

Researchers in Focus Series

Mission Statement: To provide excellence in rehabilitative care through advances in research, education and patient advocacy.



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Welcome to the Winter, 2014-2015 edition of *Researchers in Focus* highlighting the research accomplishments of the University of Kentucky's Department of Physical Medicine and Rehabilitation (PM&R) in collaboration with Cardinal Hill Rehabilitation Hospital. This issue focuses on the research projects of two of our residents. The first is a double-blind, randomized, placebo-controlled study investigating the use of transcranial direct current stimulation in modulating neuropathic pain. The second study is a recently completed retrospective study examining the incidence of spinal abscess and non-prescription schedule I substance abuse before and after implementation of a state wide policy mandating stricter regulation of prescription medications. Finally, we are extremely proud of Dr. Lumy Sawaki's involvement and contributions to the "Walk Again Project", which was showcased at the opening of the 2014 World Cup Games in Brazil and described in several presentations at last year's Society for Neuroscience Annual meeting.

Researcher in Focus: Vinod Muniswamy, MD

Dr. Vinod Muniswamy (PGY3) is working with Dr. Lumy Sawaki (Associate Professor) on a project titled "Modulating Neuropathic Pain with Transcranial Direct Current Stimulation". Neuropathic pain is considered to be a maladaptive process by which disruption of normal pain signaling results in aberrant sensitization or spontaneous neuronal activity. Recent findings suggest that in some conditions neuropathic pain is associated with maladaptive functional reorganization and hyper-excitability of the somatosensory and motor cortical regions. Therefore, strategies that modulate cortical excitability/reorganization have the potential to reduce or eliminate neuropathic pain and significantly improve quality of life. One such strategy is the use of non-invasive transcranial direct current stimulation (tDCS). However, no studies exist that confirm the ability of tDCS to modulate neuropathic pain in such a way as to significantly improve quality of life. We will conduct a small, double-blind, randomized controlled study to better understand the efficacy of tDCS on two types of chronic neuropathic pain: complex regional pain syndrome (CRPS) and phantom limb pain (PLP). The aims of this study are to 1) determine the efficacy of tDCS on limiting pain and improving quality of life, and 2) identify whether the efficacy of tDCS is optimized by cortical region specificity (dorsolateral prefrontal cortex, or DLPFC, versus primary motor cortex, or M1).



Vinod Muniswamy, MD

This small prospective study will have three stimulation conditions: 1) anodal stimulation over DLPFC, 2) anodal stimulation over M1, and 3) sham. Subjects will undergo identical protocols of intervention and evaluation. Subjects will be stratified based on pain intensity and duration of neuropathic pain, and then randomly assigned to one of the following three treatment groups: Group 1: anodal tDCS over DLPFC, Group 2: anodal tDCS over M1, Group 3: sham tDCS over DLPFC.

Each subject will receive four evaluation sessions and 10 treatment sessions. The primary outcome of this study will be assessment of pain using the Short-Form McGill Pain Questionnaire. The SF-36 Health Survey also will be used to assess changes in quality of life. Data from both instruments will be collected and evaluated by individuals who are blinded to the treatment conditions. We hypothesize that both groups receiving active tDCS (i.e., DLPFC and M1) will have improved scores on the McGill Pain Questionnaire compared to the sham group. Additionally, we expect that the group receiving tDCS over the DLPFC will have improved scores on the mental health portion of the SF-36, while the group receiving tDCS over M1 will have improved scores on the physical health portion of the SF-36. Achieving these aims will help advance the potential use of non-pharmacological interventions in neuropathic pain. The proposed work also supports our long-range goals for designing a large, randomized and multi-center study.

Researcher in Focus: Vittal Nagar, MBBS

Dr. Vittal Nagar (PGY3) working with Drs. Sara Salles (Professor) and Joe E. Springer (Professor) recently completed a retrospective study titled: "Increased Incidence Of Spinal Abscess And Substance Abuse After Implementation of State Mandated Prescription Drug Legislation". Spinal infection typically begins in the bone and can lead to a spinal abscess, resulting in swelling and inflammation around the spinal cord. The risk factors for spinal infection include age (mean of 50-60 years of age), diabetes mellitus, malignancy, alcoholism, immunosuppression (steroid use, organ transplant, HIV infection, and chronic renal failure), genitourethral manipulation, dental procedure, recent abdominal operation, systemic infection, and intravenous abuse of controlled substances. Abuse of intravenous drugs has been associated with a higher prevalence of spinal abscess due, in part, to hematogenous spread of bacteria from contaminated syringes and needles. Several studies have documented primary pyogenic infection of the spine in intravenous drug users, and several case studies have reported spinal abscess in patients who are heroin addicts.



