NRC *newsletter*

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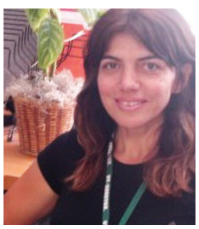
Functional Recovery of Upper Limb Movements After Spinal Cord Injury

By: Nuray Yozbatiran, Ph.D., P.T. and Gerard E. Francisco, M.D.



Yozbatiran

Francisco

Abstract: Regaining arm and hand functions after spinal cord injury (SCI) has been a major goal in persons with tetraplegia. Even small improvements in upper limb residual muscle strength and motor control can significantly alter their overall function and independency in daily activities. Although the traditional focus of rehabilitation has been the use of compensation and substitution for loss of function, more interest is growing into adapting principles of activity-based interventions in designing effective treatment protocols.

Incomplete tetraplegia is the most frequent neurologic category after spinal cord injury (SCI). Each year nearly 12,000 people suffer from SCI in the U.S, and about 50% of these are reported to be injuries at cervical lesions, representing mild to severe impairment in arm and hand functions. Over years, life expectancy after injury has increased, which has increased economic burden to meet individual needs of hospitalization, home and vehicle modifications, medications, supplies and personal assistance. The average health care and living expenses are directly associated with the level of injury, where high level tetraplegia (injury level between Cervical 1- Cervical 4) accounts for highest lifetime costs. While more than half of persons with SCI reported being employed at the time of injury only 12% of them could keep their employment status one year after injury.

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Techniques for Ensuring Active Engagement in Robotic Therapy of Upper Limb Function

By Marcia K. O'Malley, Ph.D.

O'Malley

Abstract: High intensity and high repetition upper limb movements are necessary for recovery of function following neurological injury, because such actions are capable of inducing brain and spinal plasticity. Robotic devices, such as the upper limb exoskeletons developed by my group (Figure 1), are uniquely suited for delivering such intensive, repetitive therapy. However, studies have shown that passively moving the limb through prescribed trajectories is not necessarily efficacious. In order to derive maximum benefit from robot-assisted rehabilitation, it is critical that the implemented control algorithms, that govern how the robotic device and the participant interact, promote the participant's active engagement in therapy. My research group at Rice University has been developing novel approaches for ensuring cognitive engagement of the patient during robotic rehabilitation of the upper limb following stroke or incomplete spinal cord injury. In this article I present several techniques that we have used, including: 1) the development of objective measures of motor impairment that can be used for frequent feedback to the therapist and patient regarding their progress; 2) robotic control architectures intended to promote engagement and intentful movements by the participant; and 3) the design and implementation of compliant robotic hardware systems that facilitate novel control approaches such as interaction control.

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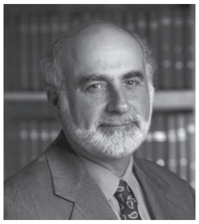
UTHealth | Neuroscience Research Center
The University of Texas Health Science Center at Houston

Director's Column

From the Director, John H. Byrne, Ph.D.



The 2013-2014 school year has proven to be another successful year of exciting events at the Neuroscience Research Center. Every fall, our Neurobiology of Disease Seminar Course educates medical and graduate students, postdoctoral fellows, residents and faculty on a current hot-topic in the field. This year was a little different as we focused on grand challenges in understanding the underlying mechanisms and future treatments of a variety of neurological diseases and disorders including: tumors, developmental and mood disorders, Alzheimer's disease, addiction, epilepsy, movement disorders, spinal cord and traumatic brain injury, and vascular diseases and stroke. In addition, diagnostic and therapeutic methods including neurological imaging and stem cell therapies were also discussed. UTHealth faculty lecturers gave a broad perspective, leading to interesting discussions on future opportunities in multiple areas. The course began with a special guest lecture from Dr. Tom Jacobs, the Assistant Vice Chancellor for Federal Relations from the University of Texas System, on the national perspective of neuroscience research in 2014.

The fall semester was filled with discussions of current research and future collaborations through two annual events. At the 2013 annual meeting of the Society for Neuroscience, held this year in San Diego, California, our largest group of current and former UTHealth neuroscientists met to discuss their work, what they had learned at the meeting, and future collaborations. In addition, the 20th annual Neuroscience Poster Session was our largest to date and included neuroscientists from the UTHealth NRC, Baylor College of Medicine Department of Neuroscience, and Rice University's Departments of Psychology, and Electrical and Computer Engineering

Discussion of research collaborations continued as the NRC hosted Dr. Huda Zoghbi as our 2014 Distinguished Lecture in the Neurosciences on March 27th. Since 1992, this annual event has brought internationally renowned scientists to Houston to deliver a lecture on their work. Fortunate for us, our esteemed guest is located across the street at Baylor College of Medicine. Dr. Zoghbi is also an Investigator at the Howard Hughes Medical Institute and Director of the Jan and Dan Duncan Neurological Research Institute at Texas Children's Hospital. Her lecture on "Genetic and Neurobiological Approaches to Neuropsychiatric Disorders" was very well attended and many UTHealth faculty had the opportunity to meet with her throughout her visit to the Center.

