

University of Kentucky Physical Medicine & Rehabilitation



21ST
ANNUAL PM&R
RESEARCH DAY
May 28, 2009

Cardinal Hill
Rehabilitation Hospital
Center of Learning
2050 Versailles Road
Lexington, Kentucky

PROGRAM AND ABSTRACTS

21st Annual

Physical Medicine and Rehabilitation Research Day

May 28, 2009

Cardinal Hill Rehabilitation Hospital

Lexington, KY

The logo for UK HealthCare, featuring the letters 'UK' in a bold, blue, sans-serif font. The 'U' and 'K' are connected, with a small white silhouette of a building tower integrated into the 'K'. To the right of 'UK' is the word 'HealthCare' in a blue, sans-serif font.



21st Annual

**Physical Medicine and Rehabilitation
Research Day**

May 28, 2009
Cardinal Hill Rehabilitation Hospital
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**UNIVERSITY OF KENTUCKY
DEPARTMENT OF PHYSICAL MEDICINE & REHABILITATION
21st ANNUAL RESEARCH DAY AGENDA**

CARDINAL HILL REHABILITATION HOSPITAL
CENTER OF LEARNING
May 28, 2009

8:30 a.m. – 8:50 a.m. Continental Breakfast (CL2)
Sponsored By: Fran Settle, Amedisys Home Health Care

8:50 a.m. – 9:00 a.m. Opening Remarks (CL4): Robert Nickerson, M.D.

PM&R RESIDENT RESEARCH PRESENTATIONS – CL4

- 9:00 a.m. – 9:10 a.m. Zach Berry, M.D., Physical Medicine & Rehabilitation
“Using Three-Dimensional Gait Analysis to Discriminate Between Gait Patterns of Children with Cerebral Palsy/Spastic Diplegia and Hereditary Spastic Paraplegia”
- 9:15 a.m. – 9:25 a.m. Kristin Caldera, D.O., Physical Medicine & Rehabilitation
“The Effect of Intrathecal Baclofen Implant as Measured by the Change in Pre-Implant and Post-Implant PODCI Scores”
- 9:30 a.m. – 9:40 a.m. Thomas Coury, D.O., Physical Medicine & Rehabilitation
“Restarting Antiplatelet Therapy Following Intracranial Hemorrhage”
- 9:45 a.m. – 9:55 a.m. Silke Bernert, M.D., Physical Medicine & Rehabilitation
“Idiopathic Toe-Walking - Review of Treatment Methods and Outcome Measures”
- 10:00 a.m. – 10:10 a.m. Jessica Colyer, M.D., Physical Medicine & Rehabilitation
“Children with Spastic Diplegic Cerebral Palsy Increase Upper Extremity Weight Bearing During Ambulation Over Time”
- 10:15 a.m. – 10:25 a.m. ***BREAK***
- 10:30 a.m. – 10:40 a.m. Oscar Ortiz, M.D., Physical Medicine & Rehabilitation
“Importance of Upper Extremity Movement in Gait Speed in Children with Spastic Hemiplegic Cerebral Palsy”
- 10:45 a.m. – 10:55 a.m. Curtis Gale-Dyer, D.O., Physical Medicine & Rehabilitation
“Extrapontine Myelinolysis and Associated Dystonia: A Case Study”
- 11:00 a.m. – 11:10 a.m. Lindsay Shroyer, M.D., Physical Medicine & Rehabilitation
“Dose-Response Relationships of Sensory-Driven Motor Recovery in Stroke Subjects with Minimal Upper Extremity Motor Function: Background”
- 11:15 a.m. – 11:25 a.m. Dorathy Lachman, M.D., Physical Medicine & Rehabilitation
“Dose-Response Relationships of Sensory-Driven Motor Recovery in Stroke Subjects with Minimal Upper Extremity Motor Function: Proposed Methods”

UNIVERSITY OF KENTUCKY
DEPARTMENT OF PHYSICAL MEDICINE & REHABILITATION
21st ANNUAL RESEARCH DAY AGENDA
(Continued)

11:35 a.m. – 12:35 p.m.

Lunch (CL2)

Sponsored By: Michele Williams, Sanofi-Aventis

POSTER PRESENTATIONS – CL3

11:35 a.m. – 12:35 p.m.

Claire Davies, C.C. PT, DPT, UK/Rehabilitation Science
“Understanding the Process Involved in Physical Therapists
Decision-Making when Assessing and Determining Interventions
for Individuals with Acute Low Back Pain”

Camille Skubik-Peplaski, MS, OTR/L, BCP, Cardinal Hill Hospital
“Humanizing Practice Environments”

Kathleen Schoch, B.S., UK/Physiology & Microbiology,
Immunology, and Molecular Genetics, SCoBIRC
“Advancing Therapeutic Approaches for Traumatic Brain Injury
Through Calpastatin Overexpression”

Samir Patel, Ph.D., Post-Doc, UK/Physiology, SCoBIRC
“Mitochondrial Targeted Interventions Following Contusion
Spinal Cord Injury”

Theresa Currier Thomas, Ph.D., Post-Doc, SCoBIRC
“Diffuse Brain Injury Increases Extracellular Glutamate in the
Whisker-Barrel Circuit of Rats”

Hanad Duale, Ph.D., UK/SCoBIRC
“Noxious Colorectal Stimulation in Spinalized Rats Reduces
The Efficacy of Pseudorabies Virus Labeling of Kidney-Related
Sympathetic Preganglionic Neurons”

