You’re Each My Favorite

I remember my mom telling me that I was her favorite son. The constant competition between my two brothers and me made this a joyous, but short-lived moment. Just a little while later, I heard her say the same thing to my younger brother. I confronted her, and she responded, “You’re each my favorite; I love one son more than the next.” With two boys of my own, I now clearly understand the sentiment, and this issue of Rehab Progress further highlights the dilemma of choosing favorites.

Michael Munin, MD, the fantastic editor of this publication and a founding faculty member in the department, wanted to provide a broader overview of our departmental research. His idea: ask the researchers to pick their two favorite papers and explain their choice in just a few sentences. Unfortunately, he wouldn’t accept my answer that they were each my favorite. In the end it was fun thinking about it and having to choose, although I still feel like I shorted some great papers.

The end product is impressive. The department’s research spans from genes that predict depression to animal models showing the lasting impact of an enriched rehabilitation on recovery from traumatic brain injury. There’s the brain-computer interface work that enabled people with significant disability to control a robotic arm with just their thoughts and show the possibilities for better bladder control in neurologic disease. There’s mobile health, public health, health related to supplements, and don’t even ask me to get started about the work related to spinal cord injury (I have a natural bias here).

What’s more impressive is that when Dr. Munin and I were part of the founding group what seems like just a few years ago, none of these researchers were even out of training, let alone at the University of Pittsburgh. I hope you enjoy this read as much as I do — don’t ask Munin or me to pick our favorites.

Sincerely,

Michael L. Boninger, MD
Director, UPMC Rehabilitation Institute
Professor and UPMC Endowed Chair
Department of Physical Medicine and Rehabilitation
Department of Physical Medicine and Rehabilitation Research Faculty

Our team of physicians and scientists is dedicated to improving the lives of people with disabilities through advanced basic research, the development of new therapies, greater understanding of physical and cognitive impairments, and assistive technology. Key areas of departmental research include: musculoskeletal, spinal cord injury and brain-computer interface, and traumatic brain injury (see Figure 1). Each specialty area is an umbrella covering individual research projects that study biomarkers, pharmacotherapy, regenerative medicine, behavioral psychology, assistive technology, neural rehabilitation, and other areas of focus.

As seen in Figure 2, the National Institutes of Health (NIH) remains the largest source of grant support for our research efforts. In 2013 we received more than $10 million in awards for research and training grants, which was the largest grant funding year in department history.

We asked our researchers, as a way to introduce themselves to the physical medicine and rehabilitation (PM&R) community, to choose one or two published articles they are most proud of and discuss their importance in relation to the field of PM&R. For those who want more information, we have provided links to the articles for your convenience.
**Area of Research: Musculoskeletal**

Fabrisia Ambrosio, PhD, MPT, has gained international recognition for her work in regenerative rehabilitation. Her translational investigations using pre-clinical and clinical models implement molecular, cellular, and functional analyses to investigate the development of approaches to both harness the body’s natural healing capacity and enhance the functional efficacy of regenerative medicine technologies. A series of published research studies from the Ambrosio laboratory has demonstrated that the application of rehabilitation modalities, such as neuromuscular electrical stimulation or muscle loading, significantly enhances the transplantation efficiency of stem cells injected into acutely injured or diseased skeletal muscle.

**Key Articles by Dr. Ambrosio**


“The findings from these and other studies suggest that a combination approach of stem cell transplantation followed by rehabilitation enhances the engraftment efficiency of donor cells and, more importantly, may enhance skeletal muscle functional outcomes. We believe this is important because, as stem cell therapeutics increasingly make their way to clinical practice, careful attention should be paid to the design of rehabilitation protocols that will optimize the effect of these innovative technologies. Our goal is to improve patient outcomes through a synergy of regenerative medicine approaches with physical therapeutics.”

**Active Research**

- Electrical Stimulation Reverses the Effect of Age on Skeletal Muscle (NIH)
Area of Research: **Musculoskeletal** continued

Gwendolyn Sowa, MD, PhD, associate professor and assistant dean of medical student research, has won national and international recognition for her research in deciphering the biology of intervertebral disc degeneration (IDD) and the subsequent development of biological and biomechanical therapies guided by the basic science of the disease process. She currently performs molecular laboratory-based, translational, and clinical research, investigating the effect of motion on inflammatory pathways and the beneficial effects of exercise. Dr. Sowa is co-director of the Ferguson Laboratory for Orthopaedic and Spine Research, a 3,000-square-foot laboratory fully equipped to perform molecular assays, including gene expression analysis, protein analysis, cell and organ culture, histology, and cellular and spinal biomechanical testing.

