

University of Kentucky
Department of
Physical Medicine and
Rehabilitation

25th Annual PM&R
Research Day

Cardinal Hill Rehabilitation Hospital
Center of Learning
Lexington, Kentucky



May 23, 2013



PROGRAM AND ABSTRACTS

25th Annual

Physical Medicine and Rehabilitation Research Day

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**UNIVERSITY OF KENTUCKY
DEPARTMENT OF PHYSICAL MEDICINE & REHABILITATION
25th ANNUAL RESEARCH DAY AGENDA**

**CARDINAL HILL REHABILITATION HOSPITAL
CENTER OF LEARNING
May 23, 2013**

7:00 a.m. – 7:50 a.m. Dr. Cohen breakfast Lecture and Roundtable with Residents
(Cardinal Hill Boardroom)

7:50 a.m. – 8:00 a.m. Opening Remarks (CL3): Gerald Klim, DO

PM&R RESIDENT RESEARCH PRESENTATIONS – CL3

8:00 a.m. – 8:15 a.m. Aaron Lyles, MD, Physical Medicine & Rehabilitation
“Acute Rehabilitation of Patient with Surgically Acquired Central Alveolar Hypoventilation Syndrome”

8:15 a.m. – 8:30 a.m. Zhangliang Ma, MD, PhD, Physical Medicine & Rehabilitation
“Study on Active HCMV Infection in Left MCA Stroke Patients”

8:30 a.m. – 8:45 a.m. Kavita Manchikanti, MD, Physical Medicine & Rehabilitation
“Post Traumatic Headaches: A Description and Comparison of Headache Patterns in Traumatic Brain Injury and Post-Traumatic Stress Disorder”

8:45 a.m. – 9:00 a.m. Praveen N. Pakeerappa, MD, Physical Medicine & Rehabilitation
“Botulinum Toxin A Injection to Facial Muscles in Patient with Stiff Person Syndrome Implanted with Baclofen Pump: A Case Report”

9:00 a.m. – 9:15 a.m. Sankar Chirumamilla, MD, Physical Medicine & Rehabilitation
“Effects of Athletics on Activities of Daily Living, Depression & Self-efficacy after Spinal Cord Injury”

9:15 a.m. – 9:30 a.m. Jason Lee, MD, Physical Medicine & Rehabilitation
“Parasagittal Interlaminar Epidural Approach Versus the Transforaminal Epidural Approach for the Treatment of Lumbar Radicular Pain: A Randomized, Blinded, Prospective Outcome Study”

9:30 a.m. – 9:45 a.m. **BREAK**

9:45 a.m. – 10:00 a.m. Francisco Angulo Parker, MD, Physical Medicine & Rehabilitation
“Knee Hyperextension after Hamstring Lengthening in Cerebral Palsy: Incidence, Predictive Factors and Cost in Gait Efficiency”

10:00 a.m. – 10:15 a.m. Radha Korupolu, MD, Physical Medicine & Rehabilitation
“Effects of Hamstring Lengthening Palsy on Pelvic, Hip and Ankle Kinematics in Children with Cerebral Palsy”

10:15 a.m. – 10:30 a.m. Erika Erlandson, MD, Physical Medicine & Rehabilitation
“Improvements in Functional Mobility after Hamstring Lengthening in Ambulatory Children with Cerebral Palsy”

**UNIVERSITY OF KENTUCKY
DEPARTMENT OF PHYSICAL MEDICINE & REHABILITATION
25th ANNUAL RESEARCH DAY AGENDA
(Continued)**

POSTER PRESENTATIONS – CL2 (Continued)

- 5 Rhada Korupolu, MD, UK/PM&R
Concurrent Acute Disseminated Encephalomyelitis and Guillain-Barré Syndrome in a Child: A Case Report
- 6 Darren M. Miller, UK/SCoBIRC
The NRF2-ARE Pathway as a Therapeutic Target for Acute Traumatic Brain Injury: Dose Response of Carnosic Acid
- 7 Francisco Angulo Parker, MD, UK/PM&R
CNS Histoplasmosis with Tetraparesis: A Case Report
- 8 Elizabeth Salmon, UK/Center for Biomedical Engineering
Discrimination of Attempted Movements from Rest Using an EEG Brain-Machine Interface for Rehabilitation from Neural Injury
- 9 Emily Salyers, UK/PM&R
Peripheral Nerve Stimulation Dose-Response Relationship in Chronic Stroke: Early Results from an Ongoing Trial
- 10 Camille Skubik-Peplaski PhD, OTR/L, BCP, FAOTA
Department of Occupational Therapy at EKU
The Therapy Gym: Is it Therapeutic?
- 11 Megan Danzl, PT, NCS, PhD, CHRH
Non-invasive Brain Stimulation Paired with a Novel Locomotor Training in Chronic Stroke: a Feasibility Study
- 12 Praveen N. Pakeerappa, MD, UK/PM&R
Botulinum Toxin A Injection to Facial Muscles in Patient with Stiff Person Syndrome Implanted with Baclofen Pump: A Case Report

AWARDS AND CLOSING REMARKS – CL3

1:45 p.m. – 2:00 p.m.

Awards & Closing Remarks

Joe Springer, PhD, Physical Medicine & Rehabilitation

Robert Nickerson, MD, Physical Medicine & Rehabilitation

PM&R Resident Presentations

ORAL PRESENTATIONS

Presenter:

Abstract Presentation:

Aaron Lyles, MD

“Acute Rehabilitation of Patient with Surgically Acquired Central Alveolar Hypoventilation Syndrome”

Zhangliang Ma, MD, PhD

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“Post Traumatic Headaches: A Description and Comparison of Headache Patterns in Traumatic Brain Injury and Post-Traumatic Stress Disorder”

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Sankar Chirumamilla, MD

“Effect of Athletics on Activities of Daily Living, Depression & Self-Efficacy after Spinal Cord Injury”

Jason Lee, MD

“Parasagittal Interlaminar Epidural Approach Versus the Transforaminal Epidural Approach for the Treatment of Lumbar Radicular Pain: A Randomized, Blinded, Prospective Outcome Study”

Francisco Angulo Parker, MD

“Knee Hyperextension after Hamstring Lengthening in Cerebral Palsy: Incidence, Predictive Factors and Cost in Gait Efficiency”

Radha Korupolu, MD

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Erika Erlandson, MD

“Improvements in Functional Mobility after Hamstring Lengthening in Ambulatory Children with Cerebral Palsy”

Giridhar Gundu, MD

“Modulating Pain in Complex Regional Pain Syndrome with Transcranial Direct Current Stimulation: Early Results from an Ongoing Study”

Thien Ngo, MD

“Identification of Sural Nociceptive Flexion Reflex Threshold and Ratio in Adult Males 20-40 Years of Age”

Dwan Perry, DO

“Knee Injury – Distance Running: A Case Report”

PM&R RESIDENT PRESENTATION

Acute Rehabilitation of Patient with Surgically Acquired Central Alveolar Hypoventilation Syndrome

Presenter:

Aaron Lyles, MD¹

Faculty Mentors/Collaborators:

Jay Hammock, MD¹

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

Abstract Text:

A 53 year old morbidly obese female with a history of two instances of intracranial hemorrhage secondary to a congenital medullary cavernous malformation underwent acute rehabilitation on a dedicated stroke unit following neurosurgical resection of the malformation. Patient was diagnosed with apnea at the acute care hospital, but formal sleep study was deferred until after rehabilitation. Patient was accepted by the rehabilitation hospital on oxygen and nocturnal Bi-PAP, a regimen which was adequately controlling hypoxia and hypercapnea at the acute care hospital. However, shortly after starting rehabilitation and for multiple reasons, the patient refused to wear the Bi-PAP machine. Hypoxia was avoided using oxygen supplementation, however patient became progressively hypercapnic secondary to her hypoventilation syndrome with symptoms of hypercapnia. Pharmacologic intervention was attempted using acetazolamide but was unsuccessful. Symptoms and hypercapnea resolved with reintroduction of Bi-PAP.

Key Words: Central Alveolar Hypoventilation Syndrome, Ondine's Curse, Congenital Medullary Cavernous Malformation, Hypercapnea, Rehabilitation

NOTES

PM&R RESIDENT PRESENTATION

Study on Active HCMV Infection in Left MCA Stroke Patients

Presenter:

Zhangliang Ma, MD, PhD¹

Faculty Mentors/Collaborators:

Jay Hammock, MD¹, Erika Erlandson, MD¹

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

Abstract Text:

It's well known that human cytomegalovirus (HCMV) causes severe medical problems in immune-compromised patients, such as the ones suffering from AIDS, organ transplant and leukemia. As HCMV is a member of the herpes family, it usually causes subclinical or asymptomatic infection if an individual is immune-competent. After an acute/active infection, the viruses can become latent in the body for the remainder of the patient's life. Should their immune systems become compromised again, the latent viruses can reactivate.

According to the CDC, about 50-80% of American adults at age 40 or older were infected with HCMV. There are about 790,000 CVA patients yearly, which means that there is one person experiencing a stroke every 45 seconds in US. This puts CVA as the 3rd leading cause of death. Because a stroke is a massive stress to the human body, it often compromises the immune system, and subsequently latent CMV may become an active infection. This is usually missed during their initial hospital stay, because the latent virus takes 7-10 days to transform into a full-blown infection. In this research, we hypothesize that a stroke forces a stress to the immune system, which results in the activation of latent CMV infections; its viremia along with flu-like symptoms will worsen the comorbidities of stroke patients during rehabilitation, increasing fatigue, exacerbating poor performance, which in turn could reduce enthusiasm to participate in rehab programs. Consequently, stroke patients with an active infection have to stay longer, thus increasing Medicaid or Medicare expense.

Key Words: Cerebrovascular Accident, HCMV, Reactive Infection, FIM Score, Rehabilitation

NOTES

PM&R RESIDENT PRESENTATION

Post Traumatic Headaches: A Description and Comparison of Headache Patterns in Traumatic Brain Injury and Post-Traumatic Stress Disorder

Presenter:

Kavita Manchikanti, MD¹

Collaborators:

Oscar Vargas Ortiz, MD²

Departmental Affiliations:

¹Department of Physical Medicine & Rehabilitation, University of Kentucky, Lexington, KY

²Veterans Affairs Medical Center, Lexington, KY

Abstract Text:

Background: Veterans with a history of traumatic brain injury (TBI) and suspected post-traumatic stress disorder (PTSD) who present with primary complaints of headache and neurobehavioral symptoms pose a clinical challenge. Headaches, impaired concentration, insomnia, and irritability are symptoms common to the diagnoses of PTSD and mild TBI. Although post-traumatic headaches are common following mild TBI, there are no typical characteristics to distinguish them from primary headaches or secondary headaches due to other pathology. Treatment is generally based on the primary headache that they most closely resemble. A multidisciplinary approach is favored, but the ability to distinguish headaches related to TBI from those primarily related to mental health concerns would aid in diagnosis and in focusing the treatment approach for these patients.

Objective: Describe and compare headache patterns in veterans with TBI versus those with PTSD.

Methods: This cross-sectional study will describe headache patterns in veterans with blast exposure during Operation Iraqi Freedom or Operation Enduring Freedom who have undergone formal neuropsychological evaluation at the Lexington Veterans Affairs Medical Center. Veterans will be grouped by diagnosis of TBI, PTSD, mixed, or neither based on neuropsychological testing. Retrospective chart review will provide information about headache onset, frequency, duration, location, severity, triggers, associated symptoms, and response to treatment. Headache patterns in the TBI and PTSD groups will then be described and compared using statistical analysis to determine if a headache pattern unique to TBI can be identified.

Key Words: Traumatic Brain Injury, Post-Traumatic Headaches, Post-Traumatic Stress Disorder

NOTES

PM&R RESIDENT PRESENTATION

Botulinum Toxin A Injection to Facial Muscles in Patient with Stiff Person Syndrome Implanted with Baclofen Pump: A Case Report

Presenter:

Praveen N. Pakeerappa, MD¹

Collaborators:

Pravardhan Birthi, MD¹, Sara Shahid Salles, DO¹

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

Abstract Text:

Settings: Outpatient rehabilitation clinic.

Patient: 48 year old Caucasian male with history of Stiff Person Syndrome (SPS).

