-directed proteoglycan synthesis following adenoviral-mediated transduction of disc cells.

Applications of gene transfer must be demonstrably safe and clinically effective. To facilitate this phase of inquiry, the Spine Research Group developed a reproducible animal model of slowly progressive disc degeneration. This model employs a shallow puncture of rabbit disc annulus (an annular "stab") using a hypodermic needle. The annular stab process was shown to produce a model similar to disc degeneration in imaging characteristics, as well as in histological and biochemical properties, including its under-expression of anabolic factors such as bone morphogenetic protein-2 (BMP-2).

The next step was to test gene therapy in this model. Dr. Gilbertson presented a relevant abstract to the European Cells & Materials group and the AO Spine Research Network (ECM IV/SRN) at their joint conference in July 2005 in Davos, Switzerland.



T2-weighted sagittal MRI of the lumbar spine of a rabbit from the saline-injected control group (A), and a rabbit from the Ad/hBMP-2 treatment group (B, injected with Ad/hBMP-2 by 30-ga. needle) — both 12 weeks after 16-ga. needle stab of discs L2-3, L3-4, and L4-5 to induce degeneration. Injection of saline or Ad/hBMP-2 was at 3 weeks post-stab. In both the saline group and the Ad/hBMP-2 group, L1-2 and L5-6 served as un-stabbed controls (arrows). Note that discs injected with Ad/hBMP-2 retained signal intensity better than those injected with saline.

In that study, "BMP-2 gene transfer alters course of disc degeneration in rabbit model," the investigators first induced disc degeneration in 13 rabbits by annular stab to three lumbar discs, leaving two lumbar discs intact in each animal to serve as controls. Degeneration was allowed to progress for three weeks, at which time the degenerating discs were injected either with adenoviral vectors carrying human BMP-2 (Ad/hBMP-2) (n = 8) or with saline-only as control (n = 5).

Progress was followed longitudinally, with mid-sagittal T2-weighted magnetic resonance imaging (MRI) at 3, 6, and 12 weeks post-stab, and with plain x-rays at 12 weeks. Additionally, nucleus pulposus was harvested at six weeks post-stab from three rabbits in the Ad/hBMP-2 group and two saline control-group animals and analyzed by ELISA for hBMP-2 synthesis. Levels of hBMP-2 were 72 ± 47 (pg/ml/mg) in the intact control discs, 34 ± 11 in the saline-injected controls, and 217 ± 124 in the Ad/hBMP-2-injected discs, showing robust transgene expression in the treated discs.

Analysis of the imaging studies is noteworthy. At 12 weeks following annular stab, the saline-injected control discs showed 49% loss in MRI index, compared to a 25% loss in the Ad/hBMP-2-treated group. The MRI findings are illustrated in the figure above. On x-ray, the researchers found no discernable differences between the treatment and the control groups as to disc height, osteophyte formation, or endplate sclerosis, and no obvious bony intervertebral fusion in either group.

The University of Pittsburgh Spine Research Group's study appears to be the first to show the ability of gene therapy to favorably alter the natural course of disc degeneration, as measured by clinically relevant MRI, in a reproducible animal model of the disorder.

"We have much more research ahead of us before we can contemplate clinical trials," Dr. Gilbertson says. "But the results so far should encourage more investigation of gene therapy as an approach to a very common and potentially disabling human problem."

Researchers join forces to solve problems of muscle injury, disease

The UPMC Institute for Rehabilitation and Research (IRR) has initiated a forward-looking translational research program to target musculoskeletal injury and disease. Some of the most prevalent causes of pain and disability are injuries and diseases of muscle. Examples include strains sustained during athletic activity, lacerations and contusions suffered in motor-vehicle accidents or armed combat, and devastating muscular diseases, especially Duchenne muscular dystrophy (DMD). Through multidisciplinary collaborations, IRR researchers are developing novel lines of therapy for these problems and exploring ways to usher them from the laboratory to the clinic.

The IRR recently recruited Fabrisia Ambrosio, PhD, MPT, as part of its research initiative in musculoskeletal disorders. She is working with renowned researcher Johnny Huard, PhD, director of Children's Hospital of Pittsburgh's Growth and Development Laboratory, one of the nation's premier programs in musculoskeletal research.