**Key Articles by Dr. Sowa**


“We decided to use our readily available model systems in the lab to address a common question in the clinic, that is: ‘Is there any benefit of glucosamine for disc degeneration and low back pain?’ While clinical data exists regarding its use in osteoarthritis, little has been done to investigate the potential response of low back pain to this commonly used supplement. Anti-inflammatory effects of glucosamine were observed in vitro and were consistent with previous research in articular cartilage. However, both in vitro model systems and in vivo experiments demonstrated a detrimental effect of glucosamine on disc matrix. Although the degree to which glucosamine may accelerate degenerative changes in human intervertebral discs remains unknown, this study raises concern over the frequent and unregulated use of glucosamine. The glucosamine research is instructive when considering biologic therapies for intervertebral disc degeneration. Just because it is natural, it cannot be assumed that it is safe. In addition, it is likely that different contributions to disc degeneration, such as age, injury, and genetic predispositions, will require different therapies. Further development of biologically based biomarkers is likely to provide the information necessary to guide regenerative treatments as well as individualize existing treatments with patient specificity. It is hoped that such advances will improve quality of life and function in low back pain.”

**Active Research**

- Alternative Treatments for Disc Degenerations: Effects on Matrix Homeostasis (NIH)
- Identification of Novel Molecular Biomarkers With Improved Sensitivity and Specificity Over Imaging-Based Assessment for Low Back Pain (American Geriatrics Society)
- Identification of Biomarkers Predictive of Response to Spinal Injections (UPMC)
Area of Research: **Spinal Cord Injury**

**Michael Boninger, MD**, professor and endowed chair, is internationally known for his research in the areas of spinal cord injury and assistive technology. Dr. Boninger is the director and principal investigator of the University of Pittsburgh Model Center on Spinal Cord Injury, a National Institute for Disability and Rehabilitation Research Center of Excellence. He was inducted into the National Spinal Cord Injury Association Hall of Fame in 2006, and has won numerous awards, including the 2011 A. Estin Comarr Award from the Academy of Spinal Cord Professionals. Dr. Boninger was also inducted into the Institute of Medicine in 2012.

**Key Articles by Dr. Boninger**


“These two publications highlight the continued importance and shortcomings of wheelchairs — the most important technology we can provide to our patients. In one, we learn that the skill with which a wheelchair user can maneuver his or her chair correlates with quality of life. Unfortunately, too few wheelchair users have the skills needed to fully navigate the environment. In the second we learn of the alarming rate of wheelchair failures. Both studies point out where further work is needed related to this important technology, and in both cases we have ongoing studies that will help to solve these problems. Both papers have collaborators from outside the University of Pittsburgh, and I truly value these relationships. Finally, the first author on one paper was a resident and on the other a doctoral student in bioengineering. Teaching brilliant students such as these is the highlight of my job.”

**Active Research**

- Collaboration on Mobility Training (COMIT) (Department of Education)
- Center of Excellence on Wheelchairs and Associated Rehabilitation Engineering (Veterans Administration)
- Longitudinal Study of Acute and Chronic Arm Pathology Following SCI (Veterans Administration)

**Jennifer Collinger, PhD**, is assistant professor in the Department of Physical Medicine and Rehabilitation at the University of Pittsburgh and a Research Biomedical Engineer at the VA Rehabilitation Research and Development Center of Excellence. Dr. Collinger received her PhD in bioengineering from the University of Pittsburgh in April 2009. Dr. Collinger’s current research is related to neurorehabilitation and brain-computer interface technology for individuals with motor impairments due to spinal cord injury and disease.