Tuoxin Cao, UK/Department of Biology
“Inflammation-Induced Neuroplasticity in the Diffuse Injured Brain
Correlates with Neurological Deficits in the Rat”

Sindhu Kizhakke Madathil, UK/SCoBIRC
“Insulin-Like Growth Factor -1 Overexpression Provides Regional
Neuroprotection Dependent on Injury Severity”

Stephen M. Onifer, Ph.D., UK/SCoBIRC
“Investigation of the Effect of Hindlimb Exercise on Adult Rat
Spinal Cord cAMP following Contusion Thoracic Injury”

Shaun Carlson, UK/SCoBIRC, Department of Physiology
“Proliferation in the Hippocampal Subgranular Zone after
Traumatic Brain Injury of IGF-1 Overexpressing Mice”

**UNIVERSITY OF KENTUCKY
DEPARTMENT OF PHYSICAL MEDICINE & REHABILITATION
21st ANNUAL RESEARCH DAY AGENDA
(Continued)**

POSTER PRESENTATIONS – CL3 (Continued)

Ayman G. Mustafa, UK/SCoBIRC
“Effects of the Lipid Peroxidation Inhibitor U-83836E on
Mitochondrial Dysfunction in the Mouse TBI Model”

Jennifer Pleasant, UK/SCoBIRC
“Impactor Tip Geometry Influences Rates of Cell Death Following
Controlled Cortical Impact

FEATURE SPEAKER – CL4

12:45 p.m. – 1:45 p.m.

Steven L. Wolf, Ph.D., PT, FAPTA, FAHA
Professor Emory University, Physical Medicine & Rehabilitation
“Constraint Induced Movement Therapy in the Treatment of
Upper Extremities Post-Stroke: Findings and Mechanisms”

1:45 p.m. – 2:00 p.m.

Awards & Closing Remarks
Joe Springer, Ph.D., Physical Medicine & Rehabilitation
Robert Nickerson, M.D., Physical Medicine & Rehabilitation

PM&R Resident Presentations

ORAL PRESENTATIONS

Presenter:

Abstract Presentation:

Zach Berry, M.D.

Using Three-Dimensional Gait Analysis to Discriminate Between Gait Patterns of Children with Cerebral Palsy/Spastic Diplegia and Hereditary Spastic Paraplegia

Kristin Caldera, D.O.

The Effect of Intrathecal Baclofen Implant as Measured by the Change in Pre-Implant and Post-Implant PODCI Scores

Thomas Coury, D.O.

Restarting Antiplatelet Therapy Following Intracranial Hemorrhage

Silke Bernert, M.D.

Idiopathic Toe-Walking, Review of Treatment Methods and Outcome Measures

Jessica Colyer, M.D.

Children with Spastic Diplegic Cerebral Palsy Increase Upper Extremity Weight Bearing During Ambulation Over Time

Oscar Ortiz, M.D.

Importance of Upper Extremity Movement in Gait Speed in Children with Spastic Hemiplegic Cerebral Palsy

Curtis Gale-Dyer, D.O.

Extrapontine Myelinolysis and Associated Dystonia: A Case Study

Lindsay Shroyer, M.D.

Dose-Response Relationships of Sensory-Driven Motor Recovery in Stroke Subjects with Minimal Upper Extremity Motor Function: Proposed Methods

Dorathy Lachman, M.D.

Dose-Response Relationships of Sensory-Driven Motor Recovery in Stroke Subjects with Minimal Upper Extremity Motor Function: Background

PM&R RESIDENT PRESENTATION

Using Three-Dimensional Gait Analysis to Discriminate Between Gait Patterns of Children with Cerebral Palsy/Spastic Diplegia and Hereditary Spastic Paraplegia

Presenter:

Zachary Berry, M.D.

Faculty Mentors/Collaborators:

Chester Tytkowski, M.D.¹ and Hank White, MSPT¹

Departmental Affiliations:

¹Shriner's Hospital for Children, Lexington, KY
University of Kentucky, Department of Physical Medicine and Rehabilitation

Abstract Text:

Objective: To determine if the use of three-dimensional gait analysis can discriminate between the gait patterns of children with cerebral palsy with spastic diplegia to those with hereditary spastic paraplegia, especially with regard to knee flexion/extension.

Proposal: Hereditary spastic paraplegia is a disease process which targets the corticospinal tracts, which in turn results in spasticity that predominates in the lower extremities. Children demonstrate physical exam findings and gait patterns which resemble children with cerebral palsy/spastic diplegia. Often times, treatment of these children is similar, if not identical, to those with spastic diplegia with goals of controlling the spasticity with medications, assistive devices, or surgical procedures. Only one study is known that has used three-dimensional gait analysis in an attempt to differentiate the between the gait patterns of hereditary spastic paraplegics and spastic diplegics. One of the results of that study showed that children with HSP and spastic diplegia have a large percentage of cases (50-60%) that demonstrate knee hyperextension during stance phase with a key difference in that the spastic diplegics have accompanied ankle plantar flexion, perhaps explaining the knee extension moment. Initial gross observation of kinematic data showed that children with HSP who have undergone a gait analysis at Lexington Shriner's Hospital might have a tendency towards knee hyperextension during the stance phase of gait, more so than their spastic diplegic counterparts. Therefore, I proposed that the HSP group would show a statistically significant difference in knee angles during the stance phase of gait.

