

University of Kentucky
Department of
Physical Medicine and
Rehabilitation

24th Annual PM&R
Research Day

Cardinal Hill Rehabilitation Hospital
Center of Learning
Lexington, Kentucky



May 22, 2012



PROGRAM AND ABSTRACTS

24th Annual

Physical Medicine and Rehabilitation Research Day

May 22, 2012

Cardinal Hill Rehabilitation Hospital

Lexington, KY

UKHealthCare



24th Annual

**Physical Medicine and Rehabilitation
Research Day**

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Cardinal Hill Rehabilitation Hospital
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Table of Contents

Agenda.....	3-5
Oral Presentations.....	6-24
Poster Presentations.....	25-41
Notes.....	42
Speaker Profile/Abstract.....	43
Speaker Presentation Handouts.....	44-56

**UNIVERSITY OF KENTUCKY
DEPARTMENT OF PHYSICAL MEDICINE & REHABILITATION
24th ANNUAL RESEARCH DAY AGENDA**

CARDINAL HILL REHABILITATION HOSPITAL
CENTER OF LEARNING
May 22, 2012

7:00 a.m. – 8:50 a.m. Dr. Whyte breakfast Lecture and Roundtable with Residents (Conference Room D)

9:00 a.m. – 9:15 a.m. Opening Remarks (CL3): Gerald Klim, D.O.

PM&R RESIDENT RESEARCH PRESENTATIONS – CL3

9:15 a.m. – 9:30 a.m. Francisco Jose Angulo Parker, M.D., Physical Medicine & Rehabilitation
“Incidence of Pneumonia Associated with the Frazier Free Water Protocol”

9:30 a.m. – 9:45 a.m. Sankar Chirumamilla, M.D., Physical Medicine & Rehabilitation
“Pancreatitis and Paroxysmal Sympathetic Hyperactivity in Traumatic Brain Injury”

9:45 a.m. – 10:00 a.m. Radha Korupolu, M.D., Physical Medicine & Rehabilitation
“Spinal Transcutaneous Direct Current Stimulation to Enhance Locomotor Training after Spinal Cord Injury”

10:00 a.m. – 10:15 a.m. Jason Lee, M.D., Physical Medicine & Rehabilitation
“Multidisciplinary Pain Treatment Following Tractor Rollover Accident and Hemipelvectomy: A Case Report”

10:15 a.m. – 10:30 a.m.

BREAK

10:30 a.m. – 10:45 a.m. Erika Erlandson, D.O., Physical Medicine & Rehabilitation
“Improvements in Functional Mobility after Hamstring Lengthening in Ambulatory Children with Cerebral Palsy”

10:45 a.m. – 11:00 a.m. Giridhar Gundu, M.D., Physical Medicine & Rehabilitation
“Modulating Pain in Complex Regional Pain Syndrome with Transcranial Direct Current Stimulation”

11:00 a.m. – 11:15 a.m. Thien Ngo, M.D., Physical Medicine & Rehabilitation
“Identification of Sural Nociceptive Flexion Reflex Index in Males 20-40 Years of Age”

11:15 a.m. – 11:30 a.m. Dwan Perry, D.O., Physical Medicine & Rehabilitation
“Retrospective Study to Determine Diagnostic Factors in Patients with Lumbosacral Radiculopathy”

11:30 a.m. – 11:45 a.m. Hena Sattar, M.D., Physical Medicine & Rehabilitation
“Influence of the Resident Training Program in Rehabilitation Technology on the Equipment and Assistive Technology Portion of the ABPMR Part 1 Scores”

UNIVERSITY OF KENTUCKY
DEPARTMENT OF PHYSICAL MEDICINE & REHABILITATION
24th ANNUAL RESEARCH DAY AGENDA
(Continued)

POSTER PRESENTATIONS (CL4) & Buffet Lunch (CL2)

- 11:45 a.m. – 1:00 p.m.
- 1 Pravardhan Birthi, M.D., UK/PM&R
Gait Changes in Patients Diagnosed with Cerebral Palsy (GMFCS Level 3), Status Post Selective Dorsal Rhizotomy – A Retrospective Study
 - 2 David T. Brough, M.D., UK/PM&R
Spontaneous Deltoid Muscle Rupture: A Case Report
 - 3 Cheryl L. Carrico, M.S., OT/L, UK/PM&R
Nerve Stimulation and Modified Constraint-Induced Therapy to Enhance Post-Stroke Neuroplasticity and Motor Recovery: A Pilot Study
 - 4 Carolyn Crowds, UK/Anatomy & Neurobiology, UK/SCoBIRC
Enhancing Endogenous Protective Mechanisms Following Spinal Cord Injury
 - 5 Megan Danzl, PT, DPT, NCS, CHRH, UK/PM&R
Non-Invasive Brain Stimulation Paired with a Novel Locomotor Training in Chronic Stroke: A Feasibility Study
 - 6 Kristin V. Day, Ph.D., MPT, NCS, CHRH, UK/Department of Rehabilitation Sciences
Pursuing Treatments for Disorders of Consciousness: Theories of Common Neural Mechanisms Underlying Consciousness and Locomotor Activity
 - 7 Nicole Etter, M.S., CCC/SLP, UK/Dept of Rehabilitation Sciences
Perioral Vibrotactile Detection Thresholds in Healthy Aging Adults
 - 8 Jay Hammock, M.D., UK/PM&R
Sinus Bradycardia Progressing to Acute Left Heart Failure Likely Secondary to Tizanidine (Zanaflex) Administration: A Case Report
 - 9 Talat Jamil, M.D., UK/SCoBIRC, UK/PM&R, CHRH
Improving Motor Function with Peripheral Nerve Stimulation in Severe Hemiparesis: Preliminary Results
 - 10 Katherine Maddy, M.S., CCC/SLP, UK/Dept of Rehabilitation Sciences, CHRH
Needs Assessment of People with Stroke in Appalachian Kentucky: the Emergence of a Theoretical Model

UNIVERSITY OF KENTUCKY
DEPARTMENT OF PHYSICAL MEDICINE & REHABILITATION
24th ANNUAL RESEARCH DAY AGENDA
(Continued)

POSTER PRESENTATIONS – CL4 (Continued)

- 11 Darren M. Miller, UK/SCoBIRC
Administration of the Nrf2-ARE Activators Sulforaphane and Carnosic Acid Attenuate 4-Hydroxy-2-Nonenal Induced Mitochondrial Dysfunction Ex Vivo
- 12 Jignesh D. Pandya, UK/SCoBIRC, UK/Anatomy & Neurobiology
Effects of CSPGs on Adult Central Nervous System Mitochondrial Bioenergetics: An *In Vitro* Study
- 13 Daisy E. Ramos, UK/SCoBIRC
Effects of Combining Task-Specific Rehabilitation with Brainstem Chondroitinase ABC Treatment on Adult Rat Forelimb Function Recovery after Cervical Spinal Cord Injury
- 14 Dexter V. Reneer, UK/SCoBIRC, UK/Anatomy & Neurobiology
Blast-Induced Brain Injury: Influence of Shockwave Components
- 15 Elizabeth Salmon, UK/Center for Biomedical Engineering
Development of an Electroencephalogram Brain-Machine Interface to Facilitate Motor Recovery from Incomplete Spinal Cord Injury: A Feasibility Study

FEATURE SPEAKER – CL3

1:00 p.m. – 2:00 p.m.

John Whyte, M.D., Ph.D.
Director of Moss Rehabilitation Research Institute and
Professor of Rehabilitation Medicine at Thomas Jefferson
University
“Pharmacologic Treatment of Neuro-Cognitive Impairments:
Gathering the Evidence to Support Practice”

2:00 p.m. – 2:30 p.m.

Awards & Closing Remarks
Lumy Sawaki, M.D., Ph.D., Physical Medicine & Rehabilitation
Robert Nickerson, M.D., Physical Medicine & Rehabilitation

PM&R Resident Presentations

ORAL PRESENTATIONS

Presenter:

Abstract Presentation:

Francisco Jose Angulo Parker, M.D.	“Incidence of Pneumonia Associated with the Frazier Free Water Protocol”
Sankar Chirumamilla, M.D.	“Pancreatitis and Paroxysmal Sympathetic Hyperactivity in Traumatic Brain Injury”
Radha Korupolu, M.D.	“Spinal Transcutaneous Direct Current Stimulation to Enhance Locomotor Training after Spinal Cord Injury”
Jason Lee, M.D.	“Multidisciplinary Pain Treatment Following Tractor Rollover Accident and Hemipelvectomy: A Case Report”
Erika Erlandson, M.D.	“Improvements in Functional Mobility after Hamstring Lengthening in Ambulatory Children with Cerebral Palsy”
Giridhar Gundu, M.D.	“Modulating Pain in Complex Regional Pain Syndrome with Transcranial Direct Current Stimulation”
Thien Ngo, M.D.	“Identification of Sural Nociceptive Flexion Reflex Index in Adult Males 20-40 Years of Age”
Dwan Perry, D.O.	“Retrospective Study to Determine Diagnostic Factors in Patients with Lumbosacral Radiculopathy”
Hena Sattar, M.D.	“Influence of the Resident Training Program in Rehabilitation Technology on the Equipment and Assistive Technology Portion of the ABPMR Part 1 Scores”

PM&R RESIDENT PRESENTATION

Incidence of Pneumonia Associated with the Frazier Free Water Protocol

Presenter:

Francisco Jose Angulo Parker, M.D.¹

Faculty Mentors/Collaborators:

Pravardhan Birthi, M.D.¹ Sara Salles, D.O.¹ (Mentor)

Participating Sites:

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

Abstract Text:

Patients with stroke commonly have dysphagia ranging from 47 to 81% depending on the location and severity of stroke. The Frazier Free Water Protocol is widely administered in the USA and Canada. However, no strong evidence-based study has been performed to ensure safety and benefits of the Frazier Free Water Protocol compared to the thickened liquids. Therefore, the goal of this proposal is to develop a prospective, randomized and controlled study to determine the safety and efficacy of the Frazier Free Water Protocol.