Dr. Ambrosio's research involves programs to facilitate moving some of the approaches that have shown promise in the Laboratory into pre-clinical and clinical trials. Her current efforts focus on stem-cell transplantation for DMD and intramuscular pharmacotherapy for muscle injury.

In 2005, researchers in the Growth and Development Laboratory isolated and identified a new line of postnatal ("adult") muscle-derived stem cells (MDSCs) with features once thought to be characteristic only of embryonic stem-cell lines. The postnatal MDSCs demonstrate several properties relevant to cellular therapeutics: multilineage plasticity; high replicative potential;

extended capacity for self-renewal; and a remarkable ability to regenerate myofibers when injected into skeletal muscle.

Dr. Huard and his colleagues are studying Duchenne muscular dystrophy using mdx mice, a murine model of the disease. DMD is a lethal, X-linked genetic disease characterized by profound and global muscle weakness caused by a lack of dystrophin expression in muscle fibers. Using a viral vector that the group engineered to carry the dystrophin gene, the researchers are using *ex vivo* transduction of MDSCs isolated from muscle biopsy. When the transduced MDSCs are re-injected in the dystrophin-deficient muscle of mdx mice, they generate myofibers that express dystrophin for up to 24 weeks. However, it is not yet known how well the muscle performs. Dr. Ambrosio, a licensed physical therapist whose background includes both a master of science in physiology-endocrinology and a doctorate in rehabilitation science and technology, is devising protocols to test the physiological response and force-generating ability of the regenerated muscle.

Clinical applications of MDSC transplantation are possible outcomes of this research. The potential benefits of cellular therapy for DMD are extraordinary, and the procedures are only minimally invasive. Autologous transplantation would entail a muscle biopsy, *ex vivo* expansion and viral transduction, and re-injection of transduced cells. This approach circumvents the problem of immune rejection of the MDSC graft, although the possibility remains of an immune response to the viral vector. Allogeneic MDSC transplantation

eliminates the vector, but it introduces the possibility of rejection of the donor cells, even though MDSCs appear to be somewhat immune-privileged. Research must settle these and many additional concerns before stem-cell therapy is ready for clinical trials.

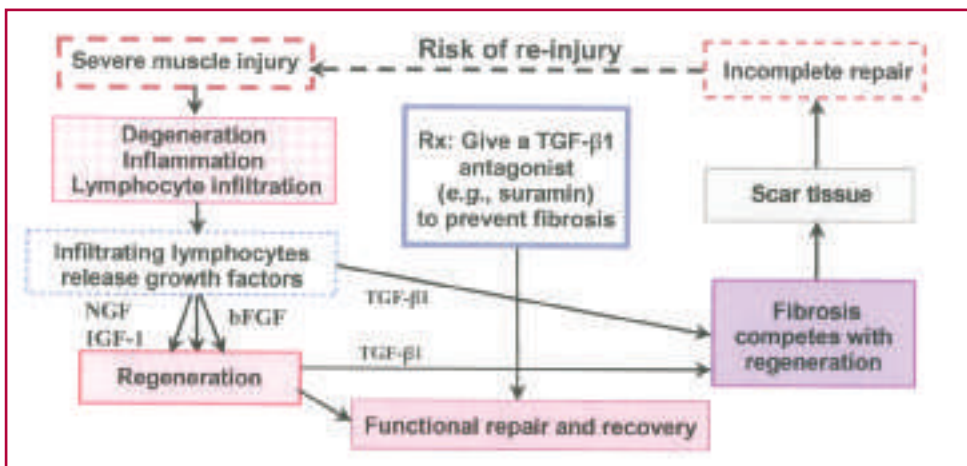
In another translational research project, Dr. Ambrosio is constructing protocols for preclinical functional assessment of muscle treated with an anti-fibrosis agent after injury.

Striated muscle can self-regenerate following injury, but concomitant fibrosis hinders the healing process. Administration of growth factors improves regeneration but cannot prevent fibrosis, which leads to scar tissue and incomplete repair, resulting in loss of muscle strength and a high risk of re-injury. Fibrosis is also a major contributor to the severe muscle weakness of Duchenne muscular dystrophy.

One of the primary mediators in the development of scar tissue following muscle injury is transforming growth factor beta 1 (TGF- β 1). Researchers in the Growth and Development Laboratory hypothesized that countering the effects of TGF- β 1 would result in improved healing (see Diagram). They have studied several TGF- β 1 antagonists, including decorin, suramin, and interferon-gamma (IFN- γ). The three work by different molecular mechanisms: Decorin combines directly with TGF- β 1; IFN- γ interferes with TGF- β 1 signal transduction, and suramin competes with TGF- β 1 receptors.