Vittal Nagar, MBBS

In July of 2012, the Kentucky general assembly passed House Bill 1 (HB1), which focuses on the strict monitoring and regulation of pain clinics and prescription drug abuse in Kentucky. One of the important changes that came into existence as a result of this landmark legislation is mandatory registration of all physicians with the state's Kentucky All Schedule Prescription Electronic Reporting system, known as KASPER. Mandatory use of KASPER is required prior to prescribing a schedule II or III controlled substance, as well as many Schedule IV controlled substances. While this legislation has proven effective in reducing the abuse of prescription medications, there is evidence of a surge in the use of illegal, non-prescription drugs, in particular intravenous use of heroin, possibly as a means to compensate for limited availability of medically approved controlled substances. Given that intravenous drug use is a risk factor for spinal abscess, we conducted a retrospective case study to identify the incidence of spinal abscess and drug abuse diagnoses admissions from 2010-2014.

The results of this study revealed that the incidence of intraspinal abscess increased 1.56 fold in 2011 (n=26) and 2012 (n=25) relative to 2010 (n=16). However, in 2013, the year following implementation of HB1 legislation, the incidence of intraspinal abscess increased 2.38 fold (n=38) and then 4.19 fold (n=67) in 2014. The incidence of intraspinal abscess in subjects with drug abuse diagnosis remained constant between 2010 (n=3) and 2012 (n=3). However, it increased two-fold (n=7) in 2013 and then nine-fold (n=27) in 2014. In addition, the ratio of cases with spinal abscess plus substance abuse diagnoses relative to those with spinal abscess diagnosis alone remained relatively flat over years 2010-2013. However, this ratio more than doubled in 2014, indicating that the increase in spinal abscess cases with substance abuse is not simply due to an overall increase in incidence of spinal abscess. It is important to note that the total number of admissions remained relatively level over the entire study time period, indicating that the increase in the number of cases with spinal abscess associated with drug abuse is not due to an increase in overall admissions.

It is tempting to speculate that the increased incidence is related to an overall increase in the abuse of schedule I substances (e.g., heroin) in response to legislation limiting the availability of similarly acting prescription medications. However, it is more likely that the increased incidence is due many factors. There is clear evidence of increased heroin usage and overdose deaths due to heroin across the United States, and this includes several states that do not have legislative measures mandating stricter oversight of prescriptions for controlled substances. Other factors contributing to the increases incidence of spinal abscess due to drug abuse may be the availability and cost of heroin over opioid-based prescription medications, as well as the reformulation of highly abused prescription pain medications. In the state of Kentucky, the cost of a single dose of highly abused opiate prescription medications is the same as approximately five doses of heroin. Regardless of the factors involved, given the nationwide increase in heroin usage, the results of this study are of relevance to physicians and patients living in other states that are experiencing similar consequences of spinal abscess related to intravenous substance abuse.

Upcoming Events, Presentations and Publications

Research Day, May 28, 2015

The 27th Annual Research Day is scheduled for Thursday, May 28, 2015. The program consists of ongoing and planned projects presented by PM&R residents, rehabilitation research projects conducted by students and postdocs from the various University of Kentucky Colleges, as well as clinicians, therapists, and researchers involved in rehabilitation research from Cardinal Hill Rehabilitation Hospital and surrounding areas.

This year, Dr. Walter Frontera has agreed to serve as the keynote speaker. Dr. Frontera is Professor and Chair of Physical Medicine and Rehabilitation, and Medical Director of Rehabilitation Services at Vanderbilt University School of Medicine. Dr. Frontera received his medical degree from the University of Puerto Rico School of Medicine in 1979, and his PhD (with distinction) in Applied Anatomy and Physiology from Boston University in 1986. He joined Vanderbilt University in 2011 and as the inaugural chair of PM&R. Prior to joining Vanderbilt University, Dr. Frontera served as Professor and Chair of PM&R at Harvard Medical School from 1996-2006, and then as Dean of the Faculty of Medicine at the University of Puerto Rico from 2006-2011.