Case Description: We present a patient with history of SPS for 17 years with stiffness prominent bilaterally in the upper and lower extremities. He failed medical management with oral benzodiazepines and experienced side effects with high doses of oral baclofen. Subsequently Baclofen pump was implanted, with some relief of symptoms. On follow up visit to the outpatient clinic, it was noticed that his stiffness reduced and his ADLs improved, but he continued to have bruxism and neck stiffness. Botulinum toxin A was then injected to the masseter muscle and paraspinal muscles.

Assessment/results: Patient experienced dramatic improvement in neck stiffness and bruxism for a period of 3 months after which he required re-injection of Botulinum toxin A with similar beneficial results.

Discussion: SPS is a rare autoimmune neurologic disorder. It is characterized by generalized rigidity, intermittent and superimposed spasms as well as increased sensitivity to external stimuli. The standard treatment for SPS has been benzodiazepines, a GABA neuromodulator. The autoimmune hypothesis of the disorder has been supported due to relief of the symptoms provided by immunotherapy. Baclofen is also another logical therapy for SPS because of its action on GABA-B receptor agonist. On the other hand, the effects of Botulinum Toxin A therapy for the treatment of SPS remains unclear. There is scant data regarding the benefit of Botulinum toxin A for the symptomatic relief of SPS. Botulinum toxin A demonstrated improvement of stiffness which was refractory to the standard treatment on SPS in our patient.

Conclusion: Botulinum toxin A can be considered as mode of management for bruxism and neck stiffness in addition to the Baclofen pump for symptomatic relief in patients with stiff person syndrome.

Key Words: Stiff Person Syndrome, Botulinum Toxin and Bruxism

NOTES

PM&R RESIDENT PRESENTATION

Effect of Athletics on Activities of Daily Living, Depression & Self-efficacy after Spinal Cord Injury

Presenter:

Sankar Chirumamilla, MD¹

Collaborators:

Silke Bernert, MD¹, Sara Shahid Salles, DO¹, Vinod Muniswamy, MBBS¹

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

Abstract Text:

Background: Major depression is the most common psychiatric disorder in individuals with spinal cord injury (SCI). In a recent longitudinal study, approximately 20 to 22% of individuals with SCI have probable major depression. The prevalence of depression ranges from 11% to 37% with significant symptoms (2). Physical activity and exercise are proven to improve overall mental health, prevent depression and are negatively related to depression (3, 4). The purpose of this study is to determine the effect of physical activity not only on depression but also on activities of daily living and self-efficacy in individuals with SCI. We also studied eleven different barriers for physical activity.

Design: Case controlled cross sectional study

Methods: Individuals with spinal cord injury greater than 18 years of age were included in the study. Participants were asked to complete a questionnaire about their ability to participate in athletic activities, age at the time of injury, income, perceived barriers for physical activity, perceived exertion scale, general self-efficacy scale, Zung Self-rated depression scale and Brunel Mood Scale. SPSS software was used to compare level of depression, mood, self-efficacy, exertion with Activities of Daily Living, level of community participation, and barriers to participation in both groups.

Results: Seventy six participants completed the survey. Of them 47 (61.8%) were male with mean age of 42.7 years and mean is 32 .8 years age at the time of injury. Forty (52.6%) identified themselves as athletes. The average score on Zung depression scale for athletes was 42 and for nonathletes was 38 ($p = 0.01$). The general self-efficacy of athletes was higher than non-athletes ($p = 0.024$). Athletes scored higher in perceived exertion scale with mean of 123 ($p = 0.013$), perhaps because of their involvement in more physical activity. The likelihood of overcoming barriers such as "nobody to go with" ($p=0.011$), "lack of local opportunities" ($p=0.019$) and "other causes" ($p=0.045$) is the key for participating in athletic activities.

Conclusion: Participating in athletics is associated with low depression in individuals with SCI. Overcoming perceived barriers such as lack of athletic partner, lack of local opportunities are important for individuals with SCI in participating in sports. Identifying these barriers and assisting them to overcome these barriers improves their quality of life.

Key Words: Spinal cord injury, athletics, depression, self efficacy

References:

- 1) Saunders LL, Krause JS, Focht KL. A longitudinal study of depression in survivors of spinal cord injury. *Spinal Cord* 2012; 50: 72-77.
- 2) Elliot TR, Frank RG. Depression following spinal cord injury. *Arch Phys Med Rehabil* 1996; 77: 816-823.
- 3) Landers DM, Arent SM. Physical activity and mental health In: Tenenbaum G, Eklund RC, eds. *Handbook of Sport psychology*. Hoboken, NJ: John Wiley & Sons, Inc., 2007: 469-491.
- 4) Galper DI, Trivedi MH, Barlow CE, Dunn AL, Kampert JB. Inverse association between physical activity and mental health in men and women. *Med Sci Sports Exerc* 2006; 38: 173-178.

NOTES

PM&R RESIDENT PRESENTATION

Parasagittal Interlaminar Epidural Approach Versus the Transforaminal Epidural Approach for the Treatment of Lumbar Radicular Pain: a Randomized, Blinded, Prospective Outcome Study

Presenter:

Jason Lee, MD¹

Collaborators:

Pravardhan Birthi, MD¹, Jay Grider, DO, PhD²

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

²Interventional Pain Medicine, University of Kentucky, Lexington, KY

Abstract Text:

Lumbosacral radicular pain is characterized by pain radiating in one, or occasionally more than one, lumbar or sacral dermatomes. Lumbar radicular pain is a common condition with an annual prevalence ranging from 9.9% to 25%. Development of radicular pain depends on both mechanical factors and concomitant nerve irritation by chemical mediators released from the disrupted disc. These chemical mediators result in an intense localized inflammatory reaction that is associated with neuritis. Local application of corticosteroids to the compressed, inflamed nerve root has emerged as a treatment option via the interlaminar and transforaminal approach. Interlaminar epidural steroid injections have been suggested to be less beneficial when compared to classic transforaminal approaches with regard to efficacy for radiculitis. A recent novel parasagittal interlaminar technique has recently been proposed by Candido et al. In this preliminary feasibility study, it was demonstrated that the parasagittal approach resulted in dye spread in lateral/foraminal epidural space suggesting that this approach could be highly effective in the application of steroid to the disc/nerve root interface in lateral recess of the spinal canal while also avoiding the vasculature of the neuroforaminal space.

Key Words: Parasagittal Interlaminar, Transforaminal Steroid Injections

NOTES

PM&R RESIDENT PRESENTATION

Knee Hyperextension after Hamstring Lengthening in Cerebral Palsy: Incidence, Predictive Factors and Cost in Gait Efficiency

Presenter:

Francisco Angulo Parker, MD¹

Collaborators:

Hank White, PhD², Henry J. Iwinski, MD³

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

²Shriners Hospital for Children, Lexington, KY

³Orthopedic Surgery, University of Kentucky, Lexington, KY

Abstract Text:

Objective (Abstract Only): Primary objective: To establish the incidence of knee hyperextension after hamstring lengthening in children with cerebral palsy with spastic diplegia.

Secondary objectives: Identify the variables in physical examination and gait analysis that can predict knee hyperextension after hamstring lengthening. Assess the cost of knee hyperextension in gait efficiency.

Design (Abstract Only): Retrospective, case control study. Regression analysis

Setting (Required for Abstracts and Case Reports): Pediatric Orthopedic Hospital

Participants (Abstracts Only): 142 subjects who had received hamstring lengthening surgery and had gait analysis pre and post surgery.

Interventions (Abstracts Only): None

Main Outcome Measures (Abstracts Only): Number and percentage of patients with knee hyperextension after hamstring lengthening. Oxygen consumption in walking test pre and post hamstring lengthening.

Results (Abstract or Case Report) or Clinical Course (Case Reports Only): 11.5 percent of our population presented with knee hyperextension after hamstring lengthening. Regression analysis showed that the main predictor of hyperextension after hamstring lengthening is knee flexion at midstance (mean of 23.9 degrees). Analysis of oxygen consumption data did not reveal any significant changes in children with hyperextended knees vs. non- hyperextended knees.

Conclusions (Required for Abstracts and Case Reports): Incidence of knee hyperextension after hamstring lengthening in our population is 11.5 percent. Pre operative knee flexion at midstance was correlated with the presence of knee hyperextension post surgery. Interestingly, there was no significant change in gait efficiency as measured by oxygen consumption in hyperextended knees vs non-hyper extended knees.

Key Words: Cerebral Palsy, Hamstring, Gait

NOTES

PM&R RESIDENT PRESENTATION

Effects of Hamstring Lengthening Palsy on Pelvic, Hip and Ankle Kinematics in Children with Cerebral Palsy

Presenter:

Radha Korupolu, MD¹

Collaborators:

Hank White, PT, PhD²

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

²Shriners Hospitals for Children, Lexington, KY

Abstract Text:

Background: Hamstring lengthening (HL) surgery is commonly performed in children with cerebral palsy (CP) to improve crouched gait. However, there is a concern that this surgery may have undesirable side effects at distant joints. The purpose of this study is to evaluate the distant joint effects of hamstring lengthening in subjects with crouched gait due to CP.

Design: Retrospective study

Methods: 147 ambulatory children with cerebral palsy were included in this study all of whom underwent hamstring lengthening in isolation or as a part of single event multilevel soft-tissue surgery. All subjects had pre-operative and post-operative clinical examination and 3-D gait analysis. Pelvic, Hip and ankle kinematic data was collected retrospectively by chart review. The mean follow up was 1.4 years.

Results: Data analysis revealed significant increase in anterior pelvic tilt post operatively. Subjects with simultaneous rectus transfer & HL were noted to have a small increase in anterior pelvic tilt compared to HL alone. There was no significant change in hip flexion during gait cycle after HL. However, Post operative ankle kinematics showed significant Improvement in our subjects.

Conclusion: HL results in distant joint effects which include undesirable increased anterior pelvic tilt post operatively. Future research is needed to evaluate the long term effects of this undesirable side effect.

Key Words: Cerebral palsy, hamstring lengthening, pelvic tilt, kinematics

NOTES

PM&R RESIDENT PRESENTATION

Improvements in Functional Mobility after Hamstring Lengthening in Ambulatory Children with Cerebral Palsy

Presenter:

Erika Erlandson, MD¹

Collaborators:

Hank White, PhD², Henry J. Iwinski, MD³

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

²Orthopedic Surgery, University of Kentucky, Lexington, KY

³Shriner's Hospital for Children, Lexington, KY

Abstract Text:

Objective: To assess the effects of hamstring lengthening procedure on gross mobility, and oxygen requirements in ambulatory children with cerebral palsy, spastic diplegia.

Design: Retrospective study of 78 children with cerebral palsy, spastic diplegia treated with a hamstring lengthening procedure performed between 1998-2010. Multiple measures related to gross mobility and functional ambulation were used for assessment as part of their comprehensive evaluations pre-operative and post-operatively. It was hypothesized that gross motor function would significantly improve and oxygen cost and consumption during ambulation would significantly decrease post-operatively.

Participants: 78 ambulatory children with a diagnosis of cerebral palsy, spastic diplegia

Interventions: Hamstring lengthening procedure.

Main Outcome Measures: Gross Motor Function Measure (GMFM) dimensions D (standing) & E (walking, running, and jumping), oxygen cost and consumption during ambulation.

Results: There was a significant decrease in oxygen consumption and cost across all groups after surgical intervention ($p < 0.001$). The GMFM dimensions D and E were significantly improved when performed barefoot for patients with a GMFCS level 3, $p = 0.004$ and 0.011 respectively, as well as FMS level 2 with $p < 0.03$ for all distances. In addition, GMFM dimension E barefoot was significantly improved in patients with GMFCS level 2 ($p = 0.048$).

Conclusion: Hamstring lengthening procedures significantly improves gross mobility, functional ambulation, and oxygen requirements for ambulation in patients with cerebral palsy, spastic diplegia who ambulate with an assistive device (GMFCS level 3, FMS level 2). In addition, significant decreases in oxygen cost and consumption for all children included in our study.