Methods: The gait analyses of 21 children with HSP were compared to an age- and GMFCS-matched sample of CP children with spastic diplegia, all of whom have undergone three-dimensional gait analysis at Shriner's Hospital in Lexington, KY. Comparison of the kinematic data was performed on initial barefoot studies to include knee angle at initial contact, midstance, and the minimum angle during stance phase. Furthermore, I compared ankle angles at initial contact and during midstance to see if ankle plantar flexion might be present in the setting of knee hyperextension.

Results: Comparison of knee angles during stance phase of gait did not show a statistically significant difference between groups. Our study showed fewer tendencies towards knee extension than the aforementioned study with only 19% of the HSP group and 9% of the SD group showing any evidence of hyperextension during stance phase. All of the subjects had a plantar flexion moment at initial contact, which could contribute all of the cases of knee hyperextension. This contradicts the previous study which stated that HSP children have hyperextension at the knee without concomitant ankle plantarflexion.

Key Words: Three-Dimensional Gait Analysis, Hereditary Spastic Paraplegia, Spastic Diplegia, Gait

PM&R RESIDENT PRESENTATION

The Effect of Intrathecal Baclofen Implant as Measured by the Change in Pre-implant and Post-implant PODCI Scores

Presenter:

Kristin Caldera, D.O.

Collaborators:

Susan McDowell, M.D.¹ and Todd Milbrandt, M.D.^{2,3}

Departmental Affiliations:

¹University of Kentucky, Department of Physical Medicine & Rehabilitation

²University of Kentucky, Department of Pediatric Orthopedic Surgery

³Shriners Hospital for Children, Lexington, Kentucky

Abstract Text:

Objectives: To assess whether there is an improvement in PODCI (Pediatric Outcomes Data Collection Instrument) scores in children with cerebral palsy (CP) who undergo intrathecal baclofen (ITB) implant, for the management of spasticity.

Design: Retrospective chart review of patients receiving implants from the years 2000-2007, with available PODCI scores.

Setting: Pediatric Orthopedic and Rehabilitation Specialty Hospital.

Participants: Children with cerebral palsy, GMFCS (Gross Motor Function Classification Scale) level IV and V who received ITB implants for management of severe spasticity.

Intervention: Intrathecal baclofen therapy in children with CP.

Main Outcome Measures: Pre intrathecal baclofen implant PODCI and post intrathecal baclofen implant PODCI.

Results: A significant difference was found between pre and post implant PODCI scores in the domain of transfers and basic mobility. A trend toward perceived improvement was seen in sports and physical function, pain, and satisfaction with symptoms. No significant change in pre and post pump happiness or treatment expectations.

Conclusion: Although the PODCI is a validated measurement tool frequently used in pediatrics, it may be beneficial to supplement outcome measures with other tools to further identify improvements in function, pain, ease of caregiving, and overall satisfaction in this population of children with cerebral palsy.

Key Words: Cerebral Palsy, PODCI, Intrathecal Baclofen

PM&R RESIDENT PRESENTATION

Restarting Antiplatelet Therapy Following Intracranial Hemorrhage

Presenter:

Thomas Coury, D.O.

Collaborators:

John "Jay" Cole, M.D.¹ and Joe E. Springer, Ph.D.²

Departmental Affiliations:

¹University of Kentucky, Department of Neurosurgery

²University of Kentucky, Department of Physical Medicine and Rehabilitation

Abstract Text:

With the advent of drug-eluting stents in the field of interventional cardiovascular medicine, many patients now find themselves on chronic antiplatelet therapy. As patients continue to sustain intracranial hemorrhages (ICH), questions have arisen about the appropriate window for re-institution of antiplatelet agents following such events.

A chart review of discharged patients from the Traumatic Brain Injury unit at Cardinal Hill Hospital over the past two years was performed, cross-referencing "plavix" with intracranial hemorrhage. Outcomes included days off of antiplatelet therapy and presence of recurrent ICH or cardiac event. Five patients met inclusion criteria. None experienced a recurrent bleed. One sustained a non-ST elevation myocardial infarction. One experienced an extremely rare post-traumatic acute inflammatory demyelinating polyneuropathy. Though a time table for restarting antiplatelet therapy was not achieved with this small sample size, this study indicates consideration could be given for restarting antiplatelet therapy early.

PM&R RESIDENT PRESENTATION

Idiopathic Toe-Walking, Review of Treatment Methods and Outcome Measures

Presenter:

Silke Bernert, M.D.

Collaborators:

Melanie McEwen, Ph.D.¹ and Todd Milbrandt, M.D.^{2,3}

Departmental Affiliations:

¹University of Kentucky, Department of Physical Medicine and Rehabilitation

²University of Kentucky, Pediatric Orthopedic Surgery

³Shriners' Hospital for Children, Lexington, Kentucky

Abstract Text:

Idiopathic toe-walking is a phenomenon of unknown cause whereby otherwise healthy children do not adopt a normal heel-toe gait as they develop but continue walking on their toes. The objective of this study was to review the treatment strategies and outcomes for 108 children treated for idiopathic toe-walking between 2001 and 2008. History and physical examination notes were reviewed. Achilles tendon lengthening was performed on all patients with plantar flexion contracture of 20 degrees or more; range of motion improved and toe-walking resolved in almost all cases. Preliminary review of the data indicates that other treatments including various combinations of physical therapy, nighttime ankle-foot orthoses (AFOs), daytime AFOs, and casts may be helpful. Children placed in nighttime AFOs, either in conjunction with physical therapy or after casts, appear to show greater improvements in gait than non-braced counterparts. Improvements in ankle dorsiflexion, assessed in knee extension, were also noted but did not seem to predict the amount of toe-walking when ankle dorsiflexion was greater than 0 degrees. Daytime AFOs did not noticeably improve gait. These findings suggest that non-operative measures can improve ankle dorsiflexion and gait; physical therapy and casting should be accompanied by nighttime orthoses, however statistical analysis is still pending. Assessments of ankle dorsiflexion during knee extension may not be a good measure of treatment outcome unless a plantar flexion contracture is present. A prospective study is needed to confirm these findings.