Dr. Frontera is the author of more than 200 scientific publications, including 75 peer-reviewed manuscripts and 10 edited books. Currently, he is editor-in-chief of *The American Journal of PM&R* and served as past-president of the International Federation of Sports Medicine. In 2008, he was elected to the Institute of Medicine of the National Academies, and in 2009, member-at-large of the National Board of Medical Examiners. Dr. Frontera's research interest is the study of the basic mechanisms that underlie skeletal muscle dysfunction in elderly men and women and in patients with chronic disease. Part of his research concerns the use of exercise to slow down and rehabilitate muscle weakness and atrophy in various patient population. His clinical interest is in the rehabilitation of sports-related injuries to the musculoskeletal system.

Recent PM&R Publications and Presentations

Resident Publications

Korupolu, R, Ngo, T, Hack, N, Escott, E, and **Salles, SS**. Rehabilitation outcomes after combined acute disseminated encephalomyelitis and Guillain-Barre syndrome in a child: A case report. *Journal of Pediatric Rehabilitation Medicine*, 2014 January, 1;7 (3): 267-72.

Nagar VR, Hooper TL, Dedrick GS, Brismée JM, Sizer PS Jr. The Effect of Recurrent Low Back Pain History on Volitional Preemptive Abdominal Activation During a Loaded Functional Reach Activity. *Spine (Phila Pa 1976)*. 2014; 2(39): E89-E96.

Nagar VR, Birthi P. Chronic Opioid Pain Management for Chronic Kidney Disease. *Journal of Pain and Palliative Care Pharmacotherapy* 2015 Jan 5; doi:10.3109/15360288.2014.997850. [Epub ahead of print].

Nagar VR, Birthi P. Implication of Bariatric Surgery on Chronic Pain and Opioid Use. *Journal of Pain and Palliative Care Pharmacotherapy*. 2015 Jan 5; doi:10.3109/15360288.2014.997851. [Epub ahead of print].

Pakeerappa, P, Salles, SS. Botulinum Toxin-A injection to Facial and Cervical Paraspinal Muscles in a Patient with Stiff Person Syndrome: A Case Report, PM&R. doi: 10.1016/j.pmrj.2014.10.013. [Epub ahead of print].

Resident Presentations

Key, J and **Erlanson, E**. Moyamoya Syndrome and Cerebral Vascular Accident as a Presenting Manifestation of Neurosyphilis: A Case Report. Poster Presentation, American Academy of Physical Medicine and Rehabilitation Annual Assembly, San Diego, CA Nov, 2014.

Resident Presentations Continued

Ma, Zhangliang, Ortiz-Vargas, Oscar, Springer, Joe, and Nickerson, Robert. Suddenly Elevated International Normalized Ratio Associated With Infections: A Case Report. Poster Presentation, American Academy of Physical Medicine and Rehabilitation Annual Assembly, San Diego, CA Nov, 2014.

Nagar, Vittal and Nickerson, Robert. Functional Improvement for Heart Failure Patients After Left Ventricular Assistive Device Placement in a Free Standing Rehabilitation Hospital. Poster Presentation, American Academy of Physical Medicine and Rehabilitation Annual Assembly, San Diego, CA Nov, 2014.

Nagar VR, Birthi P, Nickerson R, Sloan PA. A Systematic Review of Hypogonadism Associated With Chronic Opioid Therapy, Moderated e-Poster on chronic pain, 13th Annual Pain Medicine Meeting; San Francisco, CA. ASRAP-0049, American Society of Regional Anesthesia and Pain Medicine, Nov, 2014.

Nagar VR, Hooper TL, Dedrick GS, Brismée JM, Sizer PS Jr. Effect of Persistent Low Back Pain on Volitional Pre-Emptive Abdominal Activation During a Loaded Functional Reach Activity. American Academy of Physical Medicine and Rehabilitation Annual Assembly, San Diego, CA; PM&R. 2014 Sep; 6(9): S 350; Poster 469, Nov, 2014.

Pakeerappa, Praveen N and Ortiz-Vargas, Oscar. Ultrasound-Guided Injection of Steroids as a Treatment for Symptomatic Traumatic Adhesions Between the Lumbrical and Interosseous Muscles of the Hand: A Case Report. American Academy of Physical Medicine and Rehabilitation Annual Assembly, San Diego, CA, Nov, 2014.

Manchikanti, K., White, H., Iwinski, H, Salles, SS., A Retrospective Examination of Gait Changes Following Selective Dorsal Rhizotomy in Different Age Groups. AAP, Nashville, TN, February 2014.