Key Words: Cerebral Palsy, Gait, Mobility Limitation, Rehabilitation, Orthopedic Surgery

NOTES

PM&R RESIDENT PRESENTATION

Modulating Pain in Complex Regional Pain Syndrome with Transcranial Direct Current Stimulation: Early Results from an Ongoing Study

Presenter:

Giridhar Gundu, MD¹

Collaborators:

KC Chelette, MS¹, Cheryl Carrico, MS¹, Candy Pettry¹, Lumy Sawaki, MD, PhD¹

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

Abstract Text:

Complex regional pain syndrome (CRPS) is a disabling and painful condition of unclear pathophysiology. The condition has an unpredictable clinical course and is often resistant to treatments including pharmacological intervention, physical rehabilitation, and interventional pain management techniques. Recently, a non-invasive brain stimulation technique called transcranial direct current stimulation (tDCS) has emerged as promising intervention to reduce chronic and intractable pain arising from a variety of causes. However, no studies have evaluated whether tDCS may be effective in reducing pain and enhancing quality of life in subjects with CRPS. Therefore, we propose to investigate the possible benefits of tDCS as an intervention to reduce pain and enhance quality of life in subjects with CRPS.

Our proposed study has 2 specific aims:

- Specific Aim #1: Determine the effect of tDCS on pain and quality of life in subjects with CRPS. Outcome measures include standardized tests of pain and quality of life.
- Specific Aim #2: Determine the optimal tDCS electrode location for reduction of pain and enhancement of quality of life in subjects with CRPS.

We have secured approval by the University of Kentucky Institutional Review Board and begun enrollment of subjects. Three subjects with chronic CRPS were enrolled after informed consent (projected total enrollment: n=30). Each subject was randomly assigned to 1 of 3 groups: 1) anodal stimulation over left dorsolateral prefrontal cortex, 2) anodal stimulation over left primary motor cortex, or 3) sham. We delivered tDCS daily for 10 consecutive weekdays. Assessments of pain and quality of life including the Short-Form McGill Pain Questionnaire and The SF-36 Health Survey were performed by a blinded evaluator at four time points: 1-week prior to start of intervention, immediately prior to start of intervention, after intervention day 5, and after intervention day 10.

Key Words: Chronic Pain, Neuropathic Pain, Neuromodulation, Rehabilitation, Brain Stimulation

NOTES

PM&R RESIDENT PRESENTATION

Identification of Sural Nociceptive Flexion Reflex Threshold and Ratio in Adult Male 20-40 Years of Age

Presenter:

Thien Ngo, MD¹

Collaborators:

Oscar Ortiz Vargas, MD², Lumy Sawaki, MD, PhD¹

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

²Lexington Veterans Affairs Medical Center, Lexington, KY

Abstract Text:

Objective: The absence of objective instruments to measure pain makes it difficult to develop strong experimental studies in this field. The Nociceptive Flexion Reflex Threshold (NFRT) has been used in research for this purpose, but has not transcended into clinical grounds due to poor standardization and absence of normative data. We aimed to establish normative data for a limited homogeneous population of young men and to prove the concept that a ratio of the NFRT (NFRR), using the supramaximal stimulation for the sural sensory nerve action potential (SNAP), will decrease the inherent between-individual variability of the NFRT.

Design: Eleven healthy male volunteers (ages 20-40 years) participated in this study. Sural SNAP was recorded using a standard protocol. The nociceptive flexion reflex of the biceps femoris muscle was identified using surface electrodes and following a stimulation protocol that included random intermittent stimulation and a stepwise approach. Each patient scored their level of pain caused by NFRT using a visual analogue scale (VAS).

Results: Values for NFRT and NFR ranged 31-72 and 12-41 (mA), respectively. NFRT and NFR correlation with VAS was $r^2=0.154$ and $r^2=0.595$, respectively.

Conclusions: Our pilot study failed to establish a significant correlation between the NFRR and pain index in the young adult males group age between 20-40. However, biceps reflex stimulation and pain index did show a 0.59 percent correlation that is consistent with the current literature of 0.92.

Key Words: Nociceptive Flexion Reflex Threshold, Sural Sensory Nerve Action Potential, Visual Analogue Scale

NOTES

PM&R RESIDENT PRESENTATION

Knee Injury – Distance Running: A Case Report

Presenter:

Dwan Perry, DO¹

Collaborators:

Mary L. Ireland²

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

²Orthopedic Sports Medicine, University of Kentucky, Lexington, KY

Abstract Text:

History: A 37 year old male runner who presented with insidious onset of right knee pain over the past month. As a former college cross country athlete who participates in several races per year, including marathons, he began to experience medial sided right knee pain with his runs as well as during prolonged walks. There was a recent increase in mileage with his daily runs averaging 12-13 miles per day. Shortly after this regimen change, the pain manifested as sharp, intermittent, with no evidence of radiating symptoms or swelling. He denied any recent trauma, change in running style or surface prior to onset of pain. Cryotherapy and over-the-counter analgesics provided mild relief.

Physical Examination: Examination revealed no visible effusion. Palpation revealed tenderness to palpation over the medial tibial plateau just above the pes anserine tendon insertion. No effusion was appreciated. There was no joint line tenderness. There was full range of motion at the knee. Varus and valgus stability testing were negative at 0° and 30°. Lachman's, along with anterior and posterior drawer tests were negative. McMurray's test was also negative. The extremity was neurovascularly intact.

Differential Diagnosis:

1. Medial Meniscus Injury
2. Tibial Stress Fracture
3. Articular Cartilage Defect of the Medial or Patellofemoral Compartment
4. Pes Anserine Bursitis

Test and Results:

Radiographs of the Bilateral Knee, anteroposterior and lateral views:

1. No evidence of fracture or loose bodies.

MRI of the Right Knee without Contrast:

1. Reactive bone marrow edema in the medial tibial plateau.
2. Irregular edema within the fibular head indicative of early arthrosis affecting the proximal tibiofibular articulation.
3. Normal appearing medial meniscus and articular cartilage.

Final/Working Diagnosis:

Medial Proximal Tibial Plateau Stress Fracture

Treatment and Outcomes:

1. Cessation of the painful activities.
2. As symptoms resolved, it was recommended to have a gradual return to running once asymptomatic.
3. The patient began running again after pain subsided. This was followed by a recurrence of pain which prompted another period of rest from running.
4. After resolution of pain, the patient was able to return to running with no recurrence of pain at one year after initial presentation.

Key Words: Knee Pain, Stress Fracture, Tibial Plateau, Running, Athlete

NOTES

POSTER PRESENTATIONS

<u>Presenter:</u>	<u>Poster #</u>	<u>Poster Presentation:</u>
Cheryl Carrico, MS, OT/L UK/PMR	1	“Peripheral Nerve Stimulation Paired with Constraint-Induced Therapy to Enhance Post-Stroke Upper Extremity Motor Performance”
Kenneth Chelette, MS UK/PM&R	2	“Transcranial Direct Current Stimulation for Motor Recovery From Severe Post-Stroke Hemiparesis: Early Results From an Ongoing Clinical Trial”
Erika Erlandson, MD UK/PM&R	3	“Carotid-Cavernous Fistula after Traumatic Brain Injury: A Case Report”
Giridhar Gundu, MD UK/PM&R	4	“Positional Femoral Entrapment Neuropathy: A Case Report”
Radha Korupolu, MD UK/PM&R	5	“Concurrent Acute Disseminated Encephalomyelitis and Guillain-Barré Syndrome in a Child: A Case Report”
Darren M. Miller UK/SCoBIRC	6	“The NRF2-ARE Pathway as a Therapeutic Target for Acute Traumatic Brain Injury: Dose Response of Carnosic Acid”
Francisco Angulo Parker, MD UK/PM&R	7	“CNS Histoplasmosis with Tetraparesis: A Case Report”
Elizabeth Salmon UK/Ctr for Biomedical Eng.	8	“Discrimination of Attempted Movements from Rest Using an EEG Brain-Machine Interface for Rehabilitation from Neural Injury”
Emily Salyers UK/PM&R	9	“Peripheral Nerve Stimulation Dose-Response Relationship in Chronic Stroke: Early Results from an Ongoing Trial”
Camille Skubik-Peplaski, PhD OTR/L, BCP, FAOTA Dept of Occ. Therapy/EKU	10	“The Therapy Gym: Is it Therapeutic?”
Megan Danzl, PT, NCS, PhD, Cardinal Hill Rehab Hospital	11	“Non-Invasive Brain Stimulation Paired with a Novel Locomotor Training in Chronic Stroke: a Feasibility Study”
Praveen Pakeerappa, MD UK/PM&R	12	“Botulinum Toxin A Injection to Facial Muscles in Patient with Stiff Person Syndrome Implanted with Baclofen Pump: A Case Report”

POSTER PRESENTATION - 1

Peripheral Nerve Stimulation Paired with Constraint-Induced Therapy to Enhance Post-Stroke Upper Extremity Motor Performance

Presenter:

Cheryl Carrico, MS, OT/L¹

Collaborators:

KC Chelette, MS¹, Laurie Nichols, BS, OT/L^{1,2}, Lumy Sawaki, MD, PhD^{1,3}

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

²Cardinal Hill Rehabilitation Hospital, Lexington, KY

³Department of Neurology, Wake Forest University, Winston-Salem, NC

Abstract Text:

Sensory input in the form of peripheral nerve stimulation (PNS) can enhance upper extremity (UE) motor performance following stroke. Likewise, intensive task-oriented motor training can significantly enhance UE motor performance after stroke. Constraint-induced therapy (CIT) is an example of intensive task-oriented motor training. CIT compels use of the paretic UE while constraining the non-paretic UE during performance of motor tasks. No studies in stroke have evaluated whether PNS enhances the effects of CIT. Therefore, we investigated whether *active* PNS paired with CIT leads to significantly more improved UE motor function after stroke than *sham* PNS paired with CIT. Outcome measures included the Fugl-Meyer Assessment Scale (FMA; primary outcome measure), the Wolf Motor Function Test (WMFT), and the Action Research Arm Test (ARAT). Nineteen subjects with chronic, mild-to-moderate post-stroke motor deficit received 2 hours of either active (n=10) or sham (n=9) PNS preceding 4 hours of a modified form of CIT, for 10 consecutive weekdays. We used factorial ANOVA to analyze changes in FMA, WMFT, and ARAT. All outcomes showed significance at completion and 1-month follow-up compared with baseline (p<0.05). These results indicate that in cases of mild to moderate post-stroke UE motor deficit, pairing PNS with intensive task-oriented motor training can lead to more improved UE motor performance than intensive task-oriented training alone. We will finalize this study after analyzing our data collected from transcranial magnetic stimulation, which measures the neurophysiological effects of our intervention. Future research should investigate strategies to accelerate clinical translation of our findings.

Key Words: Occupational Therapy, Task-Oriented Training, Neurorehabilitation

POSTER PRESENTATION - 2

Transcranial Direct Current Stimulation for Motor Recovery From Severe Post-Stroke Hemiparesis: Early Results From an Ongoing Clinical Trial

Presenter:

KC Chelette, MS¹

Collaborators:

Cheryl Carrico, MS, OT/L¹, Laurie Nichols, BS, OT/L^{1,2}, Lumy Sawaki, MD, PhD¹

Departmental Affiliations:

¹Department of Physical Medicine & Rehabilitation, University of Kentucky, Lexington, KY

²Cardinal Hill Rehabilitation Hospital, Lexington, KY

Abstract Text:

To determine the best transcranial direct current stimulation (tDCS) electrode configuration to enhance upper extremity (UE) motor function in subjects with severe post-stroke hemiparesis, we conducted a randomized, double-blind, placebo-controlled clinical trial. Here, we present data from 26 of (projected) 44 chronic stroke subjects with severe UE motor deficit (i.e., virtually no wrist and hand movement). Subjects were assigned to 1 of 4 groups: 1. anodal tDCS to excite ipsilesional hemisphere, 2. cathodal tDCS to inhibit contralesional hemisphere, 3. dual: a simultaneous combination of anodal and cathodal tDCS, or 4. sham tDCS. All subjects participated in 10 treatment sessions consisting of 20 minutes of tDCS followed by 3 hours of occupational therapy. The primary outcome measure was the Fugl-Meyer Assessment. Secondary outcome measures included the Action Research Arm Test and Stroke Impact Scale. Evaluations were performed at baseline and post-intervention. Preliminary results indicate substantially greater improvement in the cathodal group than in other groups. Our results differ from findings in subjects with mild hemiparesis. This disparity may be due to the larger lesions of subjects with severe hemiparesis which may change tDCS current flow compared to subjects with mild hemiparesis. Furthermore, in subjects with severe hemiparesis, comparatively less ipsilesional neuronal substrate may be available for stimulation. Therefore, the anodal and the dual configurations, which rely on ipsilesional stimulation, may not prove optimal.