In conjunction with international Brain Awareness Week, Brain Night for Kids was held at The Health Museum on March 20th. We had a wonderful turnout from local families and school children this year. Our volunteer base was exceptional and included faculty and students from multiple institutions and programs this year including the UTHealth NRC, Neuroscience Graduate Program, Postdoctoral Fellow Association, as well as students from Rice University. Dr. Francie Baxter and student volunteers from Texas Woman's University led an educational, interactive booth teaching children what it would be like to lose basic abilities. In addition, Dr. Summer Ott and her team from the Memorial Hermann Ironman Sports Medicine Institute Concussion Program taught children the importance of wearing a helmet during a bicycle safety demonstration involving an egg-drop. Other activities included building a neuron out of pipe-cleaners, learning about the Stroop Effect, holding a real human brain and receiving a neurological exam from UTHealth's Dr. Pedro Mancias and his medical student volunteers.

A particularly exciting program this year was our annual Public Forum, which was held on Saturday, April 5th. This year's topic was MS Update: Advances in Diagnosis and Management of Multiple Sclerosis. Dr. Jerry Wolinsky, Director of the Multiple Sclerosis Research Group at UTHealth, and interim Chair of the Department of Neurology, co-moderated this educational program with his patient and multi-platinum recording artist, Clay Walker. After being diagnosed with MS, Mr. Walker created the "Band Against MS" foundation in 2003.

This organization provides educational information, MS research funding, and funding programs helping those living with the disease. The two led an all-star panel of UTHealth faculty from the MS Research Group: Drs. John Lincoln and John William Lindsey. Dr. Flavia Nelson, also part of this group and Associate Director of the MRI Analysis Center, as well as Dr. Nneka Ifejika, Director of Neurorehabilitation, also served as panelists at the Public Forum.

The MS Research Group was founded in 1983 by Dr. Wolinsky, and is a collaboration between the Mischer Neuroscience Institute at Memorial Hermann-Texas Medical Center and the UTHealth Medical School. This research group focuses on fundamental and applied research approaches in neuroimmunology and advanced MRI to better understand the pathogenesis and treatment of MS and has participated in over 25 clinical trials of new potential therapeutics to treat this disease. Indeed many of the trials performed through this research group were critical in the development of current FDA treatments for MS. Researchers within the group focus on innovative treatments of MS, including oral protein medications; identifying causes of MS, including possible MS-inducing infections; use of MRI to better understand the progression of MS; and MS-related cognitive impairment.

We are looking forward to the development of another successful year of educational neuroscience programs and events in the 2014-2015 academic year, and hope you will share in our efforts to promote research, education and public awareness in the neurosciences.

Distinguished Lecture in the Neurosciences

Huda Zoghbi and John Byrne prior to the Distinguished lecture in the Neurosciences.

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Grants & Awards

Congratulations to NRC Members:

Staley A. Brod. M.D., Professor of Neurology, was awarded a grant for a pilot clinical trial for the treatment of MS exacerbations.

John H. Byrne, Ph.D., Professor and Chair of Neurobiology and Anatomy, was honored for his excellence in teaching and received this year's UTHealth President's Scholar Awards for Teaching.

Pauline Filipek, M.D., Professor and Director of The Autism Center at the Children's Learning Institute, was awarded the Act Early Texas! Texas State Planning Grant (SPG) to develop a comprehensive, measurable State plan that will outline an approach to improve access to comprehensive, coordinated health care/ related services for children and youth with ASD/DDs.

Gerard Francisco, M.D., Chairman and Clinical Professor of Physical Medicine and Rehabilitation, **Georgene W. Hergenroeder, R.N., M.H.A., CCRC,** Assistant Professor of Neurosurgery, and **John Redell, Ph.D.,** Assistant Professor of Neurobiology and Anatomy, received The Center for Clinical and Translational Sciences (CCTS), Translational Technologies Core Laboratories Award to study proteomic analysis to identify biomarkers for neuropathic pain.

Ines Moreno Gonzales, Ph.D., Assistant Professor of Neurology, received The Alzheimer's Association New Investigator Research Grant (NIRG) for induction of Alzheimer's disease pathology by animal consumption.