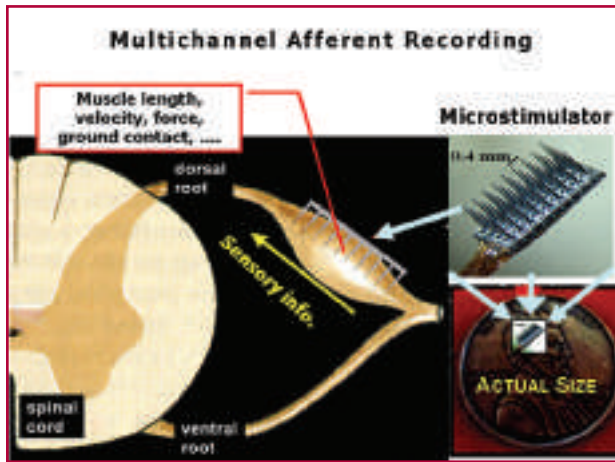
In animal models of muscle laceration, post-injury intramuscular (IM) injection of decorin resulted in improved structure and function compared to control (sham injection), and near-complete recovery of muscle strength. Injection of IFN- γ produces similar results. However, because IFN- γ treatment is associated with undesirable side effects, and decorin is not available for clinical use, Dr. Huard's group is investigating suramin, which is available; the agent is used clinically for its antiparasitic or antineoplastic properties. They studied suramin injection in a murine model of gastrocnemius laceration. Their findings suggest that suramin can prevent scar tissue formation, enhance muscle regeneration, and improve the functional recovery of lacerated muscle.

Dr. Ambrosio is formulating protocols for preclinical trials of IM suramin in a nonhuman primate model of muscle laceration. She will be designing procedures to measure outcomes such as the extent of physiological recovery and the functional response of treated muscle. Her studies will advance the goals of the Growth and Development Laboratory and the IRR to develop innovative therapies for musculoskeletal injury and disease.



Lymphocytes infiltrate the injury site, where they release cytokines, TGF- β 1, and other growth factors. TGF- β 1 is also released within the regenerating myofibers. Increasing TGF- β 1 levels prevent myogenic cells from regenerating skeletal muscle at the site of injury and promote fibrosis, which hinders regeneration. Overproduction of fibrous scar tissue leads to incomplete muscle repair, loss of muscle strength, and propensity for injury recurrence. TGF- β 1 antagonists can limit fibrosis and promote healing. **NGF** = nerve growth factor; **IGF-1** = insulin-like growth factor 1; **bFGF** = basic fibroblast growth factor.

Lab is nerve center for engineered movement and sensation



This diagram illustrates the sensory neural interface created by implanting an array of microelectrodes (top right) into the dorsal root ganglion (DRG, left). Somatosensory information flows through the DRG en route to the spinal cord. The microelectrodes detect the electrical activity associated with the flow of sensory information. Bottom right — Size of the microelectrode array relative to actual size of a US Lincoln penny.

Analysis of movement control at the neural and biomechanical levels is the foundation of the Rehab Neural Engineering Lab (RNEL) of UPMC's Department of Physical Medicine and Rehabilitation. RNEL is dedicated to the advance of rehabilitation science and practice through research and development of technologies for assisting and restoring motor function after nervous system injury or limb loss.

The laboratory is a state-of-the-art facility for studying the neurophysiology and biomechanics of walking and reaching. RNEL's 64-channel neural recording system captures single-unit activity data from large numbers of neurons simultaneously. This allows thorough inspection of activities within the neural networks responsible for transmitting and processing information related to perception and control of movement. Three-dimensional limb kinematics are measured with a six-camera motion-analysis system, and contact forces are measured with force/torque transducers. Kinematic and force data are used in mathematical models of the limb musculoskeleton, allowing estimation of individual muscles' specific contributions to the movements recorded. The combined data sets provide a comprehensive view of neural and mechanical processes and their interactions in the generation and control of limb movement.

Current investigations in the Rehab Neural Engineering Lab include studies in neural coding of sensory information; sensory and motor interfaces for control of prostheses (neuroprosthetics); and functional electrical stimulation.