**Key Articles by Dr. Collinger**


“These two publications focus on brain-computer interface (BCI) technology, which has great potential for translating intact brain activity to assistive devices in order to restore function for people with spinal cord injury. The first describes the primary outcomes of a clinical BCI study. We showed that after chronic paralysis, it is possible to extract detailed movement-related information from the brain in order to control a sophisticated robotic arm. The BCI enabled our participant to use the prosthetic arm to do skillful and coordinated reach and grasp ...”

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Jennifer Collinger, PhD  
continued from Page 5

movements that resulted in clinically significant gains in tests of upper limb function. This paper was the result of a large team effort including researchers, clinicians, our subject, and her family and caregivers, and it was a privilege to be part of such a great team. The Clinical Research Forum recognized this work as one of the top 10 clinical research achievements of 2012. We hope to replicate these results in future volunteers and begin translating this technology into the home environment, where it can be used to assist with activities of daily living. The second paper describes one step toward translation of this device. We surveyed veterans with spinal cord injury about their functional priorities and how a BCI could help with these needs. Restoration of upper limb function was a top priority for people with tetraplegia. The majority of participants in this study were interested in using a BCI, particularly for controlling functional electrical stimulation to restore lost function. Independent operation was considered to be the most important design criteria. Feedback from potential users is necessary for developing a meaningful product to restore function.”

Active Research

• Investigation of Cortical Changes Following SCI (Veterans Affairs)
• Intracortical BCI for Prosthetic Arm Control (Defense Advanced Research Projects Agency [DARPA])

Jennifer Collinger, PhD  
continued from Page 5

Brad Dicianno, MD, is associate professor in the Department of Physical Medicine and Rehabilitation and the associate medical director at the Human Engineering Research Laboratories. His research interests focus on developing and studying interventions, such as wheelchairs, adaptive sports, telemedicine, virtual reality, and preventive care programs, targeted at improving health and wellness in individuals with complex disabilities.

Key Articles by Dr. Dicianno

Outcomes of Clinicians, Caregivers, Family Members, and Adults with Spina Bifida Regarding Receptivity to Use of the iMHere mHealth Solution to Promote Wellness.
(http://telerehab.pitt.edu/ojs/index.php/Telerehab/article/view/6116)

iMHere: A Novel mHealth System for Supporting Self-Care in Management of Complex and Chronic Conditions.
(http://mhealth.jmir.org/2013/2/e10/)

“We are using telerehabilitation with the aim of improving self-management skills and medical outcomes in individuals with spina bifida. Individuals with spina bifida experience frequent and costly medical complications like urinary tract infections, wounds, and sepsis. These complications can in part be prevented with proactive wellness interventions. The two publications highlighted here demonstrate a novel system we have developed called iMHere, which is a dynamic, two-way communication system that can remind patients to perform self-care tasks and report problems, assist clinicians in quickly triaging a group of patients and intervening when problems arise, and promote patient-clinician communication in a fast and secure platform. Patients use smartphones equipped with a suite of apps and the clinician monitors a web-based portal. These papers describe the development and exciting results from our initial usability testing of the system. A full clinical trial is concluding and results will be available soon.”

Active Research

• iMHere: A Novel mHealth for Enhanced Wellness (Public Health Service)
• Rehabilitation Engineering Research Center on Telerehabilitation (Department of Education)
• National Spina Bifida Patient Registry — Clinic Demonstration Project (NIH)
Robert Gaunt, PhD, assistant professor, received his PhD in biomedical engineering at the University of Alberta (Edmonton, AB, Canada) in 2008 and completed his postdoctoral training at the University of Pittsburgh. Dr. Gaunt’s primary research interests are in the area of sensorimotor control and the development of neuroprosthetic devices. He has worked on creating methods to restore and improve bladder function using electrical stimulation of the spinal cord and peripheral nerves, and interfaces with the dorsal root ganglia to monitor natural sensory activity and generate artificial sensations. These technologies will enable advanced neuroprosthetic devices with sensory capabilities.

**Key Articles by Dr. Gaunt**


“Complications related to bladder control are significant medical and personal issues that affect many people, including almost everyone with a spinal cord injury. While some implanted stimulation devices have been used successfully to manage bladder function in people with spinal cord injuries, they have typically required additional surgical procedures that are undesirable. In the first paper, we demonstrate that electrical stimulation near the spinal cord can generate bladder contractions that may be useful for restoring bladder voiding. In the second paper, we demonstrate that a simple implantable device that contains no electronics can be used to eliminate contractions of the urethral sphincter, which commonly prevent efficient bladder voiding in people with spinal cord injuries. We hope that these technologies, along with others under development, will lead to the availability of devices that can restore normal bladder function without requiring invasive surgeries or compromising spared functions.”