Khader M. Hasan, Ph.D., Associate Professor of Diagnostic and Interventional Imaging, was awarded a grant from NASA to examine the association of diffusion tensor imaging parameters of optic tracts and cerebral white matter tracts with visual impairment and structural changes of the eyes and optic nerves in long-duration microgravity exposure.

Rodrigo Hasbun, M.D., M.P.H., Associate Professor of Internal Medicine, Infectious Diseases, was awarded a grant for the Texas NeuroAIDS Brain Bank study, part of the National NeuroAIDS Tissue Consortium's efforts to collect and distribute critical clinical data and tissue specimens from longitudinally tracked HIV-infected individuals at high risk for HIV-associated neurocognitive disorders.

Georgene W. Hergenroeder, R.N., M.H.A., CCRC, received the Texas Department of State Health Services SHS Transition Training Grant.

Georgene W. Hergenroeder, R.N., M.H.A., CCRC, and **Dong H. Kim, M.D.**, Professor and Chair of Neurosurgery and Director of the Mischer Neuroscience Institute, received funding from The Vivian L. Smith Foundation with support in kind from Zoll for the hypothermia for patients requiring evacuation of subdural hematoma.

Hongzhen Hu, Ph.D., Assistant Professor of Integrative Biology and Pharmacology, received a NIH/NIGMS grant to study the mechanisms of zinc regulation of pain-initiating TRP channels.

Hongzhen Hu, Ph.D., and **Raymond J. Grill, Ph.D.,** Associate Professor of Integrative Biology and Pharmacology, received funding from the TIRR Foundation/Mission Connect to study the targeting the TRPV4 channel to suppress cellular inflammation and improve locomotor and gastrointestinal motility dysfunction in spinal cord injury.

Susan H. Landry, Ph.D., Director of the Children's Learning Institute, was awarded two grants from the Institute of Education Sciences and the National Center for Education Research that will fund projects to compare the effectiveness of different instructional approaches and learning environments in order to improve the school readiness skills of at-risk preschool children.

Min Li, Ph.D., Associate Professor of Neurosurgery, received a grant from the Dr. Marnie Rose Foundation to identify new markers and therapeutic targets in brain tumors.

Roberta B. Ness, M.D., Dean of the School of Public Heath, received a grant from the Cancer Prevention Research Institute of Texas (CPRIT) to continue an innovative training program for cancer prevention researchers.

Hope Northrup, M.D., Professor and Director of the Division of Medical Genetics in the Department of Pediatrics, has recently received two NIH renewal grants for the study of tuberous sclerosis complex (TSC), a grant from the Tuberous Sclerosis Alliance, a renewed award from the Department of Defense Tuberous Sclerosis Research Program, and two awards from the Texas Department of State Health Services, as well as funding for two trials from the Biomarin Pharmaceutical Inc.

Grants & Awards

John O'Brien, Ph.D., Professor and Frederic B. Asche Chair of Ophthalmology and Visual Science, along with Alberto Pereda (Albert Einstein College of Medicine), received a grant from the NIDS for the generation of transgenic zebrafish to study electrical synaptic transmission.

Dawnelle Schatte, M.D., Assistant Professor of Psychiatry and Behavioral Sciences, is this year's winner of the John H. Freeman Award for Faculty Teaching.

Jair C. Soares, M.D., Professor and Chair of Psychiatry and Behavioral Sciences, received a grant from NIMH, "Searching for Endophenotypes of Bipolar Disorder," to examine the role of heritability on key brain abnormalities involved in causation of bipolar disorder.

Andrey Tsvetkov, Ph.D., Assistant Professor of Neurobiology and Anatomy, received an award from the Hereditary Disease Foundation to examine sphingosine kinase 1 as a therapeutic target in Huntington's Disease.

Kartik Venkatachalam, Ph.D., Assistant Professor of Integrative Biology and Pharmacology, received a NIH research grant to examine alterations in synaptic growth and lipid-raft organization in a fly mliv model.

JiaQian Wu, Ph.D., Assistant Professor of Neurosurgery, received a grant from the TIRR Foundation/Mission Connect to find therapeutic targets for chronic SCI using rat contusive injury model.

JiaQian Wu, Ph.D., Assistant Professor of Neurosurgery, and **Ying Liu, MD., PhD.,** Assistant Professor of Neurosurgery, received funding from the UTHealth Bentsen Stroke Center Investigator Program to identify therapeutic targets to increase neuronal differentiation efficiency of hiPSC-derived NSCs in treating stroke.