Key Words: Idiopathic Toe Walking, Treatment, Outcome Measure

PM&R RESIDENT PRESENTATION

Children with Spastic Diplegic Cerebral Palsy Increase Upper Extremity Weight Bearing During Ambulation Over Time

Presenter:

Jessica L. Colyer, M.D.

Collaborators:

Hank White, PT, Ph.D.² and Chester Tylkowski, M.D.²

Departmental Affiliations:

¹Department of Physical Medicine and Rehabilitation, University of Kentucky

²Department of Pediatric Orthopedics, Shriners Hospital for Children, Lexington, Kentucky

Abstract Text:

Objective: Multiple studies reveal that many adults with cerebral palsy (CP) lose walking ability when in adulthood. Complete explanations for discontinuation of walking have yet to be elucidated. Studies suggest that biomechanical forces, immobility, overuse injuries, and fatigue are all factors. Although many with CP will ambulate with hand-held assistive devices, little study has been performed regarding upper extremity weight bearing during ambulation. We predicted that upper extremity weight bearing would increase over time.

Design: Retrospective database review.

Setting: Outpatient gait analysis laboratory.

Patients: 1049 children had gait analysis studies available in the database. Of that number, 40 children (28 male, 12 female) with spastic diplegic CP had gait analysis on three separate occasions over time. Eighteen of this group had four discrete studies.

Methods: Gait analysis was performed with a “universal walker” that adjusts to children and adolescents of all sizes and ages. Each hand grip has a transducer which allows for collection of upper extremity weight bearing (as percent of body weight). Data was retrospectively collected and repeated measures MANOVA was performed.

Results: Participants were an average of 7.9 years at first study, 11.9 years at third study, and 12.6 years at fourth study. Among the group with three gait studies, mean weight bearing was 49.4% at first trial and 51.7% at third trial [$p=0.19$]. In the subgroup with four studies, the mean weight bearing was 47.7% at first trial and 57.3% at fourth trial, which was statistically significant [$F(3,18) = 3.75$, $p=0.016$].

Conclusions: Children with spastic diplegic CP show an increase in upper extremity weight bearing over time. Further study needs to address correlation to decreased ambulation in adulthood.

Key Words: Cerebral Palsy, Gait Analysis, Pediatrics

PM&R RESIDENT PRESENTATION

Importance of Upper Extremity Movement in Gait Speed in Children with Spastic Hemiplegic Cerebral Palsy

Presenter:

Oscar O. Ortiz-Vargas, M.D.

Departmental Affiliations:

University of Kentucky, Department of Physical Medicine and Rehabilitation
Shriner's Hospital for Children, Lexington, Kentucky

Abstract Text:

Background: Function of upper extremities (UE) in human gait is thought to be limited to helping balancing the angular momentum generated during gait. Recent studies indicate that UE movement might play a more important role, helping the inter-segmental (trunk-pelvis-legs) coordination during walking. Although this function may be trivial in normal individuals, it might become critical in patients with gait disturbances.

Methods: 159 patients with spastic hemiplegic CP with a mean age of 11.1 years were included. Medical records and gait analysis data were reviewed. Patients were classified using Winters criteria. Linear regression analysis and ANOVA were used to determine the strength of the association.

Results: Plegic elbow range of motion (ROM) observed during gait analysis was associated with gait speed, specifically in Winters type 2 ($R^2 = 0.472$, $p = 0.009$), and type 4 ($R^2 = 0.149$, $p = 0.339$) groups. Increase on stride length explains partially the changes observed in speed gait. UE ROM showed not association with O₂ consumption, and both showed an inverted U-shaped curve relationship with Winters classification. Winters classification, in turn, was inversely related to gait speed ($p = 0.008$).

Conclusions: Amplitude of movement of the plegic elbow is directly associated with gait speed in children with spastic hemiplegic CP. Lack of association between O₂ consumption and UE ROM suggests that the increased mobility of the affected elbow improves gait efficiency in this population. We can hypothesize that higher amplitude of movement in the elbow causes increment on trunk and pelvis rotation, facilitating the lengthening of the stride.

Keywords: Hemiplegic Cerebral Palsy; Gait Analysis; Upper Extremity

PM&R RESIDENT PRESENTATION

Extrapontine Myelinolysis and Associated Dystonia: A Case Study

Presenter:

Curtis Gale-Dyer, D.O.

Departmental Affiliations:

University of Kentucky Medical Center, Department of Physical Medicine and Rehabilitation

Abstract Text:

Extrapontine myelinolysis (EPM) can be caused by hyponatremia, which the latest literature says can happen with or without proper correction of the blood sodium level. One of the common symptoms associated with EPM is dystonia. This is a case of a 24 year old male who presents to an acute care hospital with a blood sodium level of 106 and subsequently developed EPM roughly 10 days later after proper correction of sodium. Associated with the EPM, he developed severe dystonia in all limbs and fascial muscles. We then started him on trihexyphenidyl (Artane®) for the dystonia with good results. This case study will then discuss the use of Artane®, the difference between spasticity and dystonia, along with a review of some of the current literature related to EPM and dystonia.