We plan to enroll 80 subjects from the Cardinal Hill Rehabilitation Hospital inpatient service. Outcomes measures include the Modified Barium Swallow, Chest X-ray, serial basic metabolic panels and patient satisfaction measures.

The central hypothesis is that subjects receiving the Frazier Free Water Protocol will have better outcomes compared to the control group receiving oral hygiene. Our proposed study has 3 specific aims:

Specific aim #1: To evaluate the incidence of pneumonia in the group receiving Frazier Free Water Protocol compared to a control group receiving oral hygiene.

Specific aim #2: To evaluate hydration status in the group receiving Frazier Free Water Protocol compared to a control group receiving oral hygiene.

Specific aim #3: To evaluate patient's satisfaction in the group receiving Frazier Free Water Protocol compared to a control group receiving oral hygiene.

Key Words: Dysphagia, Speech Therapy, Rehabilitation, Aspiration Pneumonia, Swallowing

NOTES

PM&R RESIDENT PRESENTATION

Pancreatitis and Paroxysmal Sympathetic Hyperactivity in Traumatic Brain Injury

Presenter:

Sankar Chirumamilla, M.D.¹

Faculty Mentors/Collaborators:

Silke Bernert, M.D.¹ (Mentor)

Participating Sites:

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

Abstract Text:

Acute pancreatitis presents with abdominal pain, distention and tenderness as well as nausea and vomiting. In individuals with disorders of consciousness after traumatic brain injury (TBI) symptoms may be interpreted as delayed gastric emptying or related to brain injury. Elevated pancreatic enzymes have been reported after brain injury without any clinical or radiographic evidence, and diagnosis of pancreatitis is difficult. One proposed theory for elevated pancreatic enzyme levels points towards an autonomic imbalance as a cause. Disproportionate sympathetic release or Paroxysmal Sympathetic Hyperactivity (PSH) is a well established phenomenon in TBI patients. We present a case of severe TBI with PSH. Several weeks after the brain injury, the patient developed vomiting and was found to have elevated serum amylase and lipase three times the normal limit. Conservative management including a short course of bowel rest, intravenous fluid administration and adjustment of tube feeding resulted in normalization of pancreatic enzymes. The onset of pancreatitis in our TBI patient without any premorbid risk factors for pancreatitis in the setting of PSH is the convincing evidence that PSH might be the reason for acute pancreatitis in TBI patients.

Key Words: Abdominal Pain, Disorders of Consciousness, Autonomic Imbalance, Pancreatic Enzymes, Conservative Management

NOTES

PM&R RESIDENT PRESENTATION

Spinal Transcutaneous Direct Current Stimulation to Enhance Locomotor Training after Spinal Cord Injury

Presenter:

Radha Korupolu, M.D.¹

Collaborators:

Kenneth Chelette, M.S.¹, Lumy Sawaki, M.D. Ph.D.¹ (Mentor)

Participating Sites:

¹University of Kentucky, Department of Physical Medicine & Rehabilitation

Abstract Text:

Background: Non-invasive transcranial direct current stimulation (tcDCS) has been shown to modulate cortical excitability in various studies, promising adjuvant treatment options for a variety of neurological disorders. Recent preliminary studies suggest the possibility of similar non-invasive modulation of spinal neurons by transcutaneous direct current stimulation of spinal cord (tsDCS).

Proposed objectives: We aim to study the effects of tsDCS in 3 phases-

1st Phase: Establish a reliable and reproducible spinal tsDCS methodology to modulate spinal excitability in healthy subjects. Outcomes will include measurement of motor evoked potentials (MEP) elicited by transcranial magnetic stimulation (TMS), H-reflexes and F-waves.

2nd phase: Apply the tsDCS methodology developed in phase one to subjects with spinal cord injury (SCI) to evaluate modulation of spinal excitability using same outcome measures as in 1st phase. If measures show favorable findings then we will progress to phase three.

3rd Phase: Our long term objective is to evaluate the effects of tsDCS on functional motor recovery, paired with robot-assisted training in subjects with SCI.

Proposed methods for first phase: Outcome measures will be recorded before and after spinal tsDCS for 15 mins using anodal, cathodal or sham stimulation over the spinal cord at T11 level. MEP, H-reflex and F-wave will be recorded via surface EMG over gastrocnemius muscle and abductor hallucis muscle bilaterally.

Anticipated Results: We hope to find improved motor output (increased MEPs, increased F wave and decreased H reflex) as a result of modulation of spinal excitability following cathodal stimulation.

Key Words: Spinal Cord Injuries, Transcutaneous Electrical Stimulation, Motor Activity

NOTES

PM&R RESIDENT PRESENTATION

Multidisciplinary Pain Treatment Following Tractor Rollover Accident and Hemipelvectomy: A Case Report

Presenter:

Jason Lee, M.D.¹

Collaborators:

Pravardhan Birthi, M.D.¹, Sara Salles, D.O.¹ (Mentor)

Participating Sites:

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

Abstract Text:

Setting: Level 1 trauma center, Acute inpatient rehabilitation hospital, Outpatient clinic

Patient: 16 year old previously healthy Caucasian male

Case Description: The patient was found pinned down in the middle of a field following a tractor rollover where he sustained unstable pelvis fractures and organ evisceration injury. He was taken emergently to the operating room for exploratory laparotomy with pelvic packing, femoral arterial shunt placement, and multiple catheter thrombectomies. In the subsequent days and weeks he returned to the operating room for more than 40 additional major/minor procedures including a right hemipelvectomy.

His acute pain was so severe following the trauma and operations that the only means of controlling his pain was high potency opioid medications. This case report will describe the regimens used in the successful treatment of his multifactorial pain throughout the various stages of his postoperative period and rehabilitation resulting in a successful taper from pain medication.

Results/Discussion: This patient is the perfect illustration of a success story from a rehabilitation and pain management perspective. Excellent medical, surgical, rehabilitative, and pain management combined with constant awareness of the patient's multifactorial pain levels lead to proper tapering to overcome dependence issues and adverse effects.

Key Words: Rehabilitation, Exploratory Laparotomy, Pelvis Fracture, Trauma

NOTES

PM&R RESIDENT PRESENTATION

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

Presenter:

Erika Erlandson, M.D.¹

Collaborators:

Hank White, Pt, Ph.D.² (Mentor), Henry Iwinski, M.D.² (Mentor)

Participating Sites:

¹University of Kentucky, Department of Physical Medicine and Rehabilitation

²Shriners 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 (including oxygen requirements) 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.

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 ($p = 0.048$).

Conclusions: 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

Presenter:

Giridhar Gundu, M.D.¹

Collaborators:

Cheryl Carrico, M.S.¹, Kenneth Chelette, M.S.¹, Elizabeth Levay, B.S.², Lumy Sawaki, M.D., Ph.D.¹ (Mentor)

Participating Sites:

¹University of Kentucky, Department of Physical Medicine and Rehabilitation

²Cardinal Hill Rehabilitation Hospital, Lexington, KY

Abstract Text:

Complex regional pain syndrome (CRPS) is a disabling painful condition of unclear pathophysiology and an unpredictable clinical course. The condition is often resistant to individual therapy and even with a combination of pharmacological interventions, physical rehabilitation, and interventional pain management techniques. Recently, non-invasive brain stimulation techniques such as transcranial direct current stimulation (tDCS) have emerged as promising interventions to modulate chronic and intractable pain. However, there are no studies currently available to support the hypothesis that tDCS is effective to modulate pain and quality of life as associated with CRPS. Therefore, we propose here to investigate the possible benefits of tDCS as an intervention to modulate pain and 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 associated with CRPS. The effect will be measured by standardized tests of pain and quality of life.**
- **Specific Aim #2: Determine the specificity of tDCS site for modulation of pain and quality of life associated with CRPS.**

We plan to recruit 30 subjects for this study. Each subject will undergo consent, then randomized in 1 of 3 groups: 1) anodal stimulation over DLPFC, 2) anodal stimulation over primary motor cortex, and 3) sham. We will conduct 4 evaluation sessions and 10 treatment sessions with each subject. Assessment of pain in this study will include the Short-Form McGill Pain Questionnaire and The SF-36 Health Survey.