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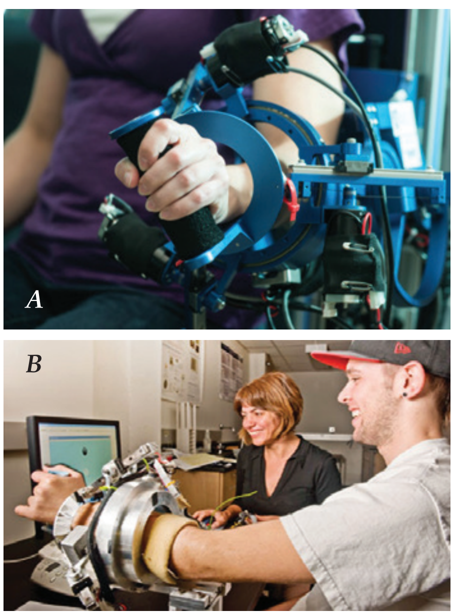

Figure 1. A, *The MAHI Exo-II, an upper limb exoskeleton robot, developed at Rice University, for rehabilitation after neurological injury.* ***B****, The upper limb robotic exoskeleton engages, both cognitively and physically, the individual in their therapeutic protocols.*

The development of objective measures of motor impairment.

In our early collaborations with UT's Department of Physical Medicine and Rehabilitation, we analyzed the correlations between four clinical measures (Fugl–Meyer (FM) upper extremity scale, Motor Activity Log, Action Research Arm Test (ARAT), and Jebsen-Taylor Hand Function Test (JTHFT)) (published by Celik et al. (2010) in IEEE Transactions on Neural Systems and Rehabilitation Engineering). The Fugl-Meyer upper extremity motor function assessment evaluates and measures recovery in post-stroke hemiplegic patients by assessing the ability of the individual to perform a variety of specified movements. The Motor Activity Log is a structured interview intended to examine how much and how well the subject uses their more-affected arm outside of the laboratory setting. The ARAT assesses upper limb functioning using observational methods. Finally, the JTHFT is a timed assessment of a broad range of unimanual hand functions required for activities of daily living (ADLs). We also selected four robotic measures (smoothness of movement, trajectory error, average number of target hits per minute, and mean tangential speed) to assess motor recovery. Data were gathered as part of a hybrid robotic and traditional upper extremity rehabilitation program for nine stroke patients. Smoothness of movement and trajectory error, quantitative measures of movement quality defined for point-to-point movements, were found to have significant moderate to strong correlations with all four of the clinical measures, and most strongly correlate to FM and ARAT, which are clinical measures focused on objective assessment of the degree of impairment due to neurological injury. The strong correlations suggest that smoothness of movement and trajectory error may be used to compare outcomes of different rehabilitation protocols and devices effectively, provide improved resolution for tracking patient progress compared to only pre- and post-treatment measurements, enable accurate adaptation of therapy based on patient progress, and deliver immediate and useful feedback to the patient and therapist.

Robotic control architectures.
More recently, we have focused on the development of novel control algorithms

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20th Annual Neuroscience Poster Session

Drs. Jack Byrne, Dora Angelaki and Behnaam Aazhang.

Graduate student and postdoctoral winners
(Students from left to right): Denise Harvey, Tammy Szu-Yu Ho, Deepna Devkar, Alexander Herman, Stuart Red, Demet Gurler, Ph.D., Juan Diego Pita-Almenar, Ph.D., Richard Dewell, Ph.D., Samantha Summerson, Curtis Neveu. *(Not pictured: Wei Huang)*

Saturday, December 7, 2013
UTHealth Cooley University Life Center

The UTHealth NRC was pleased to organize and co-host the 20th Annual Neuroscience Poster Session with Baylor College of Medicine (BCM) Department of Neuroscience, and Rice University Departments of Psychology and Electrical and Computer Engineering. This was our largest poster session to date with seventy-nine posters presented from faculty, research scientists, graduate and medical students from all three institutions.

Graduate Student Awards:
UTHealth Graduate School of Biomedical Sciences 1st Place:
The Dee S. and Patricia Osborne Endowed Scholarship in the Neurosciences: Deepna Devkar

Rice University Gertrude Maurin Cognitive Neuroscience Research Award: Denise Harvey

Rice University Department of Electrical and Computer Engineering Award: Samantha Summerson

Baylor College of Medicine Award from the Department of Neuroscience: Alexander Herman

Overall 2nd Place Prizes:
Wei Huang (BCM) and Tammy Szu-Yu Ho (BCM)

Overall 3rd Place Prizes:
Curtis Neveu (UTHealth) and Stuart Red (UTHealth)

Postdoctoral Fellow Awards
1st Place: Juan Diego Pita-Almenar (UTHealth)

2nd Place: Demet Gurler (UTHealth)

3rd Place: Richard Dewell (BCM)

Group shot of faculty judges from all three institutions.

Group shot of poster presenters from all three institutions.