PM&R RESIDENT PRESENTATION

Dose-Response Relationships of Sensory-Driven Motor Recovery in Stroke Subjects with Minimal Upper Extremity Motor Function: Background

Presenter:

Lindsay Shroyer, M.D.

Collaborators:

Dorathy Lachman, M.D., Lumy Sawaki, M.D., Ph.D., Cheryl Carrico, M.S., O.T., Laurie Nichols, B.S., O.T., and Kenneth Chelette, M.S.

Departmental Affiliations:

University of Kentucky, Department of Physical Medicine and Rehabilitation

Abstract Text:

Stroke is the third leading cause of death in the United States and the leading cause of disability among American adults. Efforts to limit the amount of tissue damaged in the acute phase of stroke have been disappointing, highlighting the need for effective therapeutic interventions after neurologic damage has occurred. The viability of such interventions is rooted in the capacity of the adult brain to undergo a degree of reorganization formerly thought to occur only during early post-natal periods. Several lines of evidence indicate that sensory training and experience can increase the capacity for this reorganization, providing great benefit in the recovery of function after brain injury. Data from animal and human models have suggested that sensory input plays an important role in motor output, possibly by influencing cortical plasticity. Our investigation of these approaches to rehabilitation has yielded further insight into the mechanisms of functional recovery. More specifically, preliminary data from ongoing studies in chronic and subacute stroke demonstrate that motor function can be substantially enhanced when peripheral nerve stimulation (PNS) is delivered **before** intensive task-oriented therapy. In these ongoing studies, the intensity of PNS has been adjusted to elicit small compound muscle action potentials of 50 to 100 μ V without inducing muscle contractions (below motor threshold). Improvement of motor function measured by behavioral testing appears to be associated with corticomotor reorganization measured by transcranial magnetic stimulation (TMS). While afferent inputs seem to play a major role in inducing behavioral motor improvement and plastic changes in stroke patients, there have been no studies directly comparing how **timing and stimulus intensity of PNS** correlate with functional motor gains. Therefore, in this study, **we propose to develop a time and dose response model**, applying PNS before and concurrent with intensive motor training as well as below and above motor threshold. The long-range goals of this research are to: (a) maximize the restoration of upper extremity motor function in post-stroke patients, and (b) determine the impact of this intervention in improving activities of daily living and quality of life and (c) collect solid data to prepare for a future randomized clinical trial.

Key Words: Neuroplasticity, Stroke, Motor Recovery, Upper Extremity, Nerve Stimulation, Transcranial Magnetic Stimulation

PM&R RESIDENT PRESENTATION

Dose-Response Relationships of Sensory-Driven Motor Recovery in Stroke Subjects with Minimal Upper Extremity Motor Function: Proposed Methods

Presenter:

Dorathy Lachman, M.D.

Collaborators:

Lindsay Shroyer, M.D., Lumy Sawaki, M.D., Ph.D., Cheryl Carrico, M.S., O.T., Laurie Nichols, B.S., O.T., and Kenneth Chelette, M.S.

Departmental Affiliations:

University of Kentucky, Department of Physical Medicine and Rehabilitation

Abstract Text:

We propose to develop a time and dose response model through the application of peripheral nerve stimulation (PNS) delivered below and above the motor threshold before and concurrent with intensive motor training. Twelve chronic stroke patients with severe upper extremity weakness following a single ischemic stroke will be recruited for this study. Subjects will participate in two assessment sessions and ten days of intervention. Assessment sessions to evaluate behavioral and neurophysiological changes will be performed using behavioral motor function tests and transcranial magnetic stimulation (TMS), respectively. Following the screening process and informed consent, an anatomical MRI will be obtained for each patient. The anatomical MRI will be used to document the lesion and to accurately construct a TMS motor map using the Brainsight™ neuronavigation system (Rogue Research Inc. Montreal, Canada). Evaluations will be performed at baseline and after the intervention period. Following baseline assessment, patients will be randomized to one of the following four groups:

Group 1: Below motor threshold PNS delivered prior to motor training

Group 2: Above motor threshold PNS delivered prior to motor training

Group 3: Below motor threshold PNS delivered concurrently with motor training

Group 4: Above motor threshold PNS delivered concurrently with motor training

The intervention period will consist of intensive motor training delivered by an upper extremity robotic system. All subjects will undergo identical protocols of evaluation and intensive motor training.

The central hypothesis is that chronic stroke patients receiving **PNS above motor threshold and during** intensive motor training will have improved motor function compared to patients receiving PNS below-motor threshold and before motor training. Further, the degree of functional gain measured by behavioral assessment will correlate with the neurophysiological changes measured by image-guided TMS.

Key Words:

Neuroplasticity, Stroke, Motor Recovery, Upper Extremity, Nerve Stimulation, Transcranial Magnetic Stimulation

POSTER PRESENTATIONS

Presenter:

Poster Presentation:

Claire Davies, C.C. PT, DPT

Understanding the Process Involved in Physical Therapists Decision-Making when Assessing and Determining Interventions for Individuals with Acute Low Back Pain

Camille Skubik-Peplaski,
MS, OTR/L, BCP

Humanizing Practice Environments

Kathleen Schoch, B.S.