Key Words: Stroke, Rehabilitation, Transcranial Direct Current Stimulation, Neuroplasticity

POSTER PRESENTATION - 3

Carotid-Cavernous Fistula after Traumatic Brain Injury: A Case Report

Presenter:

Erika Erlandson, MD¹

Collaborators:

Robert B. Nickerson, MD¹

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

Abstract Text:

A 50 year-old male involved in motorcycle collision sustained severe traumatic brain injury including traumatic subarachnoid hemorrhage and subdural hematoma. He required an emergent right hemi-craniectomy and subdural evacuation. He was admitted to acute rehabilitation five weeks following the accident. Two weeks into his acute rehabilitation (seven weeks after the accident) he developed progressive left eye proptosis without associated headache, mental status change, or visual disturbance.

The patient was sent to ophthalmology clinic for evaluation and subsequently transferred to the emergency department for computed tomography. The scan revealed an enlarged left cavernous sinus with multiple tubular areas as well as enlargement of the left superior ophthalmic vein, consistent with post-traumatic left carotid cavernous fistula. Subsequent angiography showed a type I carotid cavernous fistula. Endovascular coiling of the fistula was performed. Magnetic resonance imaging (MRI) and magnetic resonance angiogram (MRA) following the procedure were consistent with successful coiling of the fistula. Following the procedure the left eye proptosis steadily improved and eventually resolved.

Carotid cavernous fistulas are abnormal communications between the carotid artery and the cavernous sinus. In post-traumatic patients this fistula likely arises after a tear to the internal carotid artery within the cavernous sinus. They are associated with significant morbidity and mortality including vision loss and spontaneous intracerebral hemorrhage.

Post-traumatic carotid-cavernous fistulas are rare but serious complications of traumatic brain injury. It is important for rehabilitation physicians to be aware of this condition in patients with traumatic brain injury because if left untreated, it is associated with high morbidity and mortality.

Key Words: Traumatic Brain Injury, Carotid-Cavernous Sinus Fistula, Rehabilitation

POSTER PRESENTATION - 4

Positional Femoral Entrapment Neuropathy: A Case Report

Presenter:

Giridhar Gundu, MD¹

Collaborators:

Oscar Ortiz Vargas, MD²

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

²Veterans Affairs Medical Center, Lexington, KY

Abstract Text:

A 63 year old male with 8 month duration of left anterior-medial leg burning pain, radiating to the ankle, relieved with lying flat or upon standing and worse with sitting, not exacerbated with walking, nor associated with weakness. Upon physical exam, skin was intact without trophic changes, erythema, or swelling around the area of interest. There was no tenderness or allodynia on palpation, normal motor and sensory exam with symmetric deep tendon reflexes. It is noteworthy that the patient sat with left hip and knee in full extension. He had already undergone extensive diagnostic studies, including bone scan and electro-diagnostic (EDx) testing, with no abnormal results. However, considering the positional nature of reproduction of patient's symptoms, a repeat EDx testing was performed in sitting and supine positions, focusing on the left femoral nerve above and below the inguinal ligament.

Setting: Outpatient clinic.

Results: Positional dynamic EDx of the left femoral nerve revealed a partial conduction block below the inguinal ligament in the sitting position that corrects with patient in supine. Contra-lateral side did not demonstrate these findings. This highly suggests an entrapment of the femoral nerve at the left inguinal ligament associated with hip flexion.

Discussion: This is the first reported case, to our knowledge, of positional femoral entrapment neuropathy at the inguinal ligament. This case also illustrates a novel EDx approach that can be performed with patient in different positions.

Conclusions: Posture can be a possible etiology for femoral entrapment neuropathy. EDx testing being an extension of the physical exam should be adapted according to the patient's symptom presentation.

Key Words: Femoral Neuropathy, Electrodiagnosis, Conduction Block

POSTER PRESENTATION - 5

Concurrent Acute Disseminated Encephalomyelitis and Guillain-Barré Syndrome in a Child: A Case Report

Presenter:

Radha Korupolu, MBBS, MS¹

Collaborators:

Nawaz Hack, MD², Sara Shahid Salles, DO¹

Departmental Affiliations:

¹Department of Physical Medicine & Rehabilitation, University of Kentucky, Lexington, KY

²Department of Neurology, University of Kentucky, Lexington, KY

Abstract Text:

Setting: Tertiary care pediatric hospital & acute inpatient rehabilitation hospital.

Patient: A 5-year old girl with acute Tetraparesis

Case Description: The patient presented to our tertiary care hospital with tetraparesis and areflexia. Magnetic resonance imaging (MRI) of the brain and spine showed T2 hyperintense signals in bilateral thalamus and spinal cord. Cerebrospinal fluid analysis revealed elevated protein and leukocyte levels. These findings were consistent with acute disseminated encephalomyelitis (ADEM). After minimal response to intravenous steroids, she was treated with intravenous IgG. Subsequent nerve conduction studies performed due to persistent areflexia suggested acute motor-sensory axonal neuropathy, a rare variant of Guillain-Barré syndrome (GBS). Repeat MRI of spine showed increased enhancement of multiple spinal nerve roots and cauda equina, compatible with the diagnosis of GBS. The concomitance of ADEM and GBS is unusual and notable.

Clinical Course of Rehabilitation: On day 22, at admission to inpatient rehabilitation, she exhibited persistent tetraparesis with no involvement of bladder and bowel. Her balance was poor, and she required total assistance for transfers and activities of daily living. She was non-ambulatory.

She received intensive rehabilitation during a 27-day inpatient stay. At discharge, her sitting balance was fairly improved, and she was able to perform upper and lower body dressing with minimal assistance, although she required maximum assistance for transfers. She was able to ambulate in a seated walker with minimal assistance and propel a wheelchair with supervision. She was discharged to home with continued rehabilitation services via home health.

Conclusion: To our knowledge, simultaneous ADEM and GBS is rare. Little evidence in the literature addresses functional recovery in children with this diagnosis. Multidisciplinary team work, early and intensive inpatient rehabilitation, and continuum of care appear to be critical in such cases.

Key Words: Encephalomyelitis, Guillain-Barré Syndrome, Pediatrics, Rehabilitation

POSTER PRESENTATION - 6

The NRF2-ARE Pathway as a Therapeutic Target for Acute Traumatic Brain Injury: Dose Response of Carnosic Acid

Presenter:

Darren M. Miller¹

Collaborators:

Indrapal N. Singh, PhD¹, Juan A. Wang², Edward D. Hall, PhD¹

Departmental Affiliations:

¹Spinal Cord & Brain Injury Research Center; Department of Anatomy & Neurobiology, University of Kentucky, Lexington, KY

²Spinal Cord & Brain Injury Research Center, University of Kentucky, Lexington, KY

Abstract Text:

Traumatic brain injury (TBI) currently signifies a substantial health and socioeconomic dilemma in the United States with 50,000 cases resulting in death yearly. The pathophysiological importance of oxidative damage after TBI has been extensively demonstrated. The transcription factor Nrf2 mediates transcription of antioxidant/cytoprotective genes by binding to the antioxidant response element (ARE) within DNA. Upregulation of these genes constitutes a pleiotropic cytoprotective-defense pathway. Previously, we demonstrated the *in vivo* post-injury time-course of Nrf2-ARE mediated gene expression in the cortex and hippocampus of male CF-1 mice utilizing a unilateral controlled cortical impact (CCI) injury model. Interestingly, increased Nrf2-ARE mediated expression was not observed until 24 hours, whereas our recent work showed oxidative damage also peaking 24-48 hours post-TBI. Additionally, we recently demonstrated that pre-treatment 48 hours prior with either of the Nrf2-ARE activating drugs sulforaphane (5.0 mg/kg) or carnosic acid (1.0 mg/kg) could provide protection to cortical mitochondria challenged by the toxic lipid peroxidation byproduct 4-hydroxy-2-nonenal (4-HNE) *ex vivo*. Thus, we now sought to determine the *in vivo* dose response of the potent Nrf2-ARE activator carnosic acid and assess its neuroprotective potential in a mouse model of TBI. Young adult male CF-1 mice were administered carnosic acid (CA) at one of three different doses – 0.3, 1.0, or 3.0 mg/kg I.P. or vehicle at 15 minutes post-injury. At 48 hours post-injury, the ipsilateral cortex and hippocampus tissues were dissected out and levels of the oxidative damage marker 4-HNE were assessed by Western blotting. In the cortex, both 1.0 and 3.0 mg/kg doses of CA significantly ($p<0.05$) reduced levels of 4-HNE as compared to vehicle animals, whereas the 0.3 mg/kg dose did not. In the hippocampus, only the 1.0 mg/kg dose of CA significantly ($p<0.05$) reduced 4-HNE levels compared to vehicle, whereas the 0.3 and 3.0 mg/kg doses did not. The 1.0 mg/kg dose of CA was also that which we previously demonstrated to be effective at attenuating 4-HNE induced dysfunction in cortical mitochondria. Therefore, ongoing and future studies will determine the efficacy of this optimal 1.0 mg/kg CA dosing administration on attenuating post-TBI behavioral deficits and neurodegeneration. Collectively, these data demonstrate that carnosic acid may be a promising therapeutic agent for the treatment of TBI and warrants further investigation.

Key Words: Traumatic Brain Injury, Antioxidants, Gene Expression

POSTER PRESENTATION - 7

CNS Histoplasmosis with Tetraparesis: A Case Report

Presenter:

Francisco Angulo Parker¹

Collaborators:

Sara Shahid Salles, DO¹, David Brough, MD¹

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

Abstract Text:

Setting: Inpatient Rehabilitation

Patient: 13-year old girl with tetraparesis due to CNS histoplasmosis.

Case Description: The patient presented to the inpatient rehabilitation hospital with a 3-month history of recurrent headache, abdominal pain, acute deterioration in mental status, and asymmetric tetraparesis.

Assessment/Results: Magnetic resonance imaging revealed leptomeningeal enhancement along with several lacunar infarcts in basal ganglia and temporal lobes bilaterally. Cerebrospinal fluid serological test yielded positive for *Histoplasmosis capsulatum*. Intravenous antifungal therapy with amphotericin B, adequate fluid and electrolyte management, and seizure and peptic ulcer disease prophylaxis were promptly initiated. However, sequelae remained, including asymmetric tetraparesis (right greater than left), gait abnormality, balance deficits, foot drop, cognitive deficits, mood lability, and functional decline. Multidisciplinary inpatient rehabilitation was crucial to manage her condition and return her to functional independence. Specifically, occupational therapy reported independence in eating and grooming as well as minimal assist for transfers at discharge. Follow-up after discharge included neuropsychological evaluation as well as outpatient physical and occupational therapy.

Discussion: The prognosis for functional recovery associated with CNS histoplasmosis has been considered unfavorable. Literature often describes epidemiology, workup, pharmacotherapy, and sequelae; but much less is discussed in regards to the importance of multidisciplinary rehabilitation for functional recovery. Here we presented a case where restorative and adaptive rehabilitative approaches were crucial for dramatic functional recovery (as measured by Functional Independence Measure). In particular, occupational therapy ensured significant improvement towards independence in major areas of function.

Conclusion: In addition to the clinical care, multidisciplinary rehabilitation is crucial to maximize functional improvement in patients with CNS Histoplasmosis.