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that govern how the robot and participant interact during robot-assisted upper limb therapy (published by Pehlivan et al. in the 2013 Proceedings of the IEEE International Conference on Rehabilitation Robotics). A class of controllers named "assist-as-needed" addresses the requirement of promoting active engagement by providing only app ropriate assistance during movement execution. Often, these controllers depend on the definition of an optimal movement profile, against which the participant's movements are compared. We have proposed an assist-as-needed controller that introduces a novel feedback gain modification algorithm, making the controller adaptive. By modifying the gains of the feedback part of the adaptive controller directly, we are able to change the action of the adaptive controller based on the amount of error that is allowed during movement execution, while simultaneously estimating the forces provided by the participant that contribute to movement execution. We have also implemented a real-time trajectory generation algorithm based on a physiologically optimal and experimentally validated asymmetric wrist movement profile. The feedback gain modification and trajectory generation algorithms have been experimentally validated with our custom RiceWrist robotic rehabilitation system, with the modified assist-as-needed adaptive controller decreasing its feedback control action when a subject shifts his behavior from passively riding along with the robot during movement to actively engaging and initiating movements to the desired on-screen targets.

Design and implementation of compliant robotic hardware systems.

Although we can control a robot to interact with the participant in a variety of ways, there are advantages to altering the robot hardware to include physical compliance, rather than relying on the software alone to modify the robot behavior. Specifically, in Sergi et al. (2013) published in the 2013 Proceedings of the IEEE International Conference on Rehabilitation Robotics, we have proposed the inclusion of physical compliance in our robotic hardware in order to enable implementation of interaction control techniques. In the rehabilitation scenario, such control schemes assist motion by applying variable levels of mechanical assistance, with the capability of adapting to and capitalizing on the residual contributions of the subjects. Moreover, evidence from human trials with stroke subjects (published in the Journal of Rehabilitation Research and Development (2006) by Hogan et al.), and from preliminary studies on animal models of spinal cord injury (SCI) (published in Science (2012) by R. van den Brand et al.) confirms the hypothesis that interaction control schemes are more capable of promoting neuronal plasticity through mechanical interaction compared to motion control. In force-feedback interaction control, the force of interaction between the robot and the environment is measured and fed back to the controller driving the actuators, which specifies new desired force or position/velocity commands. In a Series Elastic Actuation (SEA) architecture presented by D. W. Robinson and M. M. Williamson in their MIT PhD theses (2000 and 1995 respectively), compliant elements with deflection/force measurement capabilities are intentionally introduced in series between the actuator and the load. This design choice separates the dynamic effects of some of the mechanical components of the robot from the human operator, and also enables implementation of force-feedback control laws. The introduction of physical compliance with well-known properties enables the deployment of accurate interaction control schemes, thus mimicking the traditional therapist-based physical therapy, essentially based on the adaptive and compliant transfer of support forces. In Gupta et al. (2008), published in The International Journal of Robotics Research, we have developed a prototype version of our RiceWrist robotic device which incorporates series elasticity, and will be clinically evaluating its performance in the near future.

The overarching goals of our research are to motivate the participant to remain cognitively and physically engaged during the course of their robotic upper limb therapy in order to facilitate maximum recovery of movement coordination. This article has summarized a number of techniques that address these goals. As one approach, we leverage the sensors on the robotic device to compute performance measures that track participant performance throughout therapy and provide frequent feedback to the therapist and the individual as a means of motivating their engaged participation in therapy. Another strategy is to implement novel hardware design and control architectures enabling active physical interaction between patient and robot. It is anticipated that these approaches will maximize the therapeutic benefit of robotic rehabilitation of the upper limb after neurological injury.

About the Author

Marcia O'Malley is an Associate Professor of Mechanical Engineering at Rice University where she directs the Mechatronics and Haptic Interfaces Lab. She holds a joint appointment in Computer Science at Rice, and is an Adjunct Associate Professor in the Departments of Physical Medicine and Rehabilitation at both Baylor College of Medicine and the University of Texas Medical School at Houston. In addition, she is the Director of Rehabilitation Engineering at TIRR-Memorial Hermann Hospital, and is a co-founder of Houston Medical Robotics, Inc. Her research addresses issues that arise when humans physically interact with robotic systems, with a focus on training and rehabilitation for the upper extremity in virtual environments.

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Arm and hand functions are one of the major determinants of independency in daily activities such as self-care, feeding, transferring from bed to chair or from chair to car, and work related activities. Despite extensive pre-clinical and clinical research and advancements in rehabilitation strategies, there is still no 'cure' identified for SCI and it therefore still continues to be a major cause of long-term disability. Given the fact that the majority of SCI individuals are in their most productive years of age with a life expectancy nearly approaching those of the healthy population, more aggressive treatment strategies focusing on improvement of peripheral muscle control and functions as well as recovery of central nervous system (CNS) are needed. More than half of the population with tetraplegia indicated that regaining arm and hand function would most improve their quality of life. In fact, small improvements in upper-extremity strength can make a clinically significant difference in daily activities. For example, strength of the wrist extensor muscles has a significant impact on hand function in people with C6 injuries (tenodesis effect). Despite this evidence there is a great deal of technology and focus on improving leg strength and retraining gait after SCI and not on upper extremity strength and function. Furthermore, little research has been directed at understanding and optimizing interventions of the upper extremity when compared to gait training.