**Active Research**

- Microstimulation of Pelvic and Pudendal Afferents to Restore Bladder Function (PM&R Pilot)
- Reliable Spinal Nerve Interfaces for Sensorimotor Neuroprostheses (Defense Advanced Research Projects Agency [DARPA])
- Revolutionizing Prosthetics (Defense Advanced Research Projects Agency [DARPA])
- Multichannel Microstimulation of Primary Afferent Neurons to Restore Proprioception (NIH)

Wei Wang, MD, PhD, is assistant professor and co-director of the human Rehabilitation and Neural Engineering Laboratory (hRNEL). Dr. Wang also holds secondary appointments with the Department of Bioengineering and the Clinical and Translational Sciences Institute (CTSI) at the University of Pittsburgh. Dr. Wang’s research is based on his previous investigations into how the brain controls arm and hand movement. He has developed various algorithms extracting multiple movement signals within cortical neurons that control state of the art neuroprosthetics. His investigations include brain-computer interface technology using various cortical recording techniques, with an emphasis on clinical brain-computer interface research in individuals with disabilities using electrocorticography (ECoG).

**Key Articles by Dr. Wang**


ECoG electrode location mapped to a 3D rendering of the participant’s brain. Red dots represent ECoG electrodes, and Electrodes 1 and 32 are labeled to indicate grid orientation. The black arrow indicates the central sulcus (CS) of the left hemisphere. ([PloS one. 2013 Jan;8(2):e55344](http://www.plosonline.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0055344))
"These two publications specifically highlight the current progress in using cortical surface recording (i.e., electrocorticography) to develop reliable brain-computer interface technologies for individuals with hand and arm paralysis. Cortical surface recording captures electrocorticographic (ECoG) signals that reflect local neuronal population activity. Neuroscientists have used ECoG to study various human cognitive functions, including speech and language functions, and clinicians have used ECoG to map patients’ pathological brain activity patterns for surgical treatment of epilepsy. We believe that ECoG technology offers a unique balance among various factors that are critical for a clinically viable brain interface device, such as high spatiotemporal resolution, long-term signal stability and reliability, and minimal impact to the underlying cortical tissue. Additionally, it is conceivable that ECoG technology can be further combined with other neural recording techniques, including intracortical microelectrode recordings and noninvasive scalp electroencephalography (EEG), for both research and development of future brain-computer interfaces."

**Active Research**
- Short-Term BCI Study in Individuals With Tetraplegia for Restoring Hand Function (Public Health Service)

**Martin Oudega, PhD**

Assistant professor and director of the Spinal Cord Repair Laboratory, is internationally recognized for his research on cellular and a-cellular transplants to reduce secondary injury (limit additional tissue loss), promote axonal regeneration, and increase motor and sensory outcome after injury. Dr. Oudega is a contributor and reviewer for more than 20 national and international journals, including *Journal of Neurotrauma*, *Experimental Neurology*, and *Neuroscience*.

**Key Articles by Dr. Oudega**


"These two papers highlight major research directions in my laboratory. In one paper, we show that the presence of a bone marrow stromal cell transplant in a spinal cord injury can be extended using an artificially made, degradable gel, and this leads to improved repair. Cell transplant survival is a major problem in transplantation-based repair approaches. This discovery has important consequences for the use of cell transplants for spinal cord repair and possibly other central nervous system disorders."

**Active Research**
- **Targeting Endogenous Inhibitors to Enhance Spinal Axon Regeneration After SCI (Public Health Service)**
- **Molecular Determinants Fundamental to Axon Regeneration After SCI (Department of Defense)**
- **Cell Based Strategies for Spinal Cord Repair (Industry)**
Monica Perez, PhD, assistant professor and director of the Human Motor Control Laboratory, examines how the brain and spinal cord contribute to the control of 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 transcranial magnetic (TMSCM) and electrical (TES) stimulation, and peripheral nerve stimulation techniques involving the hand and leg representation of the primary motor cortex. The overall goal of Dr. Perez’s studies is to develop strategies that can be used to maximize function of partially paralyzed muscles after spinal cord injury.