Advancing Therapeutic Approaches for Traumatic Brain Injury Through Calpastatin Overexpression

Samir Patel, Ph.D., Post-Doc

Mitochondrial Targeted Interventions Following Contusion Spinal Cord Injury

Theresa Currier Thomas, Ph.D.,
Post-Doc

Diffuse Brain Injury Increases Extracellular Glutamate in the Whisker-Barrel Circuit of Rats

Hanad Duale, Ph.D.

Noxious Colorectal Stimulation in Spinalized Rats Reduces The Efficacy of Pseudorabies Virus Labeling of Kidney Related Sympathetic Preganglionic Neurons

Tuoxin Cao

Inflammation-Induced Neuroplasticity in the Diffuse Injured Brain Correlates with Neurological Deficits in the Rat

Sindhu Kizhakke Madathil

Insulin-Like Growth Factor -1 Overexpression Provides Regional Neuroprotection Dependent on Injury Severity

Stephen M. Onifer, Ph.D.

Investigation of the Effect of Hindlimb Exercise on Adult Rat Spinal Cord cAMP Following Contusion Thoracic Injury

Ayman G. Mustafa,

Effects of the Lipid Peroxidation Inhibitor U-83836E on Mitochondrial Dysfunction in the Mouse TBI Model

POSTER PRESENTATION

Understanding the Process Involved in Physical Therapists Decision-Making when Assessing and Determining Interventions for Individuals with Acute Low Back Pain

Presenter:

Claire Davies, C.C. PT, DPT

Collaborators:

Dana Howell, Ph.D., OTD, OTR/L

Department Affiliations:

University of Kentucky, Department of Rehabilitation Science

Abstract Text:

Background: Classification systems are available to guide decision-making in low back pain (LBP). Evidence supports the proposal that if initial clinical LBP signs and symptoms are treatment matched, clinical outcomes can be improved. This is important in the population of acute LBP sufferers as many of them develop long term disability if they do not quickly recover. Initial decision-making on sub grouping LBP to guide treatments could have long term consequences. The physical therapist uses their own clinical decision-making skills to determine where the patient fits in the sub-groups.

Objectives: The aims of this study are: (1) to determine a central theory explaining the process physical therapists use to determine how to evaluate and select interventions to be used for acute LBP, (2) to observe if classification based sub grouping is used to determine interventions, (3) to determine whether the physical therapists base their diagnosis on clinical experience, biomedical knowledge, a combination of both or something different.

Methods: A qualitative design using a grounded theory approach to explore clinical decision-making. Physical therapists from different outpatient settings with varying years of experience will be purposefully selected to be interviewed. Inclusion criteria: licensed physical therapists, with any level of experience, working in a hospital based or private practice outpatient clinic and work with people with acute LBP.

Anticipated Results: Experience of physical therapists using their clinical knowledge base, to classify patients, and postgraduate training is expected to emerge from the data. This preliminary information will develop questions for a future survey.

Key Words: Decision-Making, Acute Low Back Pain, Physical Therapists

POSTER PRESENTATION

Humanizing Practice Environments

Presenter:

Camille Skubik-Peplaski, MS, OTR/L, BCP

Collaborators:

Elizabeth Hunter, Ph.D.

Departmental Affiliations:

Cardinal Hill Healthcare System

Abstract Text:

The environment has an impact on an individual's ability to recover from a traumatic insult, injury or surgery. If the client's goal is to return to their previous level of occupational participation then is a homelike setting for rehabilitation more effective to learn/relearn skills? Based on observations of several rehabilitation clinics it appears that occupational therapy practice space falls short of replicating environments that individuals would normally perform their daily routines and rituals in. In this poster we present observations of different rehabilitation environments, investigate occupational therapists perceptions of optimal clinic space and pose recommendations for the best practice. The environment of the hospital especially the therapy clinics, can be perceived as supportive or inhibitive to the client. This author further defines a supportive environment as one that is open to exploration, driven by the client's needs and goals and is accepting of the individual. Rebeiro (2001, p. 80) found that environments need to affirm the client as a "person of worth, a place to belong, and a place to be supported," and that this is what enables a client to perform their meaningful occupations. Devlin (2007) believes that the occupational treatment area needs to use environmental factors that support participation, alleviate stress and contribute to positive emotions and behaviors. In essence, if an environment is planned appropriately the client may be able to better adapt when learning new tasks. Devlin states that the clinic should have a feeling of home rather than an institution.

Key Words:

Environment, Therapy Clinic, Equipment, Occupation-Based Practice

POSTER PRESENTATION

Advancing Therapeutic Approaches for Traumatic Brain Injury Through Calpastatin Overexpression

Presenter:

Kathleen Schoch, B.S.¹

Collaborators:

Glenn Telling, Ph.D.² and Kathryn Saatman, Ph.D.¹

Departmental Affiliations:

¹University of Kentucky Medical Center, Department of Physiology

¹University of Kentucky, Spinal Cord and Brain Injury Research Center (SCoBIRC)

²University of Kentucky, Department of Microbiology, Immunology, and Molecular Genetics

Abstract Text:

Prolonged activation of calcium-activated proteases, calpains, contributes to cell death and behavioral dysfunction following traumatic brain injury (TBI). Although its inhibitor, calpastatin, is co-expressed with calpains, endogenous calpastatin levels may be insufficient to fully suppress posttraumatic proteolytic activity of calpains. We hypothesize that calpastatin overexpression will reduce calpain activity and cell death after TBI, thereby attenuating motor and cognitive behavioral deficits. Using novel transgenic mice with human calpastatin (hCAST) under control of the ubiquitous prion promoter (PrP-hCAST), we have demonstrated 3-fold greater calpastatin expression in the cortex and hippocampus and increased hCAST immunostaining in cortical and hilar regions compared to previously used mice that overexpress hCAST under the neuron-specific CaMKII promoter. We posit that PrP-hCAST mice are a better experimental tool to test our hypothesis. To this end, we have shown lower calpain activity, measured by fluorogenic assay on naïve cortical homogenates, in PrP-hCAST (n=6) compared to wildtype mice (n=5), confirming functional activity of hCAST. Immunoblots for α -spectrin revealed hCAST mice (n=11) exhibited significantly less calpain-mediated cortical α -spectrin proteolysis than wildtype littermates (n=10; p<0.01) six hours following severe controlled cortical impact (CCI). At 24 hours post-CCI, levels of calpain-specific 145 kDa spectrin breakdown product appeared attenuated in PrP-hCAST (n=3) compared to wildtype littermates (n=4), but the difference did not reach statistical significance. These preliminary results implicate a functional role for calpastatin in the acute period following severe TBI in mice. Enhancing endogenous calpastatin levels may represent a therapeutic approach for TBI.

Key Words:

Traumatic Brain Injury, Calpain, Calpain Inhibition, Calpastatin, Spectrin Proteolysis

POSTER PRESENTATION

Mitochondrial Targeted Interventions Following Contusion Spinal Cord Injury

Presenter:

Samir Patel, Ph.D., Post-Doc

Collaborators:

Travis S. Lyttle^{1,2}, Patrick G. Sullivan, Ph.D.^{1,3}, and Alexander G. Rabchevsky, Ph.D.^{1,2}

Departmental Affiliations:

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

²University of Kentucky, Department of Physiology

³University of Kentucky, Departments of Anatomy and Neurobiology

Abstract Text:

In present study, we evaluated the neuroprotective efficacy of a widely used medication for neurodegenerative diseases, acetyl-L-carnitine (ALC) in a contusion (200 kdyn) spinal cord injury (SCI) model. ALC provides sufficient influx of reducing equivalent for energy production in mitochondria, increases glutathione production, and stimulates protein and membrane phospholipid synthesis. Animals were administered i.p. either vehicle (saline) or ALC (300 mg/kg) at 15 min, 30 min or 1 hr post-injury, followed by one booster at 6 hrs post-injury (n=6). At 24 hr post-injury, mitochondria were isolated and assessed for respiration rates, activities of NADH dehydrogenase, cytochrome oxidase and pyruvate dehydrogenase, as well as NADH content. The results showed, expectedly, that SCI significantly ($p<0.05$) decreased respiration rates and activities of all the enzyme complexes. However, compared to vehicle treated-injured rats, treatment with ALC significantly ($p<0.05$) maintained mitochondrial respiration at all the time-points of administration. Moreover, compared to vehicle-treated injured rats, enzyme activities were significantly maintained after ALC administration at 15 and 30 min post-injury, but not after 1 hr. Additionally, following SCI the abnormally elevated mitochondrial NADH content was significantly ($p<0.05$) reduced by ALC treatment at all the time-points of administration. Preliminary morphological studies showed that multiple treatments with ALC at 15 min and 6 hr post-injury, followed by once daily for 7 days, significantly ($p<0.05$) spared spinal cord tissue compared to vehicle treatment. Ongoing studies with ALC treatment following contusion SCI include long-term behavioral outcome measures to correlate with tissue sparing. Supported by NIH/NINDS R01 NS049901, KSCHIRT #8-13 (AGR) and NIH/NINDS P30 NS051220.

Key Words:

Spinal Cord Injury, Mitochondrial Dysfunction, Acetyl-L-carnitine, Spinal Cord tissue Sparing

POSTER PRESENTATION

Diffuse Brain Injury Increases Extracellular Glutamate in the Whisker-Barrel Circuit of Rats

Presenter:

Theresa Currier Thomas, Ph.D., Post-Doc¹

Collaborators:

Amanda Lisembee¹, Kelley Hall¹, Katelyn McNamara¹, Tuoxin Cao¹, Greg A. Gerhardt^{2,4,5}, and Jonathan Lifshitz^{1,2,3}

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⁶University of Kentucky College of Medicine

Abstract Text:

Closed-head traumatic brain injury (TBI) causes diffuse axonal injury (axotomy) and deafferentation, resulting in circuit disruption that likely leads to neurological impairment including sensory sensitivity. One month after diffuse brain injury, rodents develop robust sensory sensitivity in response to manual whisker stimulation in comparison to sham animals which remain calm and curious. The somatosensation of whisker stimulation relies on 3 glutamatergic relays between the trigeminal nucleus, the ventral posterior medial nucleus of the thalamus (VPM), and barrel fields of the primary somatosensory cortex (S1BF); referred to as the whisker-barrel circuit. We hypothesize that the sensory sensitivity in brain-injured rats arises from circuit disruption of the glutamatergic whisker-barrel circuit. In order to test alterations in circuit disruption, male Sprague-Dawley rats received a sham (n=5) or moderate midline fluid percussion brain injury followed by electrochemical glutamate recordings at 7 or 28 days post-injury (n=4, n=8) using *in vivo* amperometry coupled to a novel multi-site microelectrode array. Measures of resting extracellular glutamate levels were used to evaluate circuit dysfunction at multiple depths through the VPM and S1BF. Resting extracellular glutamate levels were similar to sham in the VPM at 7 days post-injury, but significantly increased by 60% at 28 days post-injury. No injury-induced shifts in S1BF extracellular glutamate levels were detected. The delayed responses in the VPM correspond to the temporal development of sensory sensitivity to whisker stimulation. Similar alterations in neurotransmission may be responsible for other injury-related neurological deficits in rodents and man.