Key Words: Histoplasmosis, Tetraparesis, CNS, Functional Outcomes

POSTER PRESENTATION - 8

Discrimination of Attempted Movements from Rest Using an EEG Brain-Machine Interface for Rehabilitation from Neural Injury

Presenter:

Elizabeth Salmon¹

Collaborators:

KC Chelette, MS², Lumy Sawaki, MD, PhD², Sridhar Sunderam¹

Departmental Affiliations:

¹ Center for Biomedical Engineering, University of Kentucky, Lexington, KY

² Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

Abstract Text:

Neurological trauma, as in spinal cord injury and stroke, can severely impair normal motor functions. Brain-machine interfaces (BMIs) have been developed to decode brain signals into control commands for prosthetic devices. The sensorimotor “mu” rhythm of the electroencephalogram (EEG) is commonly used for BMI control. This idling rhythm (seen at rest) is suppressed by actual/imagined movement. Beyond their use as assistive devices, BMIs could facilitate motor recovery. Studies suggest that repetitive exercises induce beneficial neuroplastic changes in motor cortex and afferent peripheral nerve stimulation can augment this recovery. We hypothesize that stimulation-induced plastic changes could be enhanced further by selectively rewarding attempted movement with closely timed stimulation. Detection of effort directly from the brain and contingent stimulation could be accomplished using an EEG-BMI. Here, we test the feasibility of detecting cued hand movements from continuously recorded EEG. We measured EEG and grasping force in five healthy volunteers over three weekly sessions with IRB approval. Subjects responded to intermittent visual cues (6-10s apart) by squeezing a dynamometer with the left/right hand. Their EEG was classified offline based on spectral band power and other features using a linear classifier, trained on each subject's data pooled from two sessions and tested on the third. In four of five subjects with acceptable signal quality, rest, sham, left, and right samples were classified with mean accuracy of 79% (76-84%) during cross-validation within the training set, and 62% (40-73%) on the test set. Hence, EEG detection of motor intent for the proposed rehabilitation trials is feasible.

Key Words: Brain-machine Interface, Rehabilitation, Motor Injury

POSTER PRESENTATION - 9

Peripheral Nerve Stimulation Dose-Response Relationship in Chronic Stroke: Early Results from an Ongoing Trial

Presenter:

Emily Salyers¹

Collaborators:

KC Chelette, MS¹, Cheryl Carrico, MS, OT/L¹, Laurie Nichols, BS, OT/L¹, Cameron Henzman, BS², Lumy Sawaki, MD, PhD¹

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, KY

²College of Medicine, University of Louisville, Louisville, KY

Abstract Text:

Objective: To better understand the dose-response relationship of peripheral nerve stimulation (PNS) as an adjunctive intervention paired with upper extremity motor training for subjects with severe post-stroke motor deficit.

Design: Twenty-eight subjects with chronic stroke were randomly assigned to 1 of 5 groups in an ongoing double-blind study (projected total enrollment: n=60). Each subject received PNS and upper extremity motor training on a robot-assisted device. The intervention varied with respect to PNS intensity (i.e., eliciting compound action muscle potentials (CMAPs) either *above* or *below* 100 μ v, or *sham* (i.e., 0 μ v)) and PNS timing (i.e., delivered either *before* or *during* training). Baseline evaluation preceded 10 consecutive weekdays of intervention. We used the Fugl-Meyer Assessment Scale (FMA; primary outcome measure) and the Stroke Impact Scale (SIS) to measure motor performance and recovery of function.

Results: At completion evaluation, all groups showed improvement in total motor scores on the FMA. The Below/During group had greater improvement than all other groups (significant in comparing "Below/During" with "Below/Before," "Above/During," and "Sham."). SIS scores generally followed the same pattern as FMA scores, with "Below/During" showing significantly more improvement than "Sham" at completion evaluation.

Conclusions: Our preliminary data suggest that variation of PNS intensity and timing relative to motor training carries great potential to advance neurorehabilitation strategies to promote functional recovery for stroke survivors with chronic, severe upper extremity motor deficit.

Key Words: Peripheral Nerve Stimulation, Stroke, Motor Recovery

POSTER PRESENTATION - 10

The Therapy Gym: Is it Therapeutic?

Presenter:

Camille Skubik-Peplaski, PhD, OTR/L, BCP, FAOTA¹

Collaborators:

Dana Howell, PhD, OTR¹, Beth Hunter, PhD, OTR²

Departmental Affiliations:

¹Department of Occupational Therapy, Eastern Kentucky University, Richmond, KY

²Cardinal Hill Rehabilitation Hospital, Lexington, KY

Abstract Text:

Background Information: Traditionally, therapy gym environments on inpatient rehabilitation stroke programs focus on interventions that prepare an individual to perform occupations and address impairments. The profession of occupational therapy and the motor control literature espouses that therapy should focus on providing interventions that offer participation in occupations (Ferguson & Trombly, 1997; Hubbard, Parson, Neilson & Carey, 2009).

Objective: The purpose of this study was to investigate the influence of the therapy gym environment on occupational therapy interventions.

Methods: This was a three phase mixed method study completed at a 108 bed, Midwestern, freestanding rehabilitation hospital. Primary participants were five occupational therapists with secondary participants being the clients who were treated.

Data Collection and Analysis: Data was collected and analyzed simultaneously to achieve constant comparison with analysis consisting of axial coding to identify themes. Frequency data regarding the type of intervention and the overall number of sessions, time of sessions and the ratio of time to the number of sessions were calculated by a t-test. Extended observations, peer debriefing, member checking and triangulation with the literature and the quantitative outcomes ensured that the study was accurate and valid.

Results/Limitations/Conclusions: This study found that the therapists preferred to provide therapy in the gym using preparatory methods, limiting participation in occupations. The gym did provide security, habit, routines and camaraderie for the therapists. Central to occupational therapy practice is the use of occupations and the environment must support the use of occupations to foster a client's ability to return home successfully.

Key Words: Occupations, Environment and Rehabilitation

POSTER PRESENTATION - 11

Non-Invasive Brain Stimulation Paired with a Novel Locomotor Training in Chronic Stroke: a Feasibility Study

Presenter:

Megan Danzl, PT, NCS, PhD¹

Collaborators:

KC Chelette, MS², Kara Lee, PT, DPT¹, Dana Lykins, PT, DPT¹, Lumy Sawaki, MD, PhD²

Departmental Affiliations:

¹Cardinal Hill Rehabilitation Hospital, Lexington, KY

²Department of Physical Medicine & Rehabilitation, University of Kentucky, Lexington, KY

Abstract Text:

Objective:

To determine the feasibility of combining transcranial direct current stimulation (tDCS) of the lower extremity (LE) motor cortex with novel locomotor training to facilitate gait and neuroplastic change in subjects with chronic stroke.

Methodology:

Double-blind, randomized controlled study. We enrolled 10 subjects with chronic stroke; outpatient rehabilitation setting. Subjects were stratified according to baseline LE motor function then randomized to either active tDCS (20 min; 2mA) or sham tDCS for 12 sessions over 1 month. Both groups participated in identical locomotor training following each tDCS session. Training protocol (robot-assisted treadmill (Lokomat)) was designed to harness corticospinal neuroplasticity. Primary outcome measure: 10-Meter Walk Test (10MWT). Other outcome measures: Functional Ambulation Category (FAC), Timed Up and Go (TUG), Berg Balance Scale (BBS), Stroke Impact Scale-16 (SIS); cortical excitability (transcranial magnetic stimulation (TMS)).

Results:

Eight subjects completed the study (4 men; mean age 67.8 years; mean years post-stroke: 4). ANOVA trended towards improvement for both groups. Active tDCS group showed more marked improvement than sham in all measures (FAC p=0.028; 10 MWT p=0.19; TUG p=0.066; SIS p=0.062) except BBS (p=0.919). TMS recruitment curves demonstrated increased cortical excitability at completion and 1-month follow-up.

Important Findings:

It is feasible to combine tDCS targeting the LE motor cortex with novel locomotor training. It appears that tDCS has the potential to improve gait in chronic stroke. Our novel locomotor training also appears to enhance corticospinal excitability. Results warrant larger studies applying tDCS and locomotor training, particularly regarding stroke survivors with low ambulation.

Key Words: Transcranial Direct Current Stimulation, Hemiparesis, Neuroplasticity, Motor Recovery, Robotics; Lower Extremity

POSTER PRESENTATION - 12

Botulinum Toxin A Injection to Facial Muscles in Patient with Stiff Person Syndrome Implanted with Baclofen Pump: A Case Report

Presenter:

Praveen Pakeerappa, MD¹

Collaborators:

Pravardhan Birthi, MD¹, Sara Shahid Salles, DO¹

Departmental Affiliations:

¹Department of Physical Medicine & Rehabilitation, University of Kentucky, Lexington, KY

Abstract Text:

Settings: Outpatient rehabilitation clinic.

Patient: 48 year old Caucasian male with history of Stiff Person Syndrome (SPS).

Case Description: We present a patient with history of SPS for 17 years with stiffness prominent bilaterally in the upper and lower extremities. He failed medical management with oral benzodiazepines and experienced side effects with high doses of oral baclofen. Subsequently Baclofen pump was implanted, with some relief of symptoms. On follow up visit to the outpatient clinic, it was noticed that his stiffness reduced and his ADLs improved, but he continued to have bruxism and neck stiffness. Botulinum toxin A was then injected to the masseter muscle and paraspinal muscles.

Assessment/results: Patient experienced dramatic improvement in neck stiffness and bruxism for a period of 3 months after which he required re-injection of Botulinum toxin A with similar beneficial results.

Discussion: SPS is a rare autoimmune neurologic disorder. It is characterized by generalized rigidity, intermittent and superimposed spasms as well as increased sensitivity to external stimuli. The standard treatment for SPS has been benzodiazepines, a GABA neuromodulator. The autoimmune hypothesis of the disorder has been supported due to relief of the symptoms provided by immunotherapy. Baclofen is also another logical therapy for SPS because of its action on GABA-B receptor agonist. On the other hand, the effects of Botulinum Toxin A therapy for the treatment of SPS remains unclear. There is scant data regarding the benefit of Botulinum toxin A for the symptomatic relief of SPS. Botulinum toxin A demonstrated improvement of stiffness which was refractory to the standard treatment on SPS in our patient.

Conclusion: Botulinum toxin A can be considered as mode of management for bruxism and neck stiffness in addition to the Baclofen pump for symptomatic relief in patients with stiff person syndrome.

Key Words: Neck Stiffness, Bruxism, Stiff Person Syndrome

NOTES

KEYNOTE SPEAKER PRESENTATION

“Clinical Trials in Pain Medicine”



STEVEN COHEN, MD, PhD

Dr. Steven P. Cohen obtained his medical degree at the Mount Sinai School of Medicine in New York City, completed an anesthesiology residency at Columbia University, and a pain management fellowship at Massachusetts General Hospital, Harvard Medical School. Currently, he is Professor of Anesthesiology & Critical Care Medicine at the Johns Hopkins School of Medicine, and Professor at the Uniformed Services University of the Health Sciences in Bethesda, MD. He is also the Director of Medical Education and Quality Improvement for the Pain Management Division at Johns Hopkins, Director of Pain Research at Walter Reed National Military Medical Center, and the Reserve Liaison to the U.S. Army Pain Management Consultant to the Surgeon General.

Dr. Cohen has been very active in teaching and pain research in recent years, having published more than 150 peer-reviewed articles and 50 book chapters in the past 10 years. Among his major contributions are the development of a new FDA-approved technique for treating sacroiliac joint pain (lateral branch radiofrequency denervation), for which Dr. Cohen published the first reports of this technique as well as the first controlled study, inventing the intravenous ketamine test to help determine treatment strategy in patients with chronic pain, and performing the first controlled studies evaluating the local administration of tumor necrosis factor inhibitors for pain treatment. His recent placebo-controlled, dose-response and concurrent animal safety study evaluating epidural etanercept was named one of the top 3 pain research papers in 2009 by 'Anesthesiology', the leading journal in the specialty. Some of his more recent work has focused on comparative-effectiveness studies and improving pain care in wounded soldiers. These include establishing that MRI do not improve outcomes in patients with sciatica scheduled for epidural steroid injections, outcome data from the first pain clinic ever established in a combat zone (the most highly publicized article in 'Anesthesiology'), and conducting epidemiological studies evaluating a wide range of pain conditions. These full-length articles have been featured in some of the top general medical journals including "Lancet", "CMAJ", "BMJ", "Annals of Internal Medicine" and "Archives of Internal Medicine". Dr. Cohen is currently the Principal or Senior Investigator on nearly a dozen studies, including several multi-center clinical trials. He is also an author on the "Pain" chapter in the latest edition of "Cecil Textbook of Medicine", one of the premier medical textbooks in the world.

Dr. Cohen plays an active role in many organizations. He currently serves on the Editorial Boards of 'Regional Anesthesia & Pain Medicine', 'Pain Medicine', 'Pain Physician' and half a dozen other journals. He has been on the organizing committees for the American Academy of Pain Medicine and American Society of Regional Anesthesia & Pain Medicine (ASRA) for the past several years, and is the 'Chair-elect' for the 2013 Annual ASRA Pain Meeting.