Key Articles by Dr. Perez


“The corticospinal tract is a major descending pathway contributing to the control of voluntary movements, and a prominent target for investigating injury-induced plasticity and motor recovery after spinal cord injury (SCI). I chose these two publications because both highlight the need to further understand the mechanisms involved in the control of the corticospinal pathway to promote motor recovery after SCI. Specifically, the first article shows that spike timing-dependent plasticity of residual corticospinal-motoneuronal synapses provides a mechanism to improve voluntary outcome and hand dexterity after chronic incomplete SCI. Using noninvasive brain and peripheral nerve stimulation techniques, we developed a tailored protocol for precise timing of the arrival of descending and peripheral volleys at corticospinal-motoneuronal synapses of hand muscles in individuals with SCI. The second article shows the presence of aberrant plasticity in corticospinal projections to muscles located far from the injury site. These findings support the view that corticospinal degeneration does not spread rostral to the lesion, and highlight the potential of caudal regions distant from an injury to facilitate residual corticospinal output after SCI. Overall, knowledge of plasticity at these levels may contribute to the understanding of mechanisms of recovery and provide novel targets for future therapeutic strategies aimed at enhancing the recovery of motor function after SCI and other motor disorders involving corticospinal tract function.”

Active Research

• Neural Control of Bilateral Hand and Arm Movements After SCI (NIH)
• Enhancement of Hand Motor Function After Cervical Spinal Cord Injury
Amy Wagner, MD, is tenured associate professor and endowed chair of Physical Medicine and Rehabilitation research. Dr. Wagner, principal investigator of the University of Pittsburgh TBI Model Center for Neurorehabilitation Education and Rehabilomics® Research, is investigating the impact of an individual's genetics and biomarkers on treatment and outcome after TBI, with the intention of laying solid groundwork for a “personalized medicine” approach to treatment. She has coined the term "rehabilomics" to define this relatively new field of study that involves the rehabilitation-relevant properties of biomarkers and biologics as related to function, prognosis, treatment, and recovery.

Key Articles by Dr. Wagner


“I chose these particular publications to illustrate both the translational aspect of our research and the importance of moving toward a personalized medicine approach to improve outcomes after TBI. We know TBI causes significant complications, including seizures, hypogonadism, and depression. Unfortunately, it is very difficult to predict who will experience these complications, because individuals with similar trauma, and comparable hospital and rehabilitative care, often display very different outcomes. Separate investigations by my lab have shown that genetic variants can serve as strong predictors of outcome and estimate biosusceptibility to complications after TBI in humans. Over the long term, the impact of these associations can be expanded, using experimental models and other approaches, to inform relevant mechanisms and treatment targets, as well as be used as a part of clinical decision algorithms and screening/prevention programs. We are very encouraged by our work to date, as we anticipate that our research program will further refine our understanding of the role genetics, biomarkers, and pharmacologic agents have in TBI, as well as provide an infrastructure and model from which future studies can build upon to effectively optimize recovery through personalized treatment of individuals with TBI.”

Active Research

- Biomarkers: Evaluating and Treating Acute and Chronic TBI (Department of Education)
- Rehabilomics: Revolutionizing 21st Century TBI Care and Research (Department of Education)
- Genomic Variability and Symptomatology After TBI (National Institutes of Health)
- Developing Cognitive Training and Rehabilitation Paradigms for Experimental TBI (National Institutes of Health)
- University of Pittsburgh Model Center of Traumatic Brain Injury (Department of Education)
Anthony E. Kline, PhD, associate professor, has been with the department since 2002, with a research focus on the effects of TBI on neurobehavioral pathways and recovery of motor and cognitive function. Dr. Kline’s laboratory at the Safar Center for Resuscitation Research (SCRR) utilizes a controlled cortical impact (CCI) injury model to produce motor and cognitive deficits in rodents mimicking those seen in human TBI patients. Therapeutic strategies such as pharmacotherapies, environmental enrichment, and their combination are subsequently provided in an attempt to restore function and/or reduce TBI-induced deficits.