RNEL director Doug Weber, PhD, collaborates with multidisciplinary teams of investigators representing the University of Pittsburgh; Case Western Reserve University; the University of Alberta; the University of Michigan; the University of Southern California; and Washington University. For more information about the Rehab Neural Engineering Lab, visit www.rnel.health.pitt.edu

Government grant funds neuroprosthetics research

Through its Defense Advanced Research Projects Agency (DARPA), the U.S. Department of Defense has awarded a \$1 million grant to neuroprosthetics researchers working with the UPMC Institute for Rehabilitation and Research (IRR) to develop the first neuro-integrated prosthetic limb.

IRR investigators Andrew B. Schwartz, PhD, and Douglas J. Weber, PhD, are developing technology that will allow persons with prosthetic limbs to control and sense the motion of their artificial limbs through electrodes implanted in brain and spinal nerves. Dr. Schwartz, University of Pittsburgh professor of neurobiology, bioengineering, and physical medicine and rehabilitation, has pioneered development of brain-computer-interface technology that uses electrical signals recorded in the brain to control the motion of a robotic arm. Dr. Weber, assistant professor of physical medicine and rehabilitation and bioengineering, has developed techniques for recording from nerves in the dorsal root ganglia (DRG) to extract sensory signals related to proprioception. By combining their techniques, Drs. Schwartz and Weber hope to develop a new generation of prosthetic devices that interface directly with the user's nervous system to restore natural, neural control and sensation of the artificial limb.

To date, no available technology can restore proprioception or haptic sensation in artificial limbs. Dr. Weber proposes that multichannel microstimulation of primary afferent neurons in the DRG would allow tactile sensation as well as perception of limb posture, movement, and force. The primary objective of his work under the DARPA grant is to develop a new technique using electrical stimulation of nerves in the DRG to send proprioceptive information to the nervous system. The principle is similar to that of the widely successful cochlear implant, which uses patterned electrical stimulation of auditory nerves to restore hearing to people with profound deafness.

Dr. Weber's group will electrically stimulate the DRG with microstimulation patterns set to mimic the natural sensory input that occurs during limb movement, which they have studied previously. The effectiveness of DRG microstimulation will be measured in the major proprioceptive region of the primary sensory cortex (S1). Microelectrode arrays will be used to record simultaneously from populations of neurons in S1 during periods of limb movement and periods of DRG microstimulation. The S1 response to DRG microstimulation will be compared to the S1 responses observed during movement. The stimulation-evoked responses in S1 should be similar to — but smaller than — those seen during movement, because of the

limited sensory input provided by microstimulation. However, by quantifying the similarity between the movement- and stimulation-evoked S1 responses, the investigators will learn the extent to which DRG microstimulation can send movement-related information to the primary sensory cortex.

The model being developed will provide a powerful new paradigm for designing, testing, and optimizing neural interfaces that can supply proprioceptive feedback to users of prosthetic limbs. Moreover, the experimental model can be adapted to explore neural interface solutions for other problems, such as loss of tactile sensation and proprioception caused by spinal cord injury.

"Revolutionizing Prosthetics," a program within DARPA's Defense Sciences Office, purposes to have a fully functional (motor and sensory) prosthetic upper limb ready for clinical trials within four years. Limb movement will be controlled by neural signals communicated directly from the brain via cortical implant. This much is already possible, as shown by Dr. Schwartz. More elaborate and refined neuroprosthetic movement will follow as more complex algorithms are developed. Tactile and proprioceptive capabilities developed through this and other projects will help amputees to live as normally as possible despite their injuries.

Recently published

Following is a sample of recently published scholarly works by IRR faculty researchers.

Refereed papers

Ambrosio F,* Boninger ML, Souza AL, Fitzgerald SG, Koontz AM, Cooper RA. Biomechanics and strength of manual wheelchair users. *J Spinal Cord Med.* 2005;58:407–14.

Boninger ML, Koontz AM, Sisto SA, Dyson-Hudson TA, Chang M, Price R, Cooper RA. Pushrim biomechanics and injury prevention in spinal cord injury: recommendations based on CULP-SCI investigations. *J Rehabil Res Dev.* 2005;42(3)(Suppl.1):9–20.

Chen X, Li Y, Kline AE, Dixon CE, Zafonte RD, Wagner AK. Gender and environmental effects on regional brain-derived neurotrophic factor expression after experimental traumatic brain injury. *Neuroscience.* 2005;135:11–7.