Neuroplasticity of Central Nerve System

Since the work by Santiago Ramon y Cajal in 1928, the common assumption has been that the CNS is hard-wired, which means incapable of modification anatomically and incapable of repairing itself. To some extent this assumption might have affected the approach of rehabilitation specialists in designing treatment protocols so that education of compensation techniques to regain independency in daily activities, such as using assistive devices to accomplish eating, dressing and transfers, have been emphasized over more aggressive treatment strategies. However, over the last three decades the view of the CNS has undergone fundamental change. Numerous studies from basic science provide evidence that the brain is capable of producing new nerve cells and these neurons are interconnected with existing nerve cells. Even following injury or in the course of neurodegenerative diseases the brain and spinal cord have the physiological ability to reorganize synaptic connections.

Therefore, understanding brain and spinal cord plasticity will provide a basis for developing better treatment interventions to facilitate return of functions after injury. In fact, evidence from animal studies were successfully translated into clinical practice of interventions to promote recovery of walking in humans. One example for this type of plasticity is coming from basic science studies where cats with complete spinal transections respond to intense walking training in the absence of supraspinal input.

Upper Limb Interventions after SCI

Studies on motor recovery of arm and hand functions after SCI are relatively limited and generally focused on functional electrical stimulation, exercise, neuroprosthesis, Botulinum toxin injections, biofeedback or surgical interventions such as tendon transfers. In the last decade introduction of robotic devices into rehabilitation, has enabled semi-automated or automated high-intensity repetitive therapy, which otherwise would be quite labor-intensive (See accompanying article; Takahashi et al. 2008 *Brain*; Kutner et al. 2010 *Phys Ther;* Volpe et al. 2008 *Neurorehabil Neural Repair*).

Optimization of treatment protocols should not only focus on questions such as 'context' and 'when' but also on 'how much'. Recent work in neuroscience demonstrate that treatment intensity has a profound effect on motor recovery and even years after a neurological injury, neuroplasticity of the adult brain can be impacted by experience (activity)-dependent principles. Interestingly, studies that have found that robotic-assisted therapy, in addition to traditional physical and/or occupational therapy, can improve motor recovery. Robotic devices which are safe and feasible in rehabilitation have been used primarily in stroke rehabilitation (see accompanying article). To date, only a few research centers have either studied the effect of upper limb robotic-training after SCI or emphasized the importance in their reports, but no controlled clinical trial has been published so far. Bringing robotics into rehabilitation will provide additional advantages such as quantified assessment and monitoring of motor functions, brining therapy to different venues including the home, and increasing therapy efficiency with the possibility of group therapy. On the other hand, activity-based intervention in SCI rehabilitation provides constant facilitation to CNS through intense, repetitive and rhythmical activities. Robotic-assisted training or in the form of constraint-induced movement therapy are using similar principles. Evidence based randomized clinical trials are needed to promote recovery of upper limb movements within the context of facilitating neural networks at spinal and supraspinal level and thereby inducing intrinsic recovery mechanism and improving functions.

Preliminary results

Over the past five years, our laboratory has been studying the robotic-assisted combined treatment protocols in recovery of upper limb motor functions after stroke and SCI. In a recently completed project, we used MAHI Exo-II (from Dr.O'Malley's MAHI lab at Rice University) to study feasibility, safety and efficacy of robotic-assisted training of arm and hand movements in persons with incomplete SCI. The subjects have completed 12 sessions of robotic training over a course of four weeks and were tested at baseline, after treatment, and at six months for reporting changes in motor functions, and independency in daily living activities. Earlier work from this project has been published in the *Journal of Rehabilitation Medcine* (2012) by Yozbatiran et al., where a 28-year-old woman, 29 months after an incomplete SCI at the C2 level, classified as American Spinal Injury Impairment Scale C (AIS), received robotic-assisted training, based on her baseline motor abilities, either in constraint, triggered or passive modes. The number of repetitions and amount of resistance for each single-of-degree of movement at elbow, forearm and wrist, were gradu-