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

NOTES

PM&R RESIDENT PRESENTATION

Identification of Sural Nociceptive Flexion Reflex Index in Adult Males 20-40 Years of Age

Presenter:

Thien Ngo, M.D.¹

Collaborators:

Lumy Sawaki, M.D., Ph.D.¹ (Mentor), Oscar Ortiz Vargas, M.D.² (Mentor)

Participating Sites:

¹University of Kentucky, Department of Physical Medicine and Rehabilitation

²Lexington Veterans Affairs Medical Center, Lexington, KY

Abstract Text:

Background: Pain is a subjective experience, and its measurement has been traditionally based on self-reported instruments. The purpose of this pilot study is to further validate a sensory index that uses a new theoretical approach to objectively measure pain threshold called nociceptive leg flexion reflex (NFR). This technique measures a polysynaptic spinal reflex that does not require supraspinal control. This technique has been demonstrated to be reliable, reproducible and correlated well with clinical findings within subject.

Objectives: The goal of this pilot study is to begin to establish normative data of NFR in young male adults. Our proposed study has 2 specific aims:

- 1.) Specific Aim #1: Identify the sural nociceptive flexion reflex (NFR) and the sural nociceptive flexion reflex index (NFRT) in male adults of 20 to 40 years of age.
- 2.) Specific Aim #2: Measure the correlation between the NFRT and level of pain as measured by Visual Analogue Scale (VAS).

Methods: Following the screening process and informed consent, 12 healthy volunteers (convenience sample size appropriate for proof-of-concept study) will participate in a single recording session of NFR, NFRT with EMG machine and VAS session; these procedures will have an approximate duration of 2 hours.

Conclusions/Applications: We aim to further develop a standardized method to measure NFR in a limited but homogeneous population (ie, young men) to begin to establish normative data for this specific population and to apply these values for longitudinal and interventional studies in the future.

Key Words: Nociceptive Flexion Reflex Index, Sural Nerve Reflex, Visual Analog Scale, Pain Threshold

NOTES

PM&R RESIDENT PRESENTATION

Retrospective Study to Determine Diagnostic Factors in Patients with Lumbosacral Radiculopathy

Presenter:

Dwan Perry, D.O.¹

Collaborators:

Oscar Ortiz-Vargas, M.D.² (Mentor)

Participating Sites:

¹University of Kentucky, Department of Physical Medicine and Rehabilitation

²Lexington Veterans Affairs Medical Center, Lexington, KY

Abstract Text:

Background: Low back pain is the fifth most common reason for all physician visits in the United States. Lumbosacral radiculopathy (LR) is one of the most common causes of low back pain. Extensive studies evaluating the validity of symptoms, physical exam and several diagnostic tools for LR, including Electrodiagnostic testing (EDX), x-rays, computed tomography, and magnetic resonance imaging; have been published. However, their accuracy for the diagnostic of LR remains controversial, mainly due to the absence of a validated gold standard test for definite diagnosis. We propose to re-evaluate the validity of anamnesis, physical exam, imaging studies, and EDX, using for comparison the natural history of RL.

Methods/Design: We plan a retrospective cohort study evaluating the charts of patients with history of low back and leg pain seen in the Lexington Veterans Affairs Medical Center, in Lexington, Kentucky, between 2009 and 2012. Data on medical history, physical examination, imaging studies, and EDX will be systematically collected. Using Weber's results of a 10-year study evaluating the natural history of LR as our gold standard test to identify patients with LR, will evaluate the validity of the most common diagnostic factors used for the diagnosis of RL.

Hypothesis: We hypothesize that the controversial results in the accuracy of diagnostic tools seen in the literature are due to lack of consensus for the diagnosis of LR, which is mainly caused by the absence of a validated gold standard test. We propose the use of natural history of LR as gold standard for diagnosis.

Key Words: Back Pain, Sciatica, Natural History, Physical Examination, Electrodiagnosis, Magnetic Resonance Imaging, Computed Tomography

NOTES

PM&R RESIDENT PRESENTATION

Influence of the Resident Training Program in Rehabilitation Technology on the Equipment and Assistive Technology Portion of the ABPMR Part 1 Scores

Presenter:

Hena Sattar, M.D.¹

Collaborators:

Robert Nickerson, M.D.¹ (Mentor)

Kathy Sheppard-Jones Ph.D.²

Participating Sites:

¹University of Kentucky, Department of Physical Medicine and Rehabilitation

²University of Louisville, Frazier Rehabilitation Center, Department of Physical Medicine and Rehabilitation

Abstract Text:

Objective: The Resident Training Program in Rehabilitation Technology was developed to provide PM&R residents with training, knowledge and skills in Assistive Technology. The program consists of web-based training modules along with a field rotation in the delivery and planning of rehabilitation technology services in vocational, rural/agricultural and other community settings.

The objective of this study was to evaluate the effectiveness of the training modules on Assistive Technology as measured by the scores on the Equipment and Assistive Technology portion of the ABPMR Part 1 exam.

We predicted scores on the Equipment and Assistive Technology portion on ABPMR Part 1 to increase with the addition of the training modules.

Design: Two PM&R residency programs participated in the study. This was an analytic cohort study comparing average scores (before and after the implementation of the training modules) in the ABPMR part 1 Equipment and Assistive Technology portion. Average scores (from 2005-2011) of first time test takers were compared to that of the national average. Linear regression models were applied to evaluate the trends in test scores before and after the implementation of the modules.

Results: While no significant differences were found between the participating institutions compared to the national average, linear regression models showed trends for greater scores after the implementation of the web-based training.

Conclusion: With the addition of training modules in Rehabilitation Technology, we have seen an improvement in first time test taker scores on the ABPMR part I Equipment and Assistive Technology portion at one institution.

Key Words: Rehabilitation Technology, Assistive Technology, Physiatrist

NOTES

POSTER PRESENTATIONS

<u>Presenter:</u>	<u>Poster #</u>	<u>Poster Presentation:</u>
Pravardhan Birthi, M.D. UK/PM&R	1	“Gait Changes in Patients Diagnosed with Cerebral Palsy (GMFCS Level 3), Status Post Selective Dorsal Rhizotomy – A Retrospective Study”
David T. Brough, M.D. UK/PM&R	2	“Spontaneous Deltoid Muscle Rupture: A Case Report”
Cheryl L. Carrico, M.S., OT/L UK/PM&R	3	“Nerve Stimulation and Modified Constraint-Induced Therapy to Enhance Post-Stroke Neuroplasticity and Motor Recovery: A Pilot Study”
Carolyn Crowds UK/Anatomy & Neurobiology UK/SCoBIRC	4	“Enhancing Endogenous Protective Mechanisms Following Spinal Cord Injury”
Megan Danzl, PT, DPT, NCS Cardinal Hill Rehab Hospital UK/PM&R	5	“Non-Invasive Brain Stimulation Paired with a Novel Locomotor Training in Chronic Stroke: A Feasibility Study”
Kristin V. Day, Ph.D., MPT, NCS Cardinal Hill Rehab Hospital UK/Dept of Rehab Sciences	6	“Pursuing Treatments for Disorders of Consciousness: Theories of Common Neural Mechanisms Underlying Consciousness and Locomotor Activity”
Nicole Etter, M.S., CCC/SLP UK/Dept of Rehab Sciences	7	“Perioral Vibrotactile Detection Thresholds in Healthy Aging Adults”
Jay Hammock, M.D. UK/PM&R	8	“Sinus Bradycardia Progressing to Acute Left Heart Failure Likely Secondary to Tizanidine (Zanaflex) Administration: A Case Report”
Talat Jamil, M.D. UK/SCoBIRC, UK/PM&R Cardinal Hill Rehab Hospital	9	“Improving Motor Function with Peripheral Nerve Stimulation in Severe Hemiparesis: Preliminary Results”
Katherine Maddy, M.S., CCC/SLP UK/Dept of Rehab Sciences Cardinal Hill Rehab Hospital	10	“Needs Assessment of People with Stroke in Appalachian Kentucky: the Emergence of a Theoretical Model”
Darren M. Miller UK/SCoBIRC	11	“Administration of the Nrf2-ARE Activators Sulforaphane and Carnosic Acid Attenuate 4-Hydroxy-2-Nonenal Induced Mitochondrial Dysfunction Ex Vivo”
Jignesh D. Pandya UK/SCoBIRC UK/Anatomy & Neurobiology	12	“Effects of CSPGs on Adult Central Nervous System Mitochondrial Bioenergetics: An <i>In Vitro</i> Study”

POSTER PRESENTATIONS

<u>Presenter:</u>	<u>Poster #</u>	<u>Poster Presentation:</u>
Daisy E. Ramos UK/SCoBIRC	13	“Effects of Combining Task-Specific Rehabilitation with Brainstem Chondroitinase ABC Treatment on Adult Rat Forelimb Function Recovery after Cervical Spinal Cord Injury”
Pravardhan Birthi, M.D. UK/PM&R	14	“Incomplete Paraplegia in an Adult with SCIWORA with Bowel and Bladder Continence Despite Absence of Sacral Sensation”
Elizabeth Salmon UK/Ctr for Biomedical Eng.	15	“Development of an Electroencephalogram Brain-Machine Interface to Facilitate Motor Recovery from Incomplete Spinal Cord Injury: A Feasibility Study”

POSTER PRESENTATION - 1

Gait Changes in Patients Diagnosed with Cerebral Palsy (GMFCS Level 3), Status Post Selective Dorsal Rhizotomy – A Retrospective Study

Presenter:

Pravardhan Birthi, M.D.¹

Collaborators:

Hank White, PT, Ph.D.², Robert Nickerson, M.D.¹, Henry Iwanski, M.D.²

Participating Sites:

¹University of Kentucky Spinal Cord & Brain Injury Research Center

²Shriners Hospital for Children, Lexington, KY

Abstract Text:

Selective Dorsal Rhizotomy (SDR) has been used as an option for management of spasticity for a long time, but the procedure remains controversial¹. However despite controversy, SDR has been shown to reduce spasticity, improve gait and normalize gait pattern².