Key Articles by Dr. Kline

(http://online.liebertpub.com/doi/pdfplus/10.1089/neu.2012.2560)

(http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2604904/)

“The selected papers encompass the two major research interests of my laboratory. The first highlights a translational approach and shows that the cognitive benefits we have found after exposure to environmental enrichment (EE) are long-term, meaning they remain intact long after rehabilitation has been withdrawn. This important finding suggests that enrichment is a relevant preclinical model of neurorehabilitation. The second study highlights another avenue of the laboratory, which is to identify currently used pharmacological approaches that may be deleterious to the recovery process after TBI. Antipsychotics (APDs) are provided after TBI to attenuate agitation, yet their effect on the recovering brain is not well understood. The paper by Hoffman et al., shows that daily administration of haloperidol or risperidone after TBI impairs the rats’ ability to learn a cognitive task. A paper in review shows that the deleterious effects persist even after a three-month washout period.”

Active Research

• Environmental Enrichment and Cholinergic Mechanisms After TBI (NIH)
• Understanding the Impact of Anti-Psychotic Drugs on Recovery After TBI (NIH)
Additional Clinical Research from the Department of Physical Medicine and Rehabilitation

Michael C. Munin, MD, is professor, vice chair of clinical program development, and medical director of the University of Pittsburgh EMG labs at UPMC Presbyterian and UPMC Shadyside. Dr. Munin is involved in industry-funded clinical research examining outcomes with botulinum toxin therapy and methods to improve localization of chemodenervation agents using ultrasound. He is an experienced clinician who has been cited by America’s Top Doctors and Castle Connelly’s Best Doctors listing for more than a decade.

Key Articles by Dr. Munin


“I am proud to have helped develop clinical techniques that will benefit patients. In the paper in *Muscle and Nerve*, we demonstrated that within a cohort of patients with cervical dystonia, ultrasound guidance for administering botulinum toxin injections eliminated clinical symptoms of dysphagia. In the paper in *Laryngoscope*, we highlighted our electrodiagnostic technique for measuring turns within the thyroarytenoid muscle. Turns reflect the number of motor units firing and their complexity. This technique is very easy for any electromyographer to perform and helps to quantify the degree of nerve impairment in recurrent laryngeal neuropathies. This data minimizes subjective interpretation that is problematic.”

**Active Research**

- Prospective, Double-Blind, Placebo-Controlled, Randomized, Multi-Center Study With an Open-Label Extension Period to Investigate the Efficacy and Safety of NT 201 in the Treatment of Post-Stroke Spasticity of the Upper Limb (Industry)
- Adult Spasticity International Registry on BOTOX® Treatment (ASPIRE) (Industry)

Amy Houtrow, MD, PhD, MPH, is associate professor and vice chair in the Department of Physical Medicine and Rehabilitation for Pediatric Rehabilitation Medicine. She also serves as director of the ACGME-accredited Pediatric Rehabilitation Fellowship, chief of Pediatric Rehabilitation Medicine, and medical director of the Rehabilitation Institute at Children’s Hospital of Pittsburgh of UPMC. Dr. Houtrow’s research focus is recognizing the impact raising children with disabilities has on families and developing channels to improve health care delivery. The goal of her research and clinical work is to maximize the health, function, and well-being of children with disabilities.

Key Articles by Dr. Houtrow


“The first article examines the outcomes studied in clinical trials that involve children. We highlight how infrequently outcomes that would be considered important to children and their families are included in research that could impact children’s health. We used the International Classification of Disability, Functioning and Health to categorize whether the outcome of each study was at the level of body functions and structures or at the level of activities and participation. We encourage pediatric research to attend to outcomes that are meaningful to children and families instead of focusing only on the biomedical outcomes. The second article describes inpatient care for children with spina bifida. This study highlights potential areas for advancing medical care for these children who experience high rates of hospitalization compared to other children. We also show that many children with spina bifida receive care in centers that may not have the same resources that one would expect at a children’s hospital. We support additional research to ensure that children with spina bifida receive optimal care.”

**Active Research**

- Management of Myelomeningocele Study 2: A Follow-Up of MOMS (NIH)
- Spina Bifida Registry Project (CDC)