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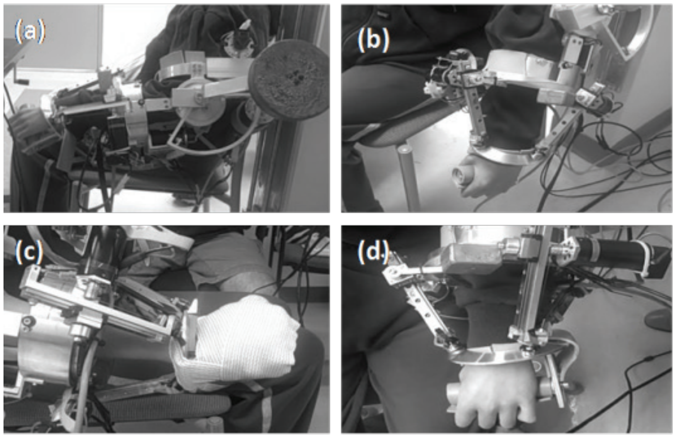


***Figure 1**. Training with the MAHI Exo-II exoskeleton. Subject is performing (a) elbow flexion/extension, (b) forearm pronation/supination elbow extended, (c) wrist flexion/extension, (d) wrist radial/ulnar deviation.*

ally increased over the period of four weeks. The positive gains in arm and hand movements suggested that highly repeatable active single-joint movements delivered through a rehabilitation robotic device can be safely implemented in treatment of upper extremity training after cervical SCI.

Our research is also focusing on developing novel treatment protocols and understanding underlying mechanisms of recovery. One approach is combining modalities; in addition to pharmaceutical interventions, neuromodulation therapies such as non-invasive brain stimulation might be used as an add-on intervention to standard physical therapies. To date several studies have found that combining motor cortical stimulation with behavioral therapies such as occupational therapy and repetitive rehabilitative training may augment recovery after stroke compared with movement alone. In this context, transcranial direct stimulation (tDCS) or transcranial magnetic stimulation (TMS) with robotic or functional exercise training can be implemented in augmenting outcomes from treatment. For example, a study published in *Neurorehabilitation and Neural Repair* (2010) by Kumru et al. found that adults with incomplete SCI demonstrated significant improvement in lower limb motor score, walking speed, and in muscle tonus, when their gait training was coupled with repetitive TMS. The potential mechanism for such improvement were attributed to modified corticospinal influences which might have increased corticospinal inhibitory input and reduced segmental spinal excitability and thus reduced spasticity in patients with incomplete SCI. Similarly, a study by Roche et al. (2009) in the *Journal of Physiology* showed that tDCS applied over motor cortex does not only modulate brain excitability but also modifies excitability of monosynaptic and non-monosynaptic spinal reflex pathways. For example, effects of anodal tDCS applied over leg motor cortex at 2mA for 20 minutes induced changes on lumbar spinal network excitability by decreasing reciprocal inhibition of soleus Ia afferents, and increasing recurrent inhibition and thus aiding to restore impaired co-contraction between tibialis anterior and solues muscles to improve standing balance and walking. These findings were published by Roche et al. (2011), also in the *Journal of Physiology*. Although further clinical trials are required to test the modulatory effects of rTMS and tDCS in various neurological diseases affecting central nervous system, it holds a strong promise as an add-on modality in rehabilitation protocols.

Conclusion

Given the strong evidence both from clinical practice and research, individuals with tetraplegia have a great desire to improve control of their arm and hand functions. This evidence should lead rehabilitation researchers to combine their effort with engineers and neuroscientists to design and develop treatment protocols with optimized frequency, intensity, duration and type of training.

About the Author

Nuray Yozbatiran is an Assistant Professor in the Department of Physical Medicine and Rehabilitation at the University of Texas Health Science Center at Houston. She received her Ph.D. training in physical therapy program from Dokuz Eylul University in Turkey and completed her postdoctoral training at the University of California, Irvine and at Department of PM&R at UTHealth. She joined UTHealth in 2007. The research focuses on using neuromodulation techniques, i.e., transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) and robotic exoskeletons in functional recovery after injury to spinal cord and brain. She also uses neuroimaging techniques such as diffusion tensor imaging to study underlying mechanism of neurorecovery.

About the Author

Gerard Francisco is Chairman and Professor of Physical Medicine and Rehabilitation at UTHealth. He is also Chief Medical Officer at TIRR Memorial Hermann, where he directs the NeuroRecovery Research Center, which houses various laboratories: Rehabilitation Robotics; Neuromodulation and Neural Interfaces; Neurorehabilitation; and MyoNeural Engineering for Rehabilitation. His clinical and research activities include brain injury and stroke rehabilitation, spasticity management, motor recovery, robot-assisted rehabilitation, and neuromodulation to facilitate neurologic and functional recovery.

Brain Awareness Week 2014

The UTHealth NRC organized two events in association with Brain Awareness Week 2014. These programs are held annually, are free, and open to the public. Special thanks to our many dedicated volunteers and public advocacy groups that were involved in making Brain Night and the Public Forum such a success.