The purpose of this retrospective study was to evaluate changes in gait pattern specifically in patients with cerebral palsy with GMFCS-3 level who underwent SDR.

Overall our results are consistent with those reported by Steinbok et al, which demonstrated improvement in ambulation distances, increased stride lengths and improved hip, knee and ankle motions after undergoing a SDR.² Also results from this retrospective study are consistent with previous report of increase hip extension during stance by Boscarino et al. Our study also reported a similar finding by Boscarino et al that a non-statistical significant increase in walking speed was found to be due to a statistically significant increase in stride length³. In our data, less ankle plantar flexion throughout the gait cycle and less hip and knee flexion during stance were reported. Lastly, our kinematic data are inconsistent with Nivedita et al. who reported an increase in hip and knee flexion one year after undergoing a SDR.

Key Words: Cerebral Palsy, Dorsal Rizotomy, Spasticity and Gait Disorder

POSTER PRESENTATION - 2

Spontaneous Deltoid Muscle Rupture: A Case Report

Presenter:

David Brough, M.D.¹

Collaborators:

Pravardhan Birthi, M.D.¹, Oscar Ortiz-Vargas, M.D.²

Participating Sites:

¹University of Kentucky, Department of Physical Medicine & Rehabilitation

²Lexington Veterans Affairs Medical Center, Lexington, KY

Abstract Text:

A 78 year old, right handed male presented with four months of progressive left shoulder weakness. He denied any history of trauma, but recalled pushing a lawnmower the week prior to the onset of symptoms. There was no pain, weakness, nor loss of function during this activity; or the week that followed. When symptoms began he noticed ecchymosis of the left upper extremity and a raised, rounded area of soft tissue with a central defect disrupting the contour of the anterior deltoid. The patient initially reported only minimal weakness. We present a unique case of spontaneous deltoid rupture diagnosed through a combination of physical exam, ultrasound, and MRI. Although our patient recalled pushing a lawnmower, there was no recollection of injury. Moreover, he was asymptomatic for one week with no trauma or strenuous activity during that time. Rupture of the deltoid has been rarely reported. The etiologies of these cases include trauma, repeated hydrocortisone injections around the shoulder joint, and chronic large rotator cuff tears. Reported cases of traumatic deltoid rupture have involved a clear event that preceded the onset of symptoms. Our patient had no such history, nor did he ever receive steroid injections. The proposed mechanism of deltoid rupture associated with rotator cuff tear involves movement of the humeral head superiorly. This may increase friction between the greater tuberosity and inferior deltoid; placing the deltoid at risk of degeneration. Shoulder hydrocortisone injections may accelerate this process. Our case of spontaneous deltoid rupture is rare, particularly in a patient without an associated trauma or previous steroid injection.

Key Words: Deltoid Muscle, Rupture, Ultrasound, MRI

POSTER PRESENTATION - 3

Nerve Stimulation and Modified Constraint-Induced Therapy to Enhance Post-Stroke Neuroplasticity and Motor Recovery: A Pilot Study

Presenter:

Cheryl Carrico, M.S., OT/L¹

Collaborators:

Kenneth C. Chelette II, M.S.¹, Laurie Nichols, B.S., OT/L^{1,2}, and Lumy Sawaki, M.D., Ph.D.^{1,3}

Participating Sites:

¹University of Kentucky, Department of Physical Medicine and Rehabilitation

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Abstract Text:

Research has shown that peripheral nerve stimulation (PNS) can enhance motor learning. No studies have shown whether PNS combined with motor training will have functional relevance in stroke. Therefore, we conducted a pilot study of PNS combined with a form of post-stroke motor training called constraint-induced therapy (CIT). CIT is one of the most current, well-validated approaches to post-stroke motor rehabilitation. CIT involves restraining the stronger, unaffected upper extremity during intensive, task-oriented motor training of the paretic upper extremity. We hypothesized that in subjects with stroke, CIT paired with *active* PNS would lead to significantly more improved motor function in the affected upper extremity than CIT paired with *sham* PNS. 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 chronic stroke subjects with mild to moderate upper extremity motor deficit received 2 hours of either active (n=10) or sham (n=9) PNS preceding 4 hours of CIT for 10 consecutive weekdays. Changes in FMA, WMFT, and ARAT were analyzed using factorial ANOVA. Results show significance ($p < 0.05$) in all measures at completion evaluation compared with baseline evaluation (FMA ($p = 0.005$); WMFT ($p = 0.030$); ARAT ($p = 0.020$)) and at 1-month follow-up compared with baseline (FMA ($p = 0.048$); WMFT ($p = 0.045$); ARAT ($p = 0.047$)). Thus, PNS paired with CIT shows enormous promise to enhance upper extremity motor recovery in individuals with mild to moderate post-stroke motor deficit.

Key Words: Neurorehabilitation, Upper Extremity, Occupational Therapy, Task-Oriented Therapy, Sensory

POSTER PRESENTATION - 4

Enhancing Endogenous Protective Mechanisms Following Spinal Cord Injury

Presenter:

Carolyn Crowdus^{1,2}

Collaborators:

Chen-Guang Yu, M.D., Ph.D.^{1,2}, Ranjana Singh^{1,2}, Ronan Power, Ph.D.³, James Geddes, Ph.D.^{1,2}

Participating Sites:

¹University of Kentucky, Department of Anatomy and Neurobiology

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

³Alltech, Nicholasville, KY

Abstract Text:

Spinal cord injury (SCI) continues to be a prevalent clinical problem, and dietary selenium supplementation represents a potential strategy to attenuate damage following a primary mechanical injury. We hypothesize that supplementation with selenized yeast will intervene in the secondary injury cascade following SCI by acting as an essential co-factor for antioxidant enzymes. Selenized yeast was supplemented to female Sprague-Dawley rats prior to receiving a moderate (150kdyn) contusive spinal cord injury. One group of animals was monitored for locomotor functional recovery over six weeks following injury. Additionally, the number of days until bladder function was recovered in each rat was examined as a marker for functional recovery. A separate group of animals received SCI and mitochondria were isolated from the spinal cords. Mitochondrial respiration was measured by looking at overall oxygen consumption rate. Selenium supplementation resulted in no significant changes in locomotor function recovery. However, we did observe a significant improvement in recovery of bladder function after SCI with selenium supplementation. Animals maintained on selenium showed improved oxygen consumption rates in mitochondria as compared to animals on the control diet. While selenium supplementation did not improve locomotor functional recovery after SCI, the improvement in bladder function recovery represents an improvement of high importance for SCI patients. The increased mitochondrial respiration provides a preliminary look at the mechanism of action for selenium as a neuroprotective agent. For high-risk populations, an effective dietary supplement could serve as a pre-treatment approach to attenuate the damage that follows neurotrauma.

Key Words: Spinal Cord Injury, Antioxidant, Selenium

POSTER PRESENTATION - 5

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

Presenter:

Megan Danzl, PT, DPT, NCS^{1,3}

Collaborators:

Kenneth C. Chelette, M.S.², Kara Lee, PT, DPT³, Dana Lykins, PT, DPT³, Lumy Sawaki, M.D., Ph.D.²

Participating Sites:

¹University of Kentucky, Department of Rehabilitation Sciences

²University of Kentucky, Department of Physical Medicine and Rehabilitation

³Cardinal Hill Rehabilitation Hospital, 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: Neuroplasticity, Stroke, Transcranial Direct Current Stimulation, Robotics, Lower Extremity

POSTER PRESENTATION - 6

Pursuing Treatments for Disorders of Consciousness: Theories of Common Neural Mechanisms Underlying Consciousness and Locomotor Activity

Presenter:

Kristin V. Day, Ph.D., MPT, NCS^{1,2}

Collaborators:

Lumy Sawaki, M.D., Ph.D.³

Participating Sites:

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Abstract Text:

Following a severe traumatic brain injury, the majority of individuals emerge from coma, but many are slow or fail to regain consciousness. These individuals are diagnosed with a disorder of consciousness, such as vegetative state or minimally conscious state. Currently, we have limited evidence for effective treatments to stimulate arousal and awareness, both components of consciousness. However, an abundance of evidence from basic science and human clinical literature demonstrates that experience-dependent neural plasticity can occur in the injured nervous system through intensive physical interventions, such as locomotor training with bodyweight support and treadmill. Additionally, a synthesis of this literature with other scientific work, including sleep and respiratory research, reveals commonalities in neural substrates and feedback mechanisms underlying consciousness and physical activity. Based on this synthesis, two newly-generated mechanistic theories will be presented: the posture and locomotion theory and the aerobic drive theory. These theories will discuss 1) the role of the locus coeruleus in both sleep-wake cycle regulation as well as static and dynamic postural control, 2) the mesencephalic locomotor region and reticular activating system as common components of the pedunculo-pontine tegmental nucleus, 3) the evidence describing enhanced cognition post-aerobic exercise in aging adults and persons with neurological disorders, and 4) the overlap in neural circuitry responsible for breathing, locomotion, and arousal. We hypothesize that physical exercise, in particular locomotor-like activity, is capable of priming the reticular activating system for arousal, thus preparing the cortex to receive, process, and respond to afferent information via thalamocortical pathways.