Key Words:

Diffuse Brain Injury, Glutamate, Whisker-Barrel Circuit, *In Vivo* Amperometry

POSTER PRESENTATION

Noxious Colorectal Stimulation in Spinalized Rats Reduces the Efficacy of Pseudorabies Virus Labeling of Kidney-Related Sympathetic Preganglionic Neurons

Presenter:

Hanad Duale, Ph.D.¹

Collaborators:

T.S. Lyttle¹, B.N. Smith² and A.G. Rabchevsky^{1,2}

Departmental Affiliations:

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

²University of Kentucky, Department of Physiology

Abstract Text:

Pseudorabies virus (PRV) has been widely used as a transynaptic tracer for synaptic connectivity in the spinal cord. We have recently reported a significant attenuation of the effectiveness of PRV-152 in labeling the intermediolateral cell column (IML) in chronic spinalized rats versus uninjured sham rats at 96 hours after viral inoculation of the left kidney. We have also observed a significant ($p<0.05$) increase in noxious colorectal distention (CRD)-evoked c-fos expression in spinal cords of injured versus sham animals. To assess whether enhancing neuronal activity in spinalized rats would increase PRV-152 labeling, we subjected awake spinalized rats to either: 1) 1.5 hours of intermittent CRD prior to PRV inoculation or 2) 1.5 hours of intermittent CRD 96 hours after inoculation ($n=3$ /group). Additionally, equal numbers of spinalized rats received PRV-152 inoculation without CRD (unstimulated). Following 96 hours post inoculation, fixed spinal and left celiac ganglionic tissues were processed to assess the distribution of labeled cells. In the cohort that received the CRD stimulation prior to PRV injection, we observed a marked reduction in labeled cells in the IML and left celiac ganglion compared to unstimulated rats. In contrast, the cohort that received CRD 96 hours after PRV-152 inoculation showed no qualitative difference in the distribution of labeled cells in either the IML or left celiac ganglion in stimulated compared to unstimulated spinalized rats. Together, these results infer that in the injured paradigm, increased neuronal activity (c-fos expression) prior to but not after PRV injection suppresses PRV-152 uptake, perhaps through lasting changes in cellular activity induced by the CRD or the down-regulation of PRV-specific receptors, transcription and/or translation factors.

Key Words:

Spinal Cord Injury, Viral Infection, Sympathetic Preganglionic Neurons

POSTER PRESENTATION

Inflammation-Induced Neuroplasticity in the Diffuse Injured Brain Correlates with Neurological Deficits in the Rat

Presenter:

Tuoxin Cao

Collaborators:

Jonathan Lifshitz, Ph.D.

Departmental Affiliations:

Spinal Cord & Brain Injury Research Center (SCoBIRC), Department of Biology, Department of Physical Medicine & Rehabilitation, University of Kentucky

Abstract Text:

At least 1.4 million civilian traumatic brain injuries (TBI) occur in the United States each year, with most of them resulting in mild to moderate injury and treated in the emergency department. TBI survivors often exhibit behavioral morbidity and changes in personality after the initial recovery, which span a spectrum of neuropsychological functions. The primary mechanical forces of TBI initiate neuroinflammatory processes that can promote neuroplasticity. An unregulated increase in neuroplasticity can result in the formation of maladaptive circuits, which may underlie post-traumatic morbidities. The purpose of this study is to identify the time course of injury-induced neuroinflammatory and neuroplasticity processes by quantifying the gene expression in the diffuse injured rat brain that may correlate with behavioral deficits.

Diffuse brain injury was induced to rats (male, Sprague-Dawley, 350-400g) by midline fluid percussion (1.9-2.0 atmospheres). Brain regions (cortex, thalamus and hippocampus) were isolated from brain-injured and uninjured rats at one or four weeks post-injury (n=3-4/group). From those tissue samples, mRNA was isolated, and then converted to cDNA, using standard procedure provided by the manufacturer. Gene expression was quantified using real-time polymerase chain reaction (rtPCR; Step-One, Applied Biosciences) using the TaqMan gene expression assays. The relative expression level of each gene was compared between time points and correlated with behavioral deficits.

Reliable quantification of relative gene expression was achieved for uninjured and brain injured S1BF, thalamus and hippocampus at 7d and 28d post-injury. As expected, chronic inflammatory processes were confirmed by the sustained increase in the inflammatory TSPO gene expression after FPI in all brain regions studied. Regional specific changes in inflammation-driven plasticity genes (GAP-43, synaptophysin) were evident over the experimental time course. In S1BF, plasticity markers continually increased, whereas plasticity markers in VPM and hippocampus initially decreased and then returned to uninjured levels. Therefore, brain injury results in neuroplastic events over a four week time course that could develop maladaptive circuits. The formation of maladaptive circuits correlates with the onset of aberrant behavioral responses to whisker stimulation; a behavior subserved by these brain regions. The sustained injury-induced inflammation also disrupts glutamatergic neurotransmission as evidenced by initial reduction and later rise in the gene expression for glutamate transporter genes (Glut1, EAAT3), suggesting that neurotransmitter reuptake is disrupted post-injury. As the transient disruption in glutamate reuptake subsides, the homeostasis is