Two boys learn about the challenges they might face if they are not able to help themselves due to a spinal cord injury.

A UTHealth medical student and volunteer performs a neurological examination on a young child.

Brain Night at The Health Museum
March 20, 2014

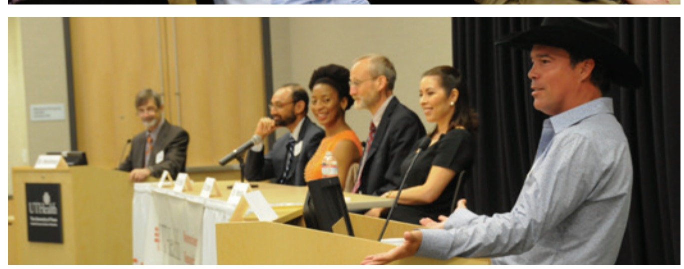
Brain Night is an event designed for elementary school children and their families. This event included mini-lectures and brain-related demonstrations. Over 300 children and their family members enjoyed brain awareness activity booths. Children learned the importance of helmet-safety, saw a real human brain, received a neurological examination, built neurons with pipe-cleaners, and much more.

UTHealth volunteers are ready to explain brain anatomy at an activity station.

19th Annual Public Forum
April 5, 2014

"MS Update: Advances in Diagnosis and Management of Multiple Sclerosis"

The event was moderated by country music performing artist, Clay Walker, and his physician, Dr. Jerry Wolinsky, Director of the Multiple Sclerosis Research Group at UTHealth. The panelists included MS experts from UTHealth: Drs. Nneka Ifejika, John A. Lincoln, John W. Lindsey, and Flavia Nelson. Local MS support groups were available after the Forum to provide continued support to MS patients and their family members.



Upcoming Events

Neurobiology of Disease Seminar Course: Central Nervous System Imaging in Health and Disease

Wednesdays
from Noon to 1:00 pm,
from August 27 to December 10, 2014

UTHealth Medical School Building 7.037. The topics include basic principles of imaging followed by a series of lectures that deal with the application of neuroimaging to normal brain development, psychiatric disorders, epilepsy, and multiple sclerosis. Lectures will be given by UTHealth faculty with a special guest lecture. Course contact: Ponnada.A.Narayana@uth.tmc.edu

Neurobiology of Disease Course Guest Lecture

Wednesday,
October 22, 2014 at Noon

UTHealth MSB 7.037. Dr. Peter Fox, Director of the Research Imaging Institute at the University of Texas Health Science Center at San Antonio will lecture on modeling based on large data sets in health and disease.

Neuroscience Poster Session

Saturday,
December 6, 2014, 9 am to Noon

UTHealth Cooley University Life Center,
7400 Cambridge St., Houston, TX.

Distinguished Lecture in the Neurosciences

Thursday,
February 12, 2015, 4:00 pm

UTHealth Medical School Building 3.001, Dr. Bruce McEwen, Alfred E. Mirsky Professor and Head of the Harold and Margaret Milliken Hatch Laboratory of Neuroendocrinology at The Rockefeller University.

Brain Night at The Health Museum

Thursday,
March 19, 2015, 6:00 to 8:00 pm

The Health Museum, 151 Hermann Drive, Houston, TX. Free event for children and their families; open to the public.

20th Annual Public Forum: The Brain on Drugs

Coming in April - stay tuned for more details!

This event will be moderated by Dr. Joy Schmitz , Director of the Center for Neurobehavioral Research on Addictions and Professor of Psychiatry and Behavioral Sciences at UTHealth. Free and open to the public.

The NRC is able to host events free to the public because of the continued support and generosity of individuals in the community.

Please support us by making a tax-deductible donation online at: ***http://giving.uthouston.org/nrc***

Check out the Neurofax calendar of neuroscience events on-line!

The Neurofax includes seminars, grand rounds, research colloquia, symposia, and local or national conferences that are sponsored by UTHealth, the Texas Medical Center, and other Houston area universities and research institutions. To submit your event to this calendar, please send an email to **nba-nrc@uth.tmc.edu** and include the Event Name, Contact, Date, Time and Location.

UTHealth® | Neuroscience Research Center
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Health Science Center at Houston

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Keep in Touch!

Website: http://med.uth.edu/nrc

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Questions? Comments?

Contact us at 713-500-5538
or E-mail: nba-nrc@uth.tmc.edu

This Newsletter is distributed by mail to individuals and groups engaged in neuroscience research within the TMC and worldwide and features research, neuroscience accomplishments and outreach efforts performed at UTHealth. Past issues are available on the NRC website.

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