Key Words: Severe brain injury, Locomotion, Consciousness, Neural Mechanisms

POSTER PRESENTATION - 7

Perioral Vibrotactile Detection Thresholds in Healthy Aging Adults

Presenter:

Nicole Etter, M.S., CCC/SLP¹

Collaborators:

Richard Andreatta, Ph.D.¹

Participating Sites:

¹University of Kentucky, Department of Rehabilitation Sciences

Abstract Text:

The lower face is a highly coordinated yet adaptive sensorimotor system. Unfortunately, little is currently known about the adaptive neural mechanisms underlying normal and disordered orofacial activities, particularly in aging populations, who as a cohort are especially vulnerable to degradation of speech and feeding behaviors as a function of normal aging, disease and acquired neurological injury. Recently, orofacial perceptual sensitivity in a group of 15 healthy aging adults were characterized (ages 65+) against previously published data in healthy young adults (aged 18-29).^{1,2,3,4} Healthy aging adults demonstrated significantly elevated lip vibrotactile detection thresholds (less sensitivity) compared to younger participants and substantially greater variance in the stability of their detection performance. These data suggest that perceptual detection reliability in the aging orofacial system may undergo aging-related alterations, with such alterations potentially influencing speech intelligibility. The implications for such changes in compromised aged populations are unknown.

These data are the foundation of planned investigations to determine the relationship between oromotor skill performance and orosensory perceptual abilities in healthy aging adults and aged patients with non-progressive motor speech disorders. Given our initial finding of decreased orosensory perception in healthy aging, we hypothesize that oromotor skill performance may be affected similarly. Current interventions for speech disorders focus almost exclusively on motor training and performance-based goals. Given the theoretical position that clinical interventions are driven primarily through sensory channels⁵, the combination of sensory and motor goals in novel interventions for speech dysarthria will be aided by greater understanding of the perception-action changes that occur with aging.

Key Words: Speech, Aging, Vibrotactile Detection, Orofacial, Orosensory

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POSTER PRESENTATION - 8

Sinus Bradycardia Progressing to Acute Left Heart Failure Likely Secondary to Tizanidine (Zanaflex) Administration: A Case Report

Presenter:

Jay Hammock, M.D.¹

Collaborators:

Chadwick Walters, D.O.²

Participating Sites:

¹University of Kentucky, Department of Physical Medicine & Rehabilitation

²Neuro Rehab Specialists, Louisville, KY

Abstract Text:

Setting: Inpatient Rehabilitation Hospital

Patient: A 79-year-old female who was undergoing inpatient rehabilitation for mild traumatic brain injury status-post motor vehicle collision

Case Description: The patient developed severe sinus bradycardia progressing to acute left heart failure less than thirty-six hours after initiating oral tizanidine therapy. This medication was chosen due the patient's persistent complaint of myofascial pain and spasms. Initial dose was 6mg/day in divided doses. The patient had no known coronary artery disease or congestive heart failure. Subjective complaints included new onset dyspnea and easy fatigueability. Physical exam findings included jugular venous distention and bibasilar crackles. 12-lead ECG revealed severe sinus bradycardia (35 bpm), new onset first degree AV block and QT interval prolongation. β -natriuretic peptide (BNP) was elevated at 1200 pg/ml, increased from a baseline value of 178 pg/ml.

Assessment/Results: Tizanidine was suspected as the cause of her symptoms and was discontinued. Within twenty-four hours of the last dose, the patient's vital signs returned to preadmission levels and symptoms completely resolved. Due to the rapid resolution of symptoms after discontinuing tizanidine, it was thought likely to be the offending agent.

Discussion: A similar prior case study reported development of extreme sinus bradycardia with acute right heart failure. To our knowledge, this is the first reported case of extreme bradycardia with acute left heart failure after administration of a standard initial dose of oral tizanidine.

Conclusion: The serious potential cardiovascular side effects of tizanidine must be taken into consideration when treating spasticity and myofascial pain.

Key Words: Sinus Bradycardia, Left Heart Failure, Tizanidine Hydrochloride, Zanaflex

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POSTER PRESENTATION - 9

Improving Motor Function with Peripheral Nerve Stimulation in Severe Hemiparesis: Preliminary Results

Presenter:

Talat Jamil, M.D.^{1,2}

Collaborators:

Cheryl Carrico, M.S., OT/L², Laurie Nichols, B.S., OT/L^{2,3}, Kenneth Chelette, M.S.², Lumy Sawaki, M.D., Ph.D.^{2,4}

Participating Sites:

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²University of Kentucky, Physical Medicine & Rehabilitation

³Cardinal Hill Rehabilitation Hospital, Lexington, KY

⁴Wake Forest University, Department of Neurology, Winston-Salem, NC

Abstract Text:

Hypothesis: Upper extremity (UE) motor training paired with active peripheral nerve stimulation (PNS) will lead to more improved motor function in the affected UE than sham PNS paired with UE motor training in subjects with severe post-stroke motor deficit.

Number of Subjects: 34

Procedures: Double-blind, sham-controlled, randomized design. We define “severe motor deficit” as virtually no wrist and finger movement. For 10 consecutive weekdays, 18 subjects with severe post-stroke motor deficit received active PNS for 2 hours daily to the ulnar, median, and radial nerves simultaneously, preceding 4 hours of intensive, task-oriented UE motor training. The remaining 16 subjects underwent an identical protocol except that they received sham PNS. Fugl-Meyer Assessment Scale (FMA) was a primary outcome measure in evaluation of UE motor performance at baseline, completion, and 1-month follow-up testing.

Statistical Analyses: We compared baseline measures for active versus sham groups. An analysis of variance model with repeated measures was fitted to each variable. Significance level was set at 0.05.

Results: Active PNS led to greater change in FMA score from baseline than sham PNS as measured at completion ($p=0.07$) and 1-month follow-up ($p=0.01$).

Conclusions: Results suggest that UE motor performance in severe post-stroke hemiparesis improves when active PNS is coupled with intensive, task-oriented UE motor training. These results demonstrate that PNS has promising adjuvant effects with motor training to enhance functional recovery in individuals with severe post-stroke motor deficit.

Key Words: Peripheral Nerve Stimulation, Task-Oriented Therapy, Motor Recovery, Hemiparesis

POSTER PRESENTATION - 10

Needs Assessment of People with Stroke in Appalachian Kentucky: The Emergence of a Theoretical Model

Presenter:

Katherine Maddy^{1,2}

Collaborators:

Sarah Campbell¹, Megan Danzl^{1,2}, Violet Sylvia³, Elizabeth Hunter², Janice Kuperstein¹, Anne Harrison¹

Participating Sites:

¹ University of Kentucky, Department of Rehabilitation Sciences

² Cardinal Hill Rehabilitation Hospital, Lexington, KY

³ Appalachian Regional Hospital, Kentucky

Abstract Text:

Kentucky Appalachian Rural Rehabilitation Network researchers are completing an assessment of the barriers to and facilitators of community re-integration for people with stroke and their caregivers in Appalachian Kentucky. A multi-modal approach of qualitative methodology with a phenomenological approach and a quantitative instrument, the Stroke Impact Scale, was used to study the lived experience of participants, their transition through the healthcare system, return to the community and life post stroke. The purpose of this presentation is to describe the team's theoretical approach to data collection, analysis and how the integration of existing theories can enrich the findings. Elements of the Social-Ecological Model were used to analyze data at the microsystem (individual, caregiver) and exosystem levels (health care, community) to determine if there were linkages between the two (mesosystem). Components of self-determination theory (autonomy, competence, relatedness) provide an additional framework for analysis. Finally, elements of social support theories were used to identify assets and needs to facilitate community re-integration. The collaboration of theory with participants' experiences supports the need for a competent mesosystem to link the microsystem and exosystem, facilitating self-determination across the continuum of care. Preliminary analysis demonstrates a sharp decline in mesosystem support once individuals are discharged home, a time when the need and readiness for learning appear to be at high levels. Future research will focus on how the development of the mesosystem may reduce medical costs by reducing the impact of secondary complications while improving quality of life for people affected by stroke in rural regions.