In addition to his academic work in pain management, Dr. Cohen is a Colonel in the Army Reserve, and the Chief, Anesthesia & Operative Services at the 48th Combat Support Hospital in Maryland. He also serves as the Reserve Liaison to the Pain Management Consultant to the U.S. Army Surgeon General. Over the past few years, Dr. Cohen has briefed or presented data on pain management issues in service members several times to the U.S. Congress and high-ranking general officers. His research was instrumental in the passage of the 2008 Military Pain Care Act, and he served as an inaugural member of the first U.S. Army Medical Advisory Board.

NOTES

CLINICAL TRIALS IN PAIN MEDICINE

Steven P. Cohen

OBJECTIVES

- Understand the effect perspective has on the evaluation of interventional pain outcomes
- Understand the differences between "efficacy" and "effectiveness"
- Learn to identify and eliminate different forms of "bias"
- Identify the limitations of placebo-controlled studies, and their generalizability

HOW IMPORTANT IS PERSPECTIVE?

"The Philistines made frequent incursions against the Hebrews. There was almost perpetual war between the two peoples. But no Philistine writings survive, unlike the Old Testament, which is often taken at 'face value'."

Unlike the common belief, the Philistines were not unsophisticated, uncultured brutes, but advanced, refined people. In fact, for several generations their culture was years ahead of Israel's, a disparity they maintained through their martial superiority.



■ **Nonsurgical Interventional Therapies for Low Back Pain**
A Review of the Evidence for an American Pain Society Clinical Practice Guideline

Roger Chou, MD,*† Steven J. Atlas, MD, MPH,‡ Steven P. Stanos, DO,§ and Richard W. Rosenquist, MD¶

"We found insufficient evidence from randomized trials to reach reliable conclusions regarding radiofrequency denervation for presumed facet joint pain."

Spine 2009

EVIDENCE-BASED MEDICINE

Evidence-based Interventional Pain Medicine according to Clinical Diagnoses

12. Pain Originating from the Lumbar Facet Joints

Maarten van Kleef, MD, PhD, FIPP^{1,2}; Pascal Vanelnderen, MD, FIPP^{2,3}; Steven P. Cohen, MD^{3,4}; Arno Lataster, MSc^{5,6}; Jan Van Zundert, MD, PhD, FIPP^{1,2}; Nagy Mekhail, MD, PhD, FIPP^{1,7}

"Currently, the 'gold standard' for treating lumbar facetogenic pain is radiofrequency treatment (1 B+)"

Pain Pract 2010

TALE OF TWO STUDIES

- Leclaire et al. 2001
- Compared RF & sham denervation in 70 pts with axial LBP (screened 76)
- Criterion: "Significant relief > 24 h after single IA block lidocaine & steroid
- Study showed negative results
- MQ-4, CR-8
- Nath et al. 2008
- Compared RF & sham denervation in 40 pts with axial LBP (screened 376)
- Criterion: > 80% relief after 3 MBB
- Created 6 lesions without stimulation
- At 6-mo, RF > control for all outcomes
- MQ-4, CR-6

Systematic Review

Effectiveness of Therapeutic Lumbar Transforaminal Epidural Steroid Injections in Managing Lumbar Spinal Pain

Lennarth Marchianni, MD, Ricardo M. Buenaventura, MD, Karla N. Marchianni, MD, Kula Ram, MD, Saranya Gupta, MD, Howard S. Smith, MD, Paul J. Christo, MD, and Stephen F. Ward, MD

“For lumbar disc herniation, the evidence is good for transforaminal epidural with local anesthetic and steroids & fair for local anesthetics alone and the ability of transforaminal epidural injections to prevent surgery.”

Pain Physician 2012

O. Airaksinen
J. L. Brox
C. Cedraschi
J. Hildebrandt
J. Klaber-Moffett
F. Kovacs
A. F. Mannion
S. Reis
J. B. Staud
H. Urwin
G. Zanoli

**Chapter 4
European guidelines
for the management of chronic
nonspecific low back pain**

- There is no evidence for ESI in non-radicular, non-specific LBP
- Should only be considered for radicular pain, if a contained disc prolapse is the cause of the pain, and if the corticosteroid is injected close to the target (nerve root)
- The injection should be x-ray guided and aimed towards the ventral epidural space or via a transforaminal approach
- There is conflicting evidence that epidural steroids without x-ray guidance are effective for radicular pain

European Spine Journal 2006

Evidence-informed management of chronic low back pain with epidural steroid injections

Michael J. DePalma, MD^{a,b,*}, Curtis W. Slipman, MD^{c,d}

- TFESI, because they are ‘target-specific’ and are the best means to ensure anterior epidural spread, are “most appropriate” in targeting pain from an intervertebral disc
- Evidence supports non-targeted ESI for short-term improvement in nonspecific chronic LBP
 - 1-3 CESI are effective in reducing nonspecific chronic LBP in the short-term

Spine Journal 2008

Epidural Steroid Injections and Selective Nerve Root Blocks

Timothy S. Eckel, MD,* and Walter S. Bartsynski, MD†

- ESI and SNRB are the foundation for any image-guided pain management practice
- ESI are highly effective in a large proportion of patients, including those with axial pain, radiculopathy & spinal stenosis
- Sustained relief can be achieved in a substantial number of patients with both types of procedures

Tech Vasc Intervent Radiol 2009

■ Treatment of Neck Pain

Injections and Surgical Interventions: Results of the Bone and Joint Decade 2000–2010 Task Force on Neck Pain and Its Associated Disorders

Eugene J. Carragee, MD, FACS,* Eric L. Hurwitz, DC, PhD,† Ivan Cheng, MD,‡
Linda J. Carroll, PhD,§ Margaretta Nordin, PT, DMedSc,¶
Jaime Guzman, MD, MSc, FRCP(C),|| Paul Peloso, MD, MSc, FRCP(C),**
Lene W. Holm, DMedSc,†† Pierre Côté, DC, PhD,‡‡ Shelia Hogg-Johnson, PhD,§§
Gabrielle van der Walde, DC,¶¶ J. David Cassidy, DC, PhD, DMedSc,|||
and Scott Haldeman, DC, MD, PhD***

“There is support for short-term symptomatic improvement of cervical radicular symptoms with epidural steroid injections, but not long-term benefit.”

Spine 2008

FAMILY MEDICINE AND THE HEALTH CARE SYSTEM

Overtreating Chronic Back Pain: Time to Back Off?

Richard A. Deyo, MD, MPH, Sobail K. Mirza, MD, MPH, Judith A. Turner, PhD, and
Brooke J. Martin, MPH

“The efficacy of spinal injections is limited. Epidural corticosteroid injections may offer temporary relief of sciatica, but both European and American guidelines, based on systematic reviews, conclude they do not reduce the rate of subsequent surgery... Despite the limited benefit of epidural injections, Medicare claims showed a 271% increase during a recent 7-year interval.”

Journal American Board of Family Medicine 2009

Assessment: Use of epidural steroid injections to treat radicular lumbosacral pain

Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology

Carol Annas, MD, MPH; Charles E. Argoff, MD; Jeffrey Samuels, MD; and Misha Miralashvili Tschanz, MD

"In general, epidural steroid injections for lumbosacral radicular pain do not impact function, need for surgery or provide long-term pain relief beyond 3 months."

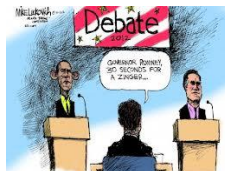
Neurology 2007

TALE OF TWO STUDIES

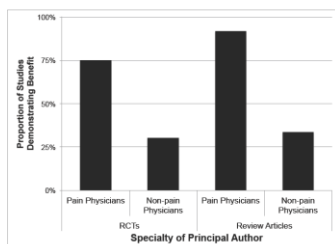
- o Carette et al. NEJM 1999
- o DB, PC study evaluating 158 pts with LSR < 12 wks 2° HNP
- o Rx group rec'd up to 3 'blind' ESI with 10 ml steroid & saline
- o Control rec'd up to 3 epidural injections with 1 ml saline
- o Both groups improved. No difference between groups from 3-12 wks
- o Ghahreman et al. Pain Med 2010
- o DB, PC study evaluating 130 pts with LSR 2° to HNP
- o Compared up to 2 injections of TF steroid & LA to TF LA, TF saline, IM steroid & IM saline
- o Fluoroscopy used
- o TF steroids > TF saline = IM steroids > IM saline & TF LA

WHY THE DIFFERENCE?

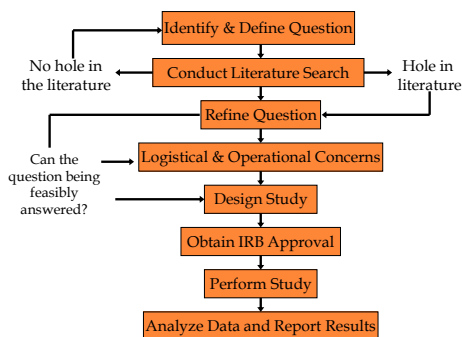
- o Confirmation bias
- o Better ability of "experts" to design studies & evaluate selection & technique
 - o Methodological vs. technical quality
- o Publication bias
- o Secondary gain
 - o Fee-for-service system awards quantity, not outcomes



ESI OUTCOMES STRATIFIED BY SPECIALTY



CONDUCTING RESEARCH



DEFINE QUESTION

- Epidemiology vs. diagnosis vs. treatment
- Must weigh magnitude of problem, likelihood of benefit & consequences of success & failure
 - Back pain vs. trigeminal neuralgia
- Avoid "mission creep"
 - Limit to 1 or 2 simple questions
 - Feasibility vs. fundability vs. interesting vs. impact



OPERATIONAL & LOGISTICAL CONCERNS

Factor

- Is the study population accessible & achievable?
 - Power analysis
- Is study ethical, and will patients enroll?
- Need for & availability of funding
- Identify outcome measures & time frame

Considerations

- Study site & culture, investigator experience, drawbacks of under- or over-powering study
- Assess need & risk of control group, need for rescue medication, consider crossover or early exit for treatment failures in placebo-controlled studies. Enrollment contingent on demographics, socioeconomic status & culture
- Cost of control >> CE studies. Utilize resources (e.g. residents & students). Tailor grant submission to organizational needs
- Are they "measurable" & validated? Who will obtain data? How frequently should surveillance occur?

INNOVATION: COMPARATIVE-EFFECTIVENESS STUDIES DONE WITHOUT FUNDING

PAIN MEDICINE

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Randomized Placebo-controlled Study Evaluating Lateral Branch Radiofrequency Denervation for Sacroiliac Joint Pain

Steven P. Cohen, M.D.,¹ Robert W. Hurley, M.D., Ph.D.,¹ Chester C. Buckenmaier III, M.D.,¹ Connie Kurland, R.N.,² Benny Morlando, R.N.,³ Anthony Dragosovich, M.D.¹

ONLINE FIRST

Effect of MRI on Treatment Results or Decision Making in Patients With Lumbosacral Radiculopathy Referred for Epidural Steroid Injections

A Multicenter, Randomized Controlled Trial

Steven P. Cohen, MD, Anita Gupta, DO, PharmD; Scott A. Strassels, PhD, PharmD; Paul J. Christo, MD, MBA; Michael A. Erdek, MD; Scott R. Griffith, MD; Connie Kurland, RN; Chester C. Buckenmaier III, MD; David Lombardi, MD; Toshiya Ito, MD, PharmD

COMPARATIVE-EFFECTIVENESS STUDIES DONE WITHOUT FUNDING

BMJ

RESEARCH

Comparison of fluoroscopically guided and blind corticosteroid injections for greater trochanteric pain syndrome: multicentre randomised controlled trial

Steven P. Cohen, associate professor;^{1,2} Scott A. Strassels, assistant professor;¹ Leslie Fraser, assistant professor;¹ Jhe Marvel, assistant professor;¹ Kayode Williams, assistant professor;¹ Matthew Crooks, assistant professor;¹ Andrew Gross, pain management fellow;¹ Connie Kurland, pain management center;² Cong Nguyen, chief;³ Neela Williams, chief¹

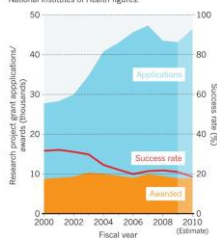
Multicenter, Randomized, Comparative Cost-effectiveness Study Comparing 0, 1, and 2 Diagnostic Medial Branch (Facet Joint Nerve) Block Treatment Paradigms before Lumbar Facet Radiofrequency Denervation

Steven P. Cohen, M.D.,¹ Kayode A. Williams, M.D., M.B.A.,¹ Connie Kurland, R.N.,¹ Cong Nguyen, M.D.,³ Cynthia Shanks, M.D.,¹ Peter Kim, M.D.,¹ Scott R. Griffith, M.D.,¹ Thomas M. Larkin, M.D.,¹ Matthew Crooks, M.D.,¹ Neela Williams, M.D.,¹ Benny Morlando, R.N.,¹ Scott A. Strassels, Pharm.D., Ph.D.¹

SOURCES OF FUNDING

- Order of Difficulty: NIH > "other government" > Private & public foundations > Internal > Industry
- Understand the organizational "needs"
 - DoD funds cancer, Alzheimer's chronic pain, SCI, TBI etc.
- Industry-sponsored studies 3.6
 - more likely to yield (+) results
 - Effect amplified more by publication bias
 - Who owns the data?
 - Influence on manuscript preparation & interpretation
 - Subtle ways to influence results
 - Industry effect on reported outcomes (e.g. Vioxx, Oxycontin & other opioids, IDET, Disc replacement etc.)