Chiaravalloti ND,* DeLuca J, Moore NB, Ricker JH. Treating learning impairments improves memory performance in multiple sclerosis: a randomized clinical trial. *Mult Scler.* 2005;11:58–68.

Chiaravalloti ND,* Hillary FG, Ricker JH, Christodoulou C, Kalnin AJ, et al. Cerebral activation patterns during working memory performance in multiple sclerosis using fMRI. *J Clin Exp Neuropsychol.* 2005;27:33–54.

Cohen LJ,* Fitzgerald SG, Lane S, Boninger ML. Development of the Seating and Mobility Script Concordance Test (SMSCT) for spinal cord injury: obtaining content validity evidence. *Assist Technol.* 2005;17:122–32.

Cooper RA, Ding D, Simpson R, Fitzgerald SG, Spaeth DM, Guo S, Koontz AM, Cooper R, Kim J, Boninger ML. Virtual reality applied to wheeled mobility: an overview of work in Pittsburgh. *Assist Technol.* 2005;17:159–70.

Dvorznak MJ,* Cooper RA, Boninger ML. Kinematic analysis for determination of bioequivalence of a modified hybrid III test dummy and a wheelchair user. *J Rehabil Res Dev.* 2005;42:343–52.

Wagner AK, Chen X, Kline AE, Li Y, Zafonte RD, Dixon CE. Gender and environmental enrichment impact dopamine transporter expression after experimental traumatic brain injury. *Exp Neurol.* 2005;195:475–83.

Wagner AK, Sokoloski JE, Ren D, Chen X, Khan AS, Zafonte RD, Michael AC, Dixon CE. Controlled cortical impact injury affects dopaminergic transmission in the rat striatum. *J Neurochem.* 2005;95:457–65.

Wilson MS, Chen X, Ma X, Ren D, Wagner AK, Reynolds IJ, Dixon CE. Synaptosomal dopamine uptake in rat striatum following controlled cortical impact. *J Neurosci Res.* 2005;80:85–91.

Wolf EJ, Pearlman J, Cooper RA, Fitzgerald SG, Kelleher AR, Collins DM, Boninger ML, Cooper R. Vibration exposure of individuals using wheelchairs over sidewalk surfaces. *Disabil Rehabil.* 2005;27:1443–9.

Abstracts and poster presentations

Arenth PA,* Ricker JH. Applications of functional near-infrared spectroscopy in neurorehabilitation. Proceedings of the 51st Annual Meeting of the Southwestern Psychological Association. 2005; 30.

Jenkins LW, Gao WM, Dixon CE, Kline AE, et al. The acute response of multiple serine-threonine kinases in a murine model of CCI using high-throughput immunoblotting. *J Neurotrauma.* 2005:251.

Majerske CW, Wagner AK, Collins MW, Ren D, Lovell MR. Concussion in sports: the effect of post-concussive exertion on symptoms and neurocognitive performance. Poster Grand Rounds, presented by Amy K Wagner, MD. AAPMR 66th Annual Assembly, October 2005, Philadelphia, Pa.

Malena R, Westergom B, Olsen A, Luthra P, Panda M, Dixon CE, Zafonte RD, Kline AE. Effects of early vs. delayed environmental enrichment on functional outcome after traumatic brain injury in adult male rats. *Soc Neurosci Abstr.* 2005, 334.8; and *J Neurotrauma.* 2005:183.

Matsuoka Y, Zafonte RD, Brewer B, Harrison T. Determining just-noticeable difference via robotic feedback: understanding perceptual gapping in TBI. Physiatric Association of Spine, Sports, and Occupational Rehabilitation 12th Annual Meeting, October 2005, Philadelphia, Pa.

Shomstein S,* Behrmann M, Ricker JH. Goal-directed attentional orienting in patients with dorsal parietal lesions. Vision Sciences Society 5th Annual Meeting. May 2005. Sarasota, Fla. [Abstract] *Vis Sci Soc Abstr.* 2005;5:195.

Westergom B, Malena R, Panda M, Olsen A, Luthra P, Dixon CE, Zafonte RD, Kline AE. The combination of a 5-HT_{1A} receptor agonist and environmental enrichment after TBI confers greater functional benefits than either treatment alone. *J Neurotrauma.* 2005:274.