Key Words: Qualitative, Theoretical, Quality of Life, Stroke, Rural

POSTER PRESENTATION - 11

**Spinal Cord & Brain Injury Research Center, University of Kentucky
College of Medicine**

Presenter:

Darren M. Miller¹

Collaborators:

Indrapal N. Singh, Ph.D.¹

Edward D. Hall, Ph.D.¹

Participating Sites:

¹University of Kentucky, Spinal Cord & Brain Injury Research Center

Abstract Text:

Traumatic brain injury (TBI) currently signifies a substantial health and socioeconomic dilemma in the United States with roughly 50,000 cases resulting in death each year. 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 occurring 24 hours post-TBI. As neuronal mitochondria have previously been shown to be susceptible to oxidative damage, we sought to mechanistically investigate whether Nrf2-ARE activation in vivo could protect mitochondria under conditions of oxidative stress ex vivo. Young adult male CF-1 mice were administered one of two known Nrf2-ARE activators I.P. – sulforaphane (5.0mg/kg) or carnosic acid (1.0mg/kg) – or their respective vehicle 48 hours prior to Ficoll isolation of cortical mitochondria. Purified mitochondria were then exposed in vitro to 30uM of 4-hydroxy-2-nonenal (4-HNE) for 15 minutes at 37 degrees Celsius. Mitochondrial bioenergetics was then assayed on the XF-24 Bioanalyzer (Seahorse Bioscience, USA). The administration of sulforaphane (SFN) and carnosic acid (CA) significantly ($p < 0.05$) attenuated 4-HNE induced inhibition of mitochondrial respiration for both Complex I and II. Furthermore, CA and SFN both significantly ($p < 0.05$) reduced 4-HNE bound mitochondria protein as determined by Western blot. These results demonstrate the capability of Nrf2-ARE induction in vivo to protect from 4-HNE toxicity to cortical mitochondria ex vivo. Ongoing studies will determine the therapeutic efficacy of Nrf2-ARE activators to attenuate post-TBI pathophysiology.

Key Words: Traumatic Brain Injury, Mitochondria, Nrf2-ARE

Acknowledgements: Supported by Grants NIH-NIDA 1T32 DA022738, NIH-NINDS 2P30 NS051220-01 and funds from the Kentucky Spinal Cord & Head Injury Research Trust.

POSTER PRESENTATION - 12

Effects of CSPGs on Adult Central Nervous System Mitochondrial Bioenergetics: An *In Vitro* Study

Presenter:

Jignesh D. Pandya^{1,2}

Collaborators:

Juan A. Wang¹, Andrea L. Moodhart¹, Edward D. Hall, Ph.D^{1,2}, Patrick G. Sullivan, Ph.D.^{1,2}, Stephen M. Onifer, Ph.D.^{1,2}

Participating Sites:

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²University of Kentucky, Department of Anatomy & Neurobiology

Abstract Text:

Compromised mitochondrial energy homeostasis together with constitutively upregulated chondroitin sulphate proteoglycans (CSPGs) and neurotrophins (brain derived neurotrophic factor, BDNF) are observed at brain and spinal cord lesions. The collaborative mechanisms of these neuronal growth inhibitors/stimulants on neurorehabilitation are being investigated. Since neuronal mitochondria are the primary target for CNS metabolic regulation, we tested the novel hypothesis that neuronal growth inhibitors/stimulants like CSPGs and/or BDNF modulate mitochondrial bioenergetics. We isolated total mitochondria from adult naive rat brain and spinal cord (n=2) and measured mitochondrial respiration following 5 minutes incubation with CSPGs and/or BDNF or Vehicles using a Clark type oxygen electrode. We measured mitochondrial ATP synthesis rates (State III) together with minimum (State IV) and maximum (State V) respiratory capacity using various mitochondrial substrates. A low dose of CSPGs (10ug/ml) impaired mitochondrial State III (18% lower) and State V (36% lower) rates compared to Vehicle. Higher dose of CSPGs (100ug/ml) showed further compromised effects on State III (55-60% lower) and State V (70-75% lower) rates. Respiratory rates remained similar to Vehicle when mitochondria were incubated with BDNF (666ng/ml). Co-incubation of CSPGs (100 or 10ug/ml) with BDNF (666ng/ml) showed reduced State III and State V respiratory rates as we observed for CSPGs alone. Using western blots, we identified full length and truncated trkB receptor for BDNF in brain and spinal cord crude mitochondrial preparations (n=3). Our preliminary data show interactions between CSPGs and CNS mitochondria which may play a crucial role in CNS injuries. The interactive signaling mechanisms will be thoroughly investigated.

Key Words: Mitochondria, Chondroitin Sulfate Proteoglycan, Brain-Derived Neurotrophic Factor, Plasticity, Neurorehabilitation, Neuroprotection, Neuroregeneration

Acknowledgements: This research is supported by the Kentucky Spinal Cord & Head Injury Research Trust #9-9 (SMO) and NIH/NINDS P30NS051220 (EDH).

POSTER PRESENTATION - 13

Effects of Combining Task-Specific Rehabilitation with Brainstem Chondroitinase ABC Treatment on Adult Rat Forelimb Function Recovery after Cervical Spinal Cord Injury

Presenter:

Daisy E. Ramos¹

Collaborators:

Andrea L. Moodhart¹, Angila D. Tolson¹, Kasem Abdallah¹, Anna X. Ming¹, Joshua H. Eason¹, Laura K. Whitnel-Smith¹, Stephen M. Onifer, Ph.D.^{1,2}

Participating Sites:

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²University of Kentucky, Department of Anatomy & Neurobiology

Abstract Text:

Improving upper extremity function is the highest priority of persons with traumatic cervical spinal cord injury (SCI). A key mechanism contributing to sensorimotor dysfunctions is chondroitin sulfate proteoglycans (CSPG) inhibition of axonal growth and failure of target neuron reinnervation. We showed that CSPG increased at adult rat cervical SCI sites and denervated brainstem cuneate nuclei (Massey et al., 2008). Administering chondroitinase ABC (chABC), a bacterial enzyme that digests CSPG, to cuneate nuclei acutely and 1 week after C6-7 dorsal column injury promoted intact forepaw primary afferents collateral spouting (Massey et al., 2006). Importantly, cutaneous stimulation of forepaw digits 1 and 2 activated more cuneate nuclei neurons compared to rats treated with control penicillinase (p-ase). We are determining whether chABC treatment affects forelimb function recovery after C6-7 SCI that damages both the dorsal columns and corticospinal tracts. Since combining daily forelimb rehabilitation with cervical SCI site chABC treatment improved forelimb function recovery compared to treatment alone (García-Alías and Fawcett, 2012), we are testing the hypothesis that daily forelimb rehabilitation also will further improve forelimb function recovery. Currently, there is a trend for improved Staircase Test pellet retrieval performance by week 3 post-SCI of chABC-treated rats undergoing daily task-specific rehabilitation. There also is a trend at week 6 for faster times in chABC-treated and p-ase-treated rats undergoing rehabilitation to attend to adhesive stickers on their forepaw palms. Our preliminary data suggest that task-specific rehabilitation combined with brainstem chABC treatment after cervical SCI has a synergistic effect on forelimb function recovery.

Key Words: Spinal Cord Injury, Forelimb Function, Plasticity, Rehabilitation, Chondroitin Sulfate Proteoglycan, Chondroitinase ABC

Acknowledgements: Support by the Kentucky Spinal Cord & Head Injury Research Trust #9-9 (SMO) and NIH/NINDS P30 NS051220 (EDH).

POSTER PRESENTATION - 14

Blast-Induced Brain Injury: Influence of Shockwave Components

Presenter:

Dexter V. Reneer¹

Collaborators:

Richard D. Hisel⁶, Julie A. Corkins¹, Carolyn A. Crowds^{1,2}, Sarbani Ghoshal¹, Joshua M. Hoffman³, Richard J. Kryscio^{4,5}, Braden T. Lusk³, and James W. Geddes, Ph.D.^{1,2}

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Abstract Text:

Blast-induced traumatic brain injury (bTBI) has been referred to as the signature injury of Operations Enduring and Iraqi Freedom (OEF/OIF). Additionally, civilians are increasingly at risk from terrorism and industrial accidents. Little is known about which components of the blast contribute to injury. We designed and built a multi-mode shock tube (McMillan Blast Device - MBD) similar to the compressed air-driven shock tube at Walter Reed Army Institute of Research. This new shock tube is able to use four driving modes (compressed air- or compressed helium-driven membrane rupture, a 2:1 mixture of H₂ and O₂ - oxyhydrogen, and RDX – the primary explosive component of C-4 plastic explosives) to generate the blast wave. Analysis of the blast waves produced by the MBD showed that compressed air-driven membrane rupture produced shockwaves that differed substantially from those produced by compressed helium-driven membrane rupture as well as those produced by chemical explosives (oxyhydrogen and RDX) with respect to the pressure-time profiles of the shockwave. Furthermore, the brains of rats exposed to compressed air-driven blasts showed more evidence of blood-brain barrier breakdown, reactive astrogliosis and microglial activation than those of rats exposed to oxyhydrogen-driven blasts. These data suggest that individual shockwave components may contribute differently to the injury, thus necessitating a unique course of clinical evaluation and/or intervention depending on the situation in which the individual was exposed.