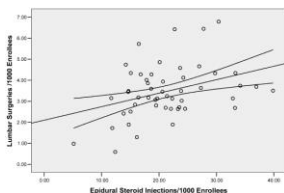
APPLICATIONS UP, SUCCESS RATES DOWN
National Institutes of Health figures.



WHAT DEFINES A "POSITIVE OUTCOME"?

- Pain scores
- Physical functioning
- Emotional functioning/sleep
- Satisfaction
- Symptoms & AE's
- Disposition (adherence to regimen & withdrawal)
- ~~Need for surgery~~
- ~~Return to work~~
- Composite or combined outcomes?
- Previous studies have demonstrated a 2-pt or 30% decrease in pain scores to be clinically significant
- Few studies have evaluated psychological functioning
- Even fewer studies have evaluated RTW

CORRELATION BETWEEN ESI & SURGERY RATE



Pearson's $r = 0.30$, $p = 0.001$, 2001 Medicare Database

Effect of ESI to Prevent Spine Surgery Randomized Controlled Trials

RCTs: Negative

- Tafazal 2009, Ng 2005, Arden 2005, Wilson-MacDonald 2005, Karppinen 2001, Carrette 1997, Dilke 1973, Cohen 2009 & 2012, Price 2005, Ghahreman 2011, Cuckler 1985, Bush 1991, Klenerman 1984, Kramer 1997, Snoek 1977, Mathews 1987, Valat 2003

RCTs: Positive

- Iversen 2011**
- Sayegh 2009

Uncontrolled Studies: Positive

- Narozny 2001
- Wang 2002
- Lin 2006 (neck)
- Manson 2013

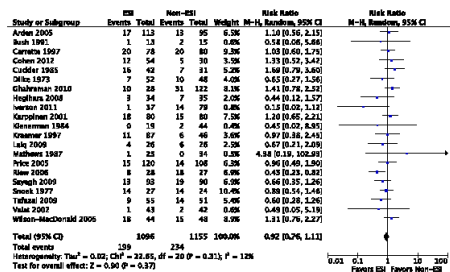
Subgroup Analyses & Primary Outcome Measures

Subgroup Analyses

- Radcliffe et al. 2012
 - In SPORT trial for HNP, more pts who rec'd ESI within 3 mos changed from surgical to nonsurgical treatment (41% vs. 12%) & fewer expressed preference for surgery (19% vs. 56%)
 - For spinal stenosis, more in surgery group who rec'd ESI changed from surgery to nonsurgical treatment (33% vs. 11%), but more in nonsurgical group who rec'd ESI crossed over to surgery (58% vs. 32%). Fewer who rec'd ESI expressed preference for surgery (62% vs. 33%)

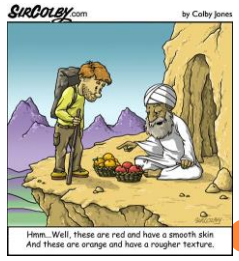
Primary Outcome

- Riew et al. JBJS 2006
- DB, RCT where 55 pts with stenosis or HNP were enrolled by 4 surgeons
- Rec'd up to 3 TFESI with 1 mL LA + saline or 1 mL LA + 1 mL betamethasone
- 18 of 27 LA pts had surgery vs. 8 of 28 steroid pts
- At 5-year f/u, 3 of 12 steroid pts followed had surgery vs. 1 of 9 LA pts



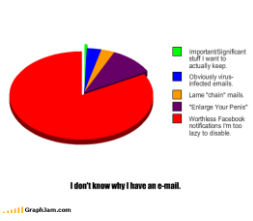
UNLESS A STUDY IS DESIGNED TO DETECT DIFFERENCES IN OPERATIVE RATES, THE CHANCE OF FINDING A SIGNIFICANT DIFFERENCE IS LITTLE TO NONE

- Need to have pts with short-duration pain, surgically amenable pathology, who are otherwise going to have surgery
- Need to have same surgeon, with standardized indications

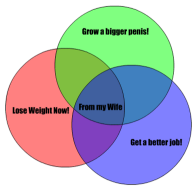


STATISTICS CAN YIELD DIFFERENT CONCLUSIONS FROM SIMILAR DATA & BE PRESENTED DIFFERENTLY

Contents of My E-Mail Inbox



The contents of my email Inbox



Annals of Internal Medicine

ORIGINAL RESEARCH

Epidural Steroids, Etanercept, or Saline in Subacute Sciatica

A Multicenter, Randomized Trial

Steven P. Cohen, MD; Ronald L. White, MD; Conner Kurland, MD; Thomas M. Laskin, MD; Audrey Chang, PhD; Scott R. Griffin, MD; Christopher Gilligan, MD; Ralph Lattin, PhD; Benny Klotzsch, MD; Paul F. Pappas, MD; Tony L. Yasko, PhD; and Cammie Nguyen, MD

“For Back Pain, Steroid Shots No More Effective Than Placebo”. Nicholas Bakalar, New York Times, April 27, 2012

Variable	ANOVA	ANCOVA	Multiple Regression
Leg Pain	0.07	0.24	< 0.001
Back Pain	0.20	0.40	0.008
Functional Capacity	0.03	0.006	0.005

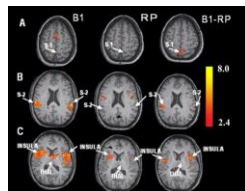
PLACEBO EFFECT “I WILL PLEASE”

- Response rates vary from 0% to > 70%
- Factors affecting response include pt and doctor expectations, brand name > generic, conditioning, genes, procedures > pills, disorder, children > adults, psych factors etc.
- Effects diminish w/ time, but expectation bias can increase with time
- Duration variable but can last months or years

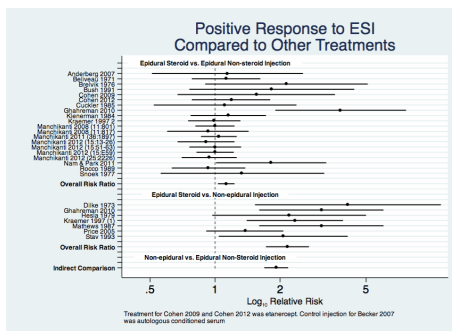


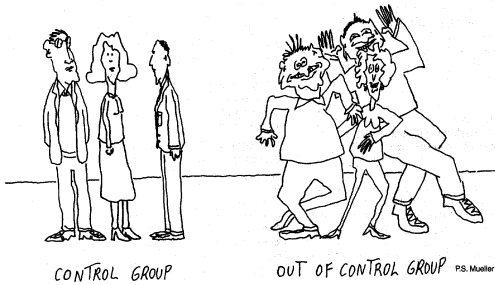
DILEMMA: IF THE DURATION AND MAGNITUDE OF PAIN RELIEF & FUNCTIONAL IMPROVEMENT ARE THE SAME FOR PLACEBO & TREATMENT, IS IT REALLY IMPORTANT- OR POSSIBLE- TO DISTINGUISH THE CONTRIBUTIONS OF EACH?

- NNT for placebo is similar to the best drugs
- Magnitude of effect is comparable
 - Can be repeated with comparable efficacy
- Brain activity between placebo and medication indistinguishable



EFFECT OF COMPARATOR GROUP





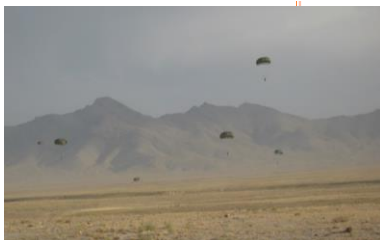
DO EPIDURAL STEROID INJECTIONS WORK"

"If one could somehow find an objective arbitrator well-versed in managing LBP to sort through the plenitude of data on ESI, they would probably conclude that ESI work, but are only beneficial in carefully selected patients with predominantly radicular symptoms, and that the effect size is modest."

Cohen SP. BMJ 2011

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell



"Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials."

OTHER "PROOFS"

- Deductive reasoning: Conclusion is logical consequence of premises
- SNRB increase diagnostic accuracy; increased accuracy leads to improved outcomes; therefore, SNRB leads to improved outcomes
- Inductive Reasoning: Moves from a specific set of facts to a general conclusion
- Selective nerve root, facet and SI joint blocks improve outcomes; therefore, discography improves outcomes



OUTCOMES NOT AMENABLE TO PLACEBO-CONTROLLED OR CLINICAL TRIAL DESIGN

Variable

- Rare complication
- Condition with very high success rate
- Outcome with extremely low success rate
- Condition with reliable treatments & dire consequences

Clinical Example

- Death after cervical TFESI
- Appendectomy for appendicitis/ acute LBP
- 5-year survival for pancreatic cancer/ chronic, non-specific LBP, on disability
- Syphilis/ surgery for cauda equina

OBSTACLES TO EVALUATING CLINICAL TRIALS

Beware of "Fishing Expeditions"

Subgroup analyses can yield important findings, but ideally should be pre-specified and corrected for



"You're going to need a bigger net."

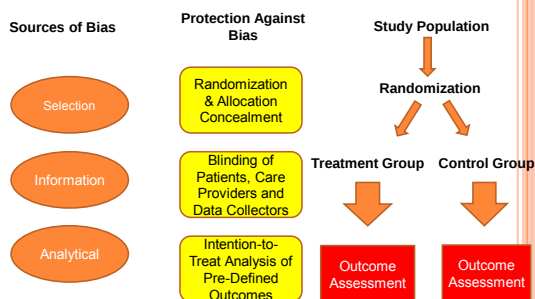
Damned if you do, damned if you don't

- Lesser disease burden more likely to improve with rx and natural course
- Short f/u studies more likely to show benefit



"We never forget you have a choice."