Korupolu R, Salmon E, Reddy L, Sawaki L. Effects of transvertebral direct current stimulation in healthy humans: early results from an ongoing study. Poster presented at: International Society of Physical Medicine and Rehabilitation Conference, Cancun, Mexico, June 2014.

Other PM&R Publications/Presentations

Cerra, F, Delaney, C, Lutfiyya, N, Shanedling, J, Pechacek, J, Pfeifle, A, and **Erlandson, E.** Nexus Innovations Incubator and the National Center Data Repository. Oral Presentation, All Together Better Health, 7th International Conference on Interprofessional Practice and Education, Pittsburg, PA, June, 2014.

Sawaki L, Butler A, Leng X, Wassenaar PA, Mohammad Y, Blanton S, Sathian K, Nichols-Larsen DS, Wolf SL, Good DC, Wittenberg GF. Differential patterns of cortical reorganization following constraint-induced movement therapy during early and late period after stroke. *NeuroRehabilitation*. 2014 Jan 1;35(3):415-26.

Combs HL, Berry DT, Pape TL, Babcock-Parziale J, Smith B, **Schleenbaker R, Shandera-Ochsner A, High WM.** The Effects of Mild TBI, PTSD, and Combined Mild TBI/PTSD on Returning Veterans. *Journal of Neurotrauma*, October 2014, doi:10.1089/neu.2014.3585 [Epub ahead of print].

Wang W-X, Visavadiya, NP, Pandya, JD, Nelson, PT, Sullivan, **Springer, JE.** Mitochondria-associated microRNAs in rat hippocampus following traumatic brain injury. *Exp. Neurol*. 2015 Jan doi: 10.1016/j.expneurol.2014.12.018. [Epub ahead of print].

Emily Salyers, BS; Cheryl Carrico; KC Chellette; Laurie Nichols; Cameron Henzman; **Lumy Sawaki.** Dose-Response Effects of Peripheral Nerve Stimulation and Motor Training in Stroke: Preliminary Data. IEEE HEALTHCOM 2014 E-health in Neurosciences Conference: October 15-18, 2014; Natal, Brazil.

Kenneth Chellette, Cheryl Carrico, Laurie Nichols, Emily Salyers, **Lumy Sawaki.** Effects of electrode configurations in transcranial direct current stimulation after stroke. IEEE HEALTHCOM 2014 E-health in Neurosciences Conference: October 15-18, 2014; Natal, Brazil.

Salmon E, Carrico CL, Nichols LR, Reddy L, **Salles S, Sawaki L.** Transcranial Direct Current Stimulation to Enhance Motor Function in Spinal Cord Injury: Pilot Data. IEEE HEALTHCOM 2014 E-health in Neurosciences Conference: October 15-18, 2014; Natal, Brazil.

Sawaki L, Donati AC, Nogueira AN, Garabello C, Gitti CM, Campos D, Yoshihara D, Pereira GA, Araújo I, Campos J, Ferreira L, Ares M, Santos M, Augusto PB, Tripodi S, Morya E, Nicoletis MAL. Novel rehabilitative strategy to facilitate EEG-triggered locomotor training in chronic spinal cord injury patients: Preliminary results of an ongoing study. Poster presented at: Neuroscience 2014--Society for Neuroscience; November 2014; Washington, DC.

Brasil FL, Muioli RC, Shokur S, Fast K, Lin AL, Peretti NA, Takigami A, Lyons K, Zielinski DJ, **Sawaki L, Joshi S, Morya E, Nicoletis MAL.** The Walk Again Project: An EEG/EMG training paradigm to control locomotion. Poster presented at: Neuroscience 2014--Society for Neuroscience; November 2014; Washington, DC.

Nicoletis MAL, Shokur S, Lin A, Muioli RC, Brasil FL, Peretti NA, Fast K, A. Takigami A, Morya E, Cheng G, **Sawaki L, Kopper R, Schwarz D, Gallo S, Lebedev M, Joshi S, Bleuler H, Rudolph A.** The Walk Again Project: Using a brain-machine interface for establishing a bi-directional interaction between paraplegic subjects and a lower limb exoskeleton. Poster presented at: Neuroscience 2014--Society for Neuroscience; November 2014; Washington, DC.

Klim GV, The Role of Rehabilitation. In: *The Art and Science of Palliative Medicine*. (Eds. Smith, HS and Pilitsis, JG), AME Publishing Company, Hong Kong. 2014.