Key Words: Blast, TBI, Military, IED, Secondary Pathology

POSTER PRESENTATION - 15

Development of an Electroencephalogram Brain-Machine Interface to Facilitate Motor Recovery from Incomplete Spinal Cord Injury: a Feasibility Study

Presenter:

Elizabeth Salmon¹

Collaborators:

Kenneth Chelette, M.S.², Lumy Sawaki, M.D., Ph.D.², and Sridhar Sunderam, Ph.D.¹

Participating Sites:

¹University of Kentucky, Center for Biomedical Engineering

²University of Kentucky, Department of Physical Medicine and Rehabilitation

Abstract Text:

Spinal cord injury and stroke can impair one's ability to perform everyday motor tasks. Brain-machine interfaces (BMIs) have been developed to decode brain signals into control commands for prosthetic devices. We are developing such a BMI to be driven by the sensorimotor or "mu" rhythm (8-12Hz) of the EEG. Mu rhythm suppression can occur with actual or imagined movement. In this protocol, approved by the IRB for healthy volunteers, scalp EEG is monitored with electrodes over sensorimotor cortex and mu band power is estimated to classify the EEG state as rest or motor imagery. The EEG classifier is constructed during a training session, in which the subject is presented with intermittent visual cues to imagine hand movement. A preliminary analysis indicated that detection of motor imagery from the EEG is feasible. Subsequently, the classifier will be used to predict motor imagery from EEG measurements in real time. Beyond their use as assistive devices, we believe that BMIs can facilitate motor recovery. Studies suggest that repetitive exercises can induce beneficial neuroplastic changes in motor cortex, and electrical stimulation of peripheral nerves or muscles can augment this recovery. We hypothesize that stimulus-induced plastic changes could be enhanced further through timing-dependent reinforcement by stimulating only in response to intended movement. To that end, we propose to use the EEG-BMI to detect the intent and then trigger electrical impulses. Following development and testing of the BMI on healthy individuals, we will investigate the effects of closed-loop stimulation on patients with incomplete spinal cord injury.

Key Words: Brain-Machine Interface, Spinal Cord Injury, Rehabilitation

NOTES

KEYNOTE SPEAKER PRESENTATION

**“Pharmacologic Treatment of
Neuro-Cognitive Impairments: Gathering
the Evidence to Support Practice”**



JOHN WHYTE, MD, PhD

Dr. Whyte is a physiatrist and experimental psychologist specializing in traumatic brain injury rehabilitation. He was the founding director of the Moss Rehabilitation Research Institute, begun in 1992, and continues in this position. He also directs the subspecialty Responsiveness Program for patients with disorders of consciousness. His research focuses on cognitive impairment after TBI, including assessment and treatment. He was a member of two Institute of Medicine policy panels, one on the “Future of Disability in America” in 2007 and one on “Cognitive Rehabilitation after TBI”, in 2011. He was the 2002 winner of the William Fields Caveness Award, from the Brain Injury Association of America, the American Congress of Rehabilitation Medicine’s 2007 Coulter Lecturer, the 2008 recipient of the Robert L. Moody Prize for Distinguished Initiatives in Brain Injury Research and Rehabilitation, the 2010 recipient of the Distinguished Academician Award from the Association of Academic Physiatrists, and the recipient of the 2012 Joel A. DeLisa Award for Excellence in Research and Education in the Field of Physical Medicine & Rehabilitation. He is a past president of the Association of Academic Physiatrists and co-director, with Michael Boninger, of the NIH-funded Rehabilitation Medicine Scientist Training Program. His research has been funded by NIH, NIDRR, the Department of Defense, and several private foundations. He has over 120 peer reviewed publications and was co-lead author of the recent report on a randomized controlled trial of amantadine in disorders of consciousness, published in the New England Journal of Medicine.



Pharmacologic Treatment of Neuro-Cognitive Impairments: Gathering the Evidence to Support Practice

John Whyte, MD, PhD

I have no conflict of interest with any financial organization regarding the material presented in this meeting





Topics

- Importance of rigorous evidence regarding pharmacologic treatments
- Obstacles and complexities that stand in the way of gathering the evidence
- Feasibility of determining pharmacologic impact in the course of clinical practice
- Examples of formal studies of pharmacologic treatment from our laboratory



IMPORTANCE OF THE EVIDENCE



For Payment and Policy

- Many insurers will not authorize treatments that they perceive to be unsupported by evidence
- Application of this standard is very inconsistent
 - Support of off-label uses in many instances
 - Denial in some arenas and for some more expensive drugs and treatments
 - Our example of zolpidem



For Patients

- In the absence of rigorous efficacy data in TBI, we rely on logical parallels from:
 - Animal models (e.g., dextroamphetamine)
 - Other patient populations (e.g., L-dopa, SSRIs, antipsychotics) BUT
- These are good sources of hypotheses but not good sources of evidence
 - Efficacy is poorly predicted from distant models and populations (e.g., dextroamphetamine, antipsychotics)
 - Adverse event profiles may differ from the original population (e.g., benzodiazepines and recovery/memory?)



OBSTACLES & COMPLEXITIES

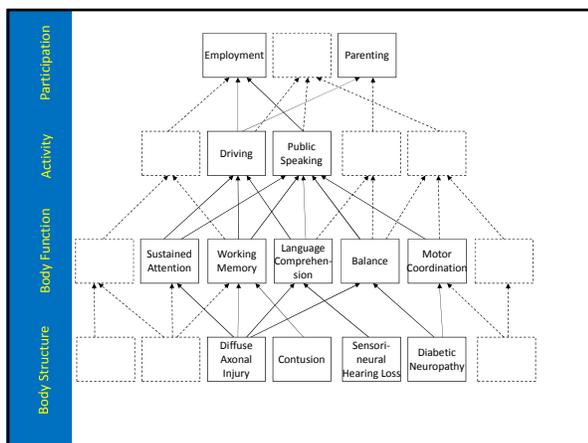
- Gap between targets of pharmacologic action and targets of therapeutic change
- Availability of sensitive and clinically relevant measures
- Confounding effects of natural recovery, intercurrent medical complications
- Variability, sample size, and logistics
- Cost

Gap between Targets

- Pharmacologic agents target cellular and subcellular processes (e.g., neurotransmitter release, uptake, membrane stability, etc.)
- Therapeutic goals are framed in terms of cognitive processes (e.g., memory storage) and functionally relevant behaviors (e.g., ability to keep appointments)
- There is no “memory” neurochemical or “keeping appointments” neurochemical – must form and test hypotheses about their relationship to cellular targets

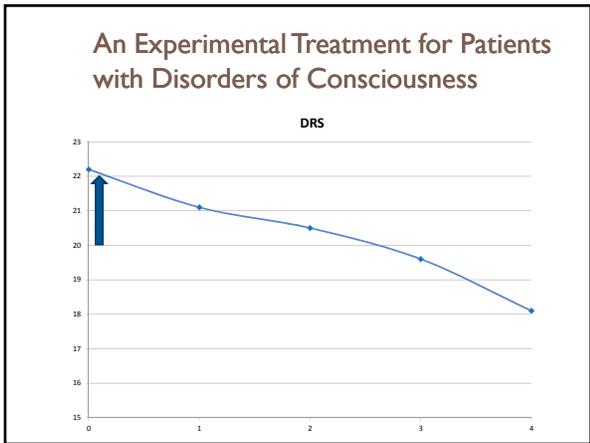
Sensitive & Relevant Measures

- In early-phase studies, measures should be sensitive to the proximal actions of the drug
 - If the hypothesis is “methylphenidate can reduce impulsive aggression by increasing frontal inhibitory function”, then let’s start with a sensitive measure of frontal inhibition
- In later-phase studies, need measures that assess functionally relevant but clinically realistic outcomes, e.g.:
 - Employment?
 - Aggressive acts with minimal provocation?



Confounding Factors

- Natural recovery
- Illness, other drug interventions, circumstantial changes



Variability & Sample Size

- Functional recovery varies greatly across patients
 - Small studies that compare a treatment and placebo group are high risk for both Type I and Type II error
 - Solutions are to:
 - Develop predictions of that variability and/or
 - Increase sample size
- Requires
 - Multicenter networks
 - Preliminary work on prediction of the outcomes of interest irrespective of pharmacologic treatment

Cost

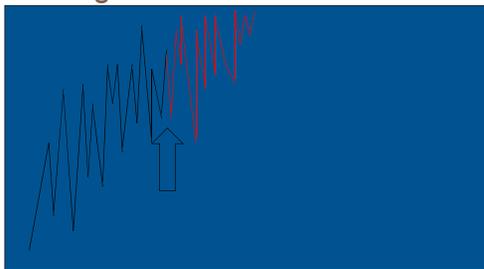
- Pharmacologic treatments are cheaper to study than behavioral treatments (a good thing)
- There may be Pharma funding to study them, but:
 - Many drugs of interest are off patent
 - Many new drugs have larger and easier-to-study target groups than TBI rehabilitation
 - There are risks in accepting Pharma funding
 - Public funding is challenging

WITH ALL THOSE OBSTACLES...