SOURCES OF BIAS IN A CLINICAL TRIAL



ELIMINATING BIAS

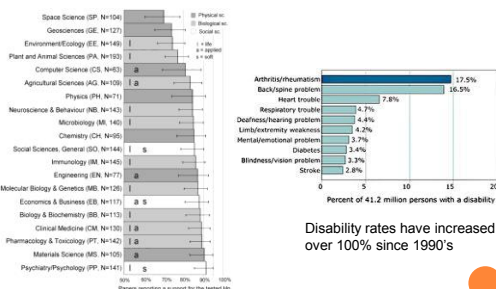
Bias Source

- Random sequence generation (selection bias)
- Allocation Concealment (selection bias)
- Blinding of subjects & investigators (performance bias)
- Blinding of outcome assessment (detection bias)
- Incomplete outcome data (attrition bias)
- Selective reporting (reporting bias)
 - AE's on opioids

Dilemma/ Remedy

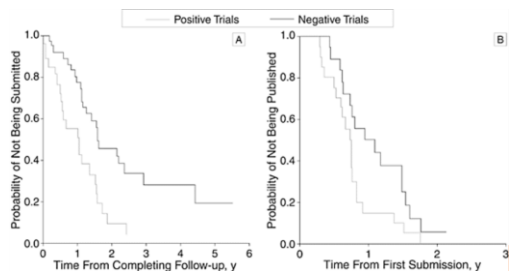
- Avoid quasi-random sequences (DOB, date of visit, alternate sequence)
- Block randomization with high #'s
- Education, debriefings, not always possible
- Despite what is written, not always possible for interventional studies
- Intention-to-treat analysis
- Analyze pre-defined outcomes, statistical corrections

IF THE CUMULATIVE EFFECT OF ALL THE POSITIVE STUDIES FOR PAIN WERE TRUE & GENERALIZABLE, THERE WOULDN'T BE A PAIN EPIDEMIC



Fanelli et al. PLoS One 2010

NEGATIVE STUDIES ARE LESS LIKELY TO BE SUBMITTED FOR PUBLICATION & TO BE PUBLISHED



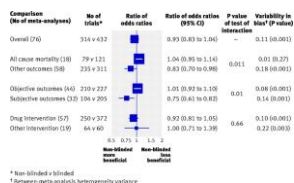
"BLINDING" DILEMMA

- Blinding essential to eliminate "expectation bias", but placebo effect integral part of benefit
 - Not needed to evaluate "effectiveness"
- Can't always blind interventionalist
- Difficult to blind "interventions"
 - Leg pain during TFESI
 - PRP and neuritis with RF
 - Psychoactive effects of analgesics



EFFECT OF BLINDING ON OUTCOMES

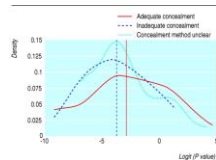
- Non-blinded assessment in RCTs exaggerates effect size by 33%
- "Blinded" studies in which adequate blinding is not confirmed are 13%-25% more likely to yield positive results
 - Effect more than doubles for subjective outcome measures
 - Increased heterogeneity



ALLOCATION CONCEALMENT

- Subversion bias occurs when researcher manipulates recruitment
- Baseline data not equivalent
- More likely to occur with small block randomization
- More prevalent than believed
- Scientific misconduct

- Hewitt et al. BMJ 2005
- Examined 234 RCTs published in 4 top journals
- 56% reported adequate, 26% unclear & 18% inadequate concealment
- Average p-value for inadequately concealed trials was 0.02 vs. 0.05 for adequate trials (test difference $p = 0.045$).



COMPARISON OF CONCEALMENT

Allocation Concealment	Effect Size OR (95% CI)	
Adequate (n=79)	1.0 (reference)	
Unclear (n=150)	0.67 (0.60-0.75)	$P < 0.01$
Inadequate (n=21)	0.59 (0.48-0.73)	

Schulz et al. JAMA 1995

WHAT IS WRONG?: AGE OF PARTICIPANTS IN MULTI-CENTER SURGICAL STUDY

Study Site	Treatment Group	Control Group
All Sites: $P < 0.01$	59	63
Site 1: $P = 0.84$	62	62
Site 2: $P = 0.60$	43	52
Site 3: $P < 0.01$	57	72
Site 4: $P < 0.001$	33	69
Site 5: $P = 0.03$	47	72
Others: $P = 0.99$	64	59

From David Torgeson, University of York

INTENTION-TO-TREAT ANALYSIS

- Pain RCTs inherently challenging to blind
- Analysis of data "as randomized" eliminates investigator bias compared to "as treated" or "per protocol"
- Analyzes subjects regardless of compliance, rx rec'd, withdrawal or deviation
 - Dilutes treatment differences
 - May exclude certain pts who never rec'd rx
 - Recommended by most major organizations



DESIGN OF CLINICAL TRIALS

- Efficacy studies need stringent IC/EC
- Difficult to design "controlled" studies
- Comparative-effectiveness studies more clinically relevant than "controlled" studies
 - Should have "liberal" IC/EC, more sites, longer f/u
 - Must weigh (-) impact of disease burden on tx group with (+) impact of natural recovery in pts with less disease burden on "control" group
- Difference between statistical significance & clinically meaningful
 - Interventional studies typically held to "higher" standard
- Must evaluate "clinical & technical" quality in addition to methodological
 - Need for specialists on panels
 - Need for imaging & contrast to confirm adequacy of procedure

EFFICACY VS. EFFECTIVENESS: WHICH IS BETTER?

Efficacy

- Highly controlled & methodological (long lists of IC & EC)
- Time-consuming & expensive
- Want "best" practitioners treating "ideal" pts; short follow-up periods maximize chance of detecting diff.
- Factors irrelevant
- Overestimate benefit in "real life" circumstances

Comparative-Effectiveness

- Should utilize more liberal IC & EC
- Easier & less expensive
- Should include more sites & longer follow-ups
- Considers utility, speed, tolerability, sustainability
- Can results in "false-negative" results for an efficacious treatment

STUDIES EVALUATING LUMBAR FACET RADIOFREQUENCY DENERVATION

- Van Kleef 1999: DB RCT. Screened **256** pts for **31** subjects
- Van Wijk 2005: DB RCT. Screened **462** pts for **81** subjects
- Nath 2008: DB RCT. Screened **376** pts for **40** subjects
- Dreyfuss 2000: Prospective audit. Screened **460** pts for **15** subjects
- *Leclaire 2001: DB RCT. Screened **76** pts for **70** subjects
- RF > placebo
- RF ≥ placebo
- RF > placebo
- 87% had ≥ 60% relief at 1-year
- *RF = placebo

RISK FACTORS FOR POOR TREATMENT OUTCOME

- Previous LBP episode
- Low education
- High physical job stress
- Physically demanding job
- Poor job satisfaction
- Obesity
- Sleep dysfunction
- Somatization
- Low levels of physical activity
- Poor coping skills
- High anxiety levels
- Depression
- "Negative" attitude
- Smoking
- Fear-avoidance
- Catastrophization
- Greater Disease burden
- Not having opportunity for reduced work load after RTD

Adapted from Cohen et al. BMJ 2009

COMPARATIVE-EFFECTIVENESS RESEARCH: HOW MANY BLOCKS IS ENOUGH?

Reasons for Performing 0 or 1 Block

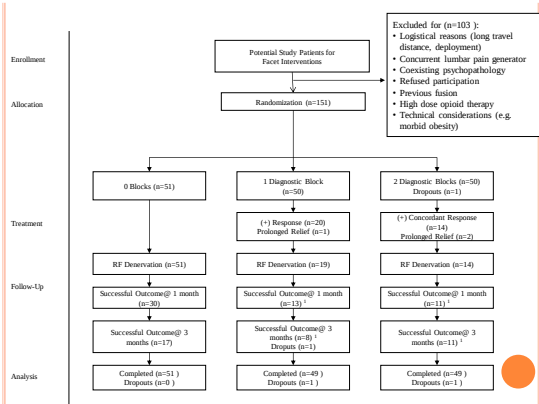
- Determine whether procedure works under "real-life" circumstances
- Reducing false-negative rate
 - Applicable if treatment is relatively safe & inexpensive
- If patient desires "relief" rather than knowing true diagnosis
- If time is important

Reasons for Performing 2 Blocks

- If one needs to determine "efficacy"
- Reducing false-positive rate
 - Applicable if rx carries much greater risk or expense than dx test
- If "diagnostic specificity" is more important than rx
- If time is unimportant

RANDOMIZED MULTI-CENTRE STUDY COMPARING 0,1 & 2 MBB BEFORE RF DENERVATION

- 151 pts randomized to receive RF denervation after 0,1 or 2 blocks
- > 50% cutoff used as criterion for (+) block
 - Pts in 2-block sub-allocated to lido-bupi or bupi-lido in blinded fashion
 - Recorded % pain relief for each block & stimulation threshold for RF lesioning
- Moderately Stringent exclusion criteria and RF parameters
- ≥ 3 months of 50% pain relief and (+) GPE success criteria



CLINICAL & TREATMENT RESULTS

	0-Block (RF)	Single-Block	Double-Block	P-Value
1 st MBB (+) (N,%)	NA	20 (40%)	29 (58%)	0.072
2 nd MBB (+)	NA	NA	14 (54%)	
Prolonged Relief from MBB		1 (2%)	2 (4%)	
Pain Score 1-mo @ Rest	2.0 (0.0 – 7.0, n=51)	2.3 (0.0 – 4.0, n=20)	1.5 (0.0 – 3.0, n=16)	0.504
Pain Score 1-mo with activity	4.5 (1.0 – 8.5)	4.3 (2.0 – 6.0)	2.8 (2.0 – 5.0)	0.370
ODI @ 1-mo	24.0 (2.0 – 46.0)	19.0 (12.0 – 38.0)	14.0 (6.0–26.0)	0.178
(+)GPE @ 1-mo	35 (70.0)	16 (80.0)	12 (75.0)	0.677
Pain Score 3-mo @ Rest	2.0 (0.0 – 6.0, n=30)	2.0 (1.5 – 3.0, n=12)	1.0 (0.0 – 1.5, n=11)	0.097
Pain Score 3-mo with activity	6.3 (1.0 – 9.0)	4.5 (2.0 – 7.0)	2.0 (1.0 – 3.0)	0.015
ODI @ 3-mo	21.0 (3.0 – 41.0)	15.5 (11.0 – 22.0)	10.0 (4.0 – 12.0)	0.008
(+) GPE @ 3-mo	23 (74.2)	11 (91.7)	11 (100.0)	0.109

SUCCESSFUL OUTCOMES BY TREATMENT GROUP

	0-Block (RF)	Single-Block	Double-Block	P-Value
Successful Outcome @ 1-Month (%)	30 (58.8)	13 (26.0)	11 (22.5)	< 0.001
Success at 1-month among persons with RF	30 (58.8, n = 51)	12 (63.2, n = 19)	9 (64.3, n = 14)	0.905
Successful Outcome @ 3-Months	17 (33.3)	8 (16.0)	11 (22.0)	0.115
Success at 3-months among persons with RF	17 (33.3, n = 51)	7 (38.9, n = 18)	9 (64.3, n = 14)	0.111

COST PER SUCCESSFUL TREATMENT

	0-Block (RF)	Single-Block	Double-Block
Cost Per Successful Treatment	\$6286.03	\$17,142.11	\$15,241.31
Cost Per Successful Treatment Excluding Medication Costs and Missed Work Days	\$6053.68	\$16,236.12	\$14,237.76
Total Cumulative Costs for Facility Fees	\$63,936	\$86,247	\$103,563
Total Cumulative Costs for Diagnostic Blocks	\$0	\$29,294.38	\$42,718.26
Total Cumulative Costs for RF Denervation	\$38,976.51	\$14,345.46	\$10,323.10
Estimated Cost of Missed Work Days	\$7650	\$10,050	\$13,350
Estimated Savings on Meds	\$3700	\$2800	\$2300

WHY DOUBLE-BLOCKS SHOULDN'T BE USED IN CLINICAL PRACTICE

Controlled Zygopophysial Joint Blocks: The Travesty of Cost-Effectiveness

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RE: cost-effectiveness of diagnostic medial branch blocks before radiofrequency denervation



Fig. 1. Cost-effectiveness analysis at treatment.

- Double-blocks are not cost-effective at current reimbursement rates
- All serious infectious complications have been associated with diagnostic blocks, not RF
- In all patient surveys, pain relief is more important than identifying "cause"

TRENDS IN CLINICAL TRIALS

- RCTs are getting larger
 - More sites
 - Prevents "fragility"
- Factorial Randomization
 - More efficient b/c each pt serves as an "active" or "control"
 - Treatment allocation completely balanced
 - Can test effect of each intervention on entire population
- Composite Outcomes
 - Ideal for outcomes with low rates
 - Eliminates statistical penalty for multiple outcomes

Outcome	Treatment (n=200)	Control (n=200)	P-Value
Trial 1			
Nerve Injury	2	10	0.09
Trial 2			
Nerve Injury	3	10	0.04

	MSO4 Active	MSO4 Placebo
Gabapentin Active	MSO4 Active	MSO4 Placebo
	Gabapentin Active	Gabapentin Active
Gabapentin Placebo	MSO4 Active	MSO4 Placebo
	Gabapentin Placebo	Gabapentin Placebo

CONCLUSIONS

- Logistical & practical concerns have led to evidence gap in pain medicine relative to other specialties
- Attention to design (i.e. early crossover for "controls" and comparative-effectiveness studies) can minimize ethical concerns and enrollment difficulties
- "Shrinking" reimbursement pie underscores need for better research & may mean more competition for patients
- Refinement of selection critical when designing "efficacy" studies