Zafonte RD, White E, Elovic EP. Atypical antipsychotics: uses and concerns for persons with acquired brain injury. AAPMR 66th Annual Assembly, October 2005, Philadelphia, Pa.

*Author was a resident or fellow at time of publication.

Pitt and CMU display elder-assist technologies in Washington, DC

Researchers from the University of Pittsburgh and Carnegie Mellon University recently visited the nation's capital to demonstrate new technologies designed to maximize independence for older adults. The occasion was the Center for Aging Services Technologies (CAST) exhibition, held last December in conjunction with the White House Conference on Aging.

Among items in the Pitt/CMU display were Pearl the Nursebot — a robot that interacts with people in assisted-living facilities; Guido — a “smart” walker that provides navigation assistance and collision avoidance for people with impaired vision who use a mobility aid; CareMedia — a video-monitoring system designed to help detect physiological and behavioral changes in patients in skilled nursing facilities who suffer from dementia; SmartWheel — a wheelchair wheel that collects data as it is used, including stroke frequency and length and average force required for propulsion; GameCycle — a videogame console interfaced with arm-cycle controls, developed to promote fitness in people with lower-extremity impairment.

According to Rory A. Cooper, PhD, distinguished professor of rehabilitation science and technology and director of the University of Pittsburgh's Human Engineering Research Laboratories, these technologies will allow older adults to continue with a more active lifestyle and to maintain their independence for a longer period of time.

“This generation is more accustomed to adopting technology than previous generations,” he adds.

Jim Osborn, executive director of Carnegie Mellon University's Medical Robotics Technology Center, notes that Carnegie Mellon and the University of Pittsburgh have complementary programs in assistive technology.

“Our work unites people who focus on geriatric issues with those who focus on rehabilitation,” he says. “Our focus on enhancing the quality of life encompasses both.”

Representatives of 32 companies and research universities participated in the exhibition.



GameCycle™ encourages cardiovascular exercise in persons with impaired lower limb function. It interfaces with commercially available video games, the user controlling speed and direction with arm cranks. The GameCycle prototype was developed at the University of Pittsburgh Human Engineering Research Laboratories under a grant from the National Institute of Child Health and Human Development and is produced and distributed by Three Rivers Holdings of Mesa, Ariz., through a technology transfer partnership. Video demonstration of GameCycle is viewable at www.3rivers.com/gamecycle.php (Photo courtesy of Three Rivers Holdings, LLC.)

Panther Rounds debuts on-line

The Department of Physical Medicine and Rehabilitation's Grand Rounds lecture series, *Panther Rounds*, presents an exceptional opportunity to share information about the newest trends and outcomes in medical practice and research. Guest lecturers are internationally known and represent diverse agencies and institutions.

Technology allows us to archive and offer this informative monthly lecture series from the Department website at no cost. *Panther Rounds* is sponsored by the University of Pittsburgh School of Medicine Center for Continuing Education in the Health Sciences, the Department of Physical Medicine and Rehabilitation, and the Accreditation Council for Continuing Medical Education and is available to anyone interested in disability medicine and research.

A new lecture is available each month. In 2006, *Panther Rounds* topics have included:

- “Novel rehabilitative approaches for recovery from traumatic brain injury.” Anthony E. Kline, PhD, assistant professor of physical medicine and rehabilitation, UPMC Institute for Rehabilitation and Research; and associate director for rehabilitation research, Safar Center for Resuscitation Research, University of Pittsburgh School of Medicine. (Jan.)

- “Using high-resolution ultrasound and prolotherapy in clinical practice: Can we see soft tissues healing?” Bradley Fullerton, MD, medical director, Spasticity Clinic, Children's Hospital of Austin, Tex. (Feb.)

Upcoming programs are scheduled for April 26, May 10, June 14, July 19, Aug. 16, and Sept. 20. Those who are in Pittsburgh at the time of a *Panther Rounds* scheduled lecture are cordially invited to attend. The University of Pittsburgh designates each *Panther Rounds* web cast for a maximum 1.0 credit towards the American Medical Association Physicians Recognition Award. Registration is required for those who wish to obtain CME credit.

To view the program and apply for CME credit on-line, follow the instructions on the website: www.rehabmedicine.pitt.edu

Presenting: IRR researchers address colleagues

Faculty members of the UPMC Institute for Rehabilitation and Research remain active and visible at national and international meetings. Following is a sampling of topics of recent presentations.