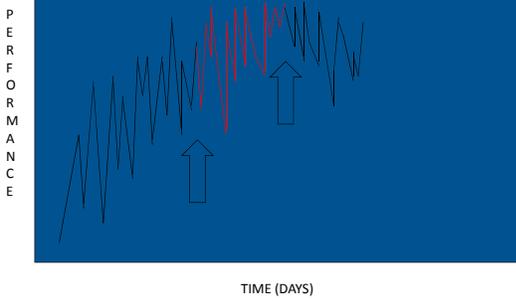
- Can we just learn from clinical practice?
- The short answer: not too often, especially during active recovery

A-B Design

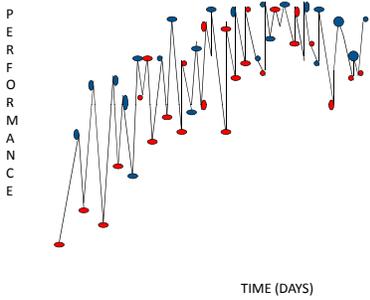
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A-B-A Design



A-B-A-B-A-B Design



STUDY EXAMPLES

Methylphenidate and Attention

- Available measures at the time were not sensitive to TBI-related attention deficits so how would treatment benefit be measured?

Computer Testing Apparatus



- Individualized durations
- Pattern mask
- Simple midline targets/foils
- Most tasks similar with minor variations

Coding of Naturalistic Behavior



- 3 independent visuo-motor tasks
- Suitable for varied ability levels
- Controlled distractions
- Videotaping

MPH (cont.)

- Attention is highly variable across patients and time
- Attention cannot be directly measured but must be inferred from patterns of performance errors or speed
- Many other deficits, not expected to respond to MPH, can also affect task errors and speed

MPH (cont.)

- Therefore: within subjects repeated cross-over design
- Each subject enrolled for 6 weeks with weekly drug changes:
 - M/P/M/P/M/P vs. P/M/P/M/P/M
 - 3 measures of each variable in each drug condition
 - Untreated deficits are “constant”

Methylphenidate Results

- Processing speed factor
 - $P < .001$, effect sizes: 0 - .48
- Family rating factor
 - $P < .01$, effect sizes: .44 - .50
- Individual inattentiveness factor
 - $P = .06$, $P = .01$, effect sizes: .15 - .62

Treatment in the Early Phase to Accelerate Recovery

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Placebo-Controlled Trial of Amantadine for Severe Traumatic Brain Injury

Joseph T. Giacino, Ph.D., John Whyte, M.D., Ph.D., Emilia Bagiella, Ph.D., Kathleen Kalmar, Ph.D., Nancy Childs, M.D., Allen Khademi, M.D., Bernd Eifert, M.D., David Long, M.D., Douglas I. Katz, M.D., Sooja Cho, M.D., Stuart A. Yablon, M.D., Marianne Luther, M.D., Flora M. Hammond, M.D., Annette Nordenbo, M.D., Paul Novak, O.T.R., Walt Mercer, Ph.D., Petra Maurer-Karattup, Dr.Rer.Nat., and Mark Sherer, Ph.D.

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Primary Aims

- Determine whether AH, given in a dose of 200 – 400 mg/day improves functional recovery from VS and MCS.
- Determine whether AH-related gains in function persist following drug discontinuation
- But...
 - 8 years of planning led up to this study...

Preliminary Tasks

- Needs to be a multi-center study
 - Planning grant: Where are these patients and where can they be studied?
 - Organizing the network: Can a group of investigators enroll patients and collect good data?
 - Natural history study: What variables can predict the variations in recovery, how many subjects can we enroll and follow, and how many would we need for a clinical trial?
 - Focus groups with families and clinicians: Can we mount a placebo controlled trial?

Inclusion Criteria

- Age ≥ 16 and ≤ 65
- Traumatic etiology
- DRS ≥ 12 at enrollment
- Unable to follow commands or communicate reliably
- At least 4 weeks but less than 16 weeks post-injury at enrollment

29

Exclusion Criteria

- Pregnancy
- Missile-type penetrating brain injury
- Premorbid CNS/developmental abnormality
- Prior exposure to AH post-TBI
- Unwillingness to discontinue psychotropic drugs
- Allergy or medical contraindication to AH
- Significant impairment of renal function
- More than 1 seizure in the 4 weeks prior to enrollment

30

Randomization

- Centralized at the DCC
- Stratified by center, time post injury (early vs. late) and diagnosis (MCS vs.VS)
- Random blocks of 4 and 6

31

Dosing Schedule

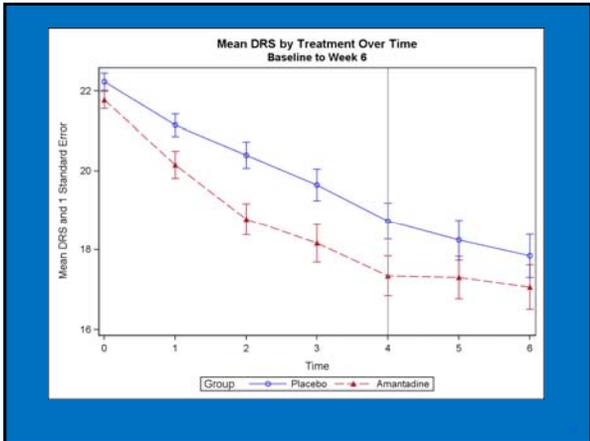
- AH/placebo started at 100 mg bid and maintained for first 2 weeks
- dose increased to 150mg bid in week 3 if DRS change < 2 points compared to baseline
- dose increased to 200mg bid in week 4 if DRS change < 2 points compared to baseline
- Drug taper down in week 5

32

Baseline Comparison

Characteristics	Amantadine (n=87)	Placebo (n=97)	P Value
Age, mean (SD)	35.5 (15.3)	37.2 (15.4)	0.44
Male, no. (%)	64 (73.6)	69 (71.1)	0.71
Hispanic or Latino	5 (5.8)	11 (11.3)	0.18
Race			0.69
Asian	1 (1.2)	1 (1.0)	
Black/African American	10 (11.5)	6 (6.2)	
White	73 (83.9)	87 (89.7)	
Other	3 (3.5)	3 (3.1)	
Education			0.31
HS or less	57 (65.5)	57 (58.8)	
At least some college	29 (33.3)	34 (35.1)	
At least some graduate	1 (1.2)	5 (5.2)	
Unknown	0 (0.0)	1 (1.0)	
Post-injury time, mean (SD)	54.7 (22.0)	53.5 (22.0)	0.71
Baseline DRS Score, mean (SD)	21.8 (2.0)	22.2 (2.1)	0.13
Baseline CRS-R Score, mean (SD)	9.6 (3.8)	9.2 (4.4)	0.47

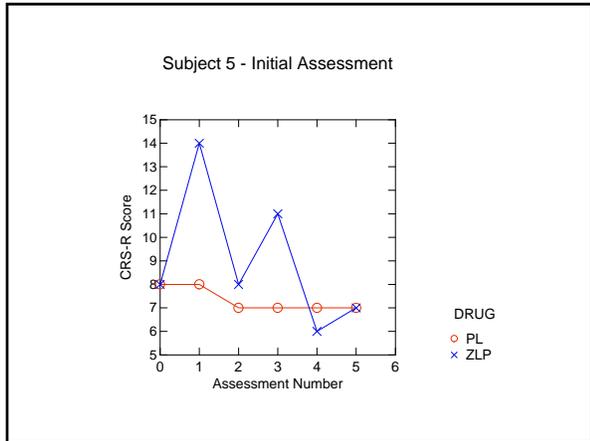
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Behavior	Percent of Sample Demonstrating Target Behavior at Enrollment		Percent of Sample Demonstrating Target Behavior at Week 4		Percent of Sample Demonstrating Target Behavior at Week 6	
	Placebo	AH	Placebo	AH	Placebo	AH
Consistent commands	0	0	32	40	39	41
Object recognition	5	2	34	44	42	45
Functional object use	1	0	26	42	32	38
Intelligible verbalization	6	5	34	39	41	36
Reliable y/n communication	0	0	27	31	29	35
Sustained attention	0	1	29	35	39	42

Zolpidem

- A case of intervention in the chronic phase



Zolpidem Results (cont.)

- No clear effects on group analysis of the 14 “non-responders”
- Thus, proportion of zolpidem responders is .07 (95% C.I.: .004 - .34)
- Need much larger sample to identify the “neural substrate” for drug response
- This design was feasible because of:
 - Improbable recovery in the chronic phase
 - Expectation of improvement within hours and reversion to baseline

Conclusions

- Twenty-five years ago we had NO medications with efficacy supported by rigorous research
- Today we have a handful that clearly have efficacy but still many questions about dose, timing, and target populations and problems
- Documentation of clinical treatment gave us very little progress
- Structured research gave us more...but it requires sustained effort and problem solving