Association of Academic Physiatrists

Annual Meeting

Daytona Beach, Fla.

March 1–4, 2006

Papers

Advancement in power wheelchair joystick technology: effects of isometric joysticks and signal conditioning on driving performance. Brad Dicianno, MD; Donald M. Spaeth, PhD; Rory A. Cooper, PhD; Shirley G. Fitzgerald, PhD; Michael L. Boninger, MD.

Motion exerts a protective effect on intervertebral discs. Gwendolyn A. Sowa, MD, PhD.

Course instruction

Residency Program and Fellowship Director Workshop: *Strategies to encourage and increase resident exposure to research.* Michael L. Boninger, MD.

New Technologies and their Application to Rehabilitation Research: *Genetic determinants of TBI recovery.* Amy K. Wagner, MD.

2nd Federal Interagency Conference on Traumatic Brain Injury: Integrating Models of Research and Service Delivery

Bethesda, Md.

March 9–11, 2006

Update on biotechnology for TBI rehabilitation. Ross D. Zafonte, DO

Gender and hormonal protective factors in TBI (workshop session). Amy K. Wagner, MD; Ross D. Zafonte, DO

The NIH TBI Clinical Trials Network: progress and promise (workshop session). Ross D. Zafonte, DO

Functional neuroimaging (workshop session). Joseph H. Ricker, PhD

Atomoxetine as a neurostimulant in severe TBI (poster presentation). Lisa A. Lombard, MD; Joseph H. Ricker, PhD; Ross D. Zafonte, DO

Perceptual gaps in robotic rehabilitation feedback (poster presentation). Yoky Matsuoka, PhD; Ross D. Zafonte, DO; Bambi Roberts-Brewer, PhD candidate; Christine Luciw-Harrison, BS.

Robotic rehabilitation of hand function after TBI (poster presentation). Yoky Matsuoka, PhD; Ross D. Zafonte, DO; Bambi Roberts-Brewer, PhD candidate; Christine Luciw-Harrison, BS

Needs assessment of persons with TBI and their families (poster presentation). Armando Rotondi, PhD; Jennifer Sinkule, BA; Michael Spring, PhD.

American Association of Neuromuscular & Electrodiagnostic Medicine

Michael C. Munin, MD, presented an invited lecture, *Laryngeal EMG Symposia: Current concepts and controversies*, at the AANEM Conference, September 21–24, 2005, in Monterey, Calif.

Medical Rehabilitation Research Training Workshop

National Center for Medical Rehabilitation Research (NCMRR)

National Institutes of Health, Rockville, Md.
Dec 5–6, 2005

What's Hot in Medical Rehabilitation Research

Quality of life technology — enhancing community participation. Rory A. Cooper, PhD

Motion exerts a protective effect on intervertebral discs. Gwendolyn A. Sowa, MD, PhD, and Sudha Agarwal, PhD (Ohio State University, Division of Oral Biology)

Anecdotes of survival and success. Gwendolyn A. Sowa, MD, PhD (panel participant).

IRR Faculty Awards

A report by **Gwendolyn A. Sowa, MD, PhD**, assistant professor of physical medicine and rehabilitation, has been named The Electrode Store's "Best Presentation Paper." The paper was presented at the Association for Academic Physiatrists Annual Meeting March 1–4, 2006 in Daytona Beach, Fla. Dr. Sowa's *in vitro* study, "Motion exerts a protective effect on intervertebral discs," seeks to describe the biochemical pathways by which mechanical force affects expression of early inflammatory mediators. The Electrode Store selects works based on their educational value in illustrating the research process, as well as for their intrinsic scientific merit.

Anthony E. Kline, PhD, assistant professor of physical medicine and rehabilitation and associate director of rehabilitation research at the University of Pittsburgh's Safar Center for Resuscitation Research, is the recipient of the American Academy of Physical Medicine and Rehabilitation President's Citation Award for his 2005 abstract, "Chronic risperidone treatment after experimental traumatic brain injury negatively impacts functional outcome."

AFFILIATE LINKS

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

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

School of Health and Rehabilitation Sciences, Department of Rehabilitation Science & Technology
www.shrs.pitt.edu/rst

Human Engineering Research Laboratories (HERL)
www.herlpitt.org

UPMC Center for Assistive Technology
www.cat.pitt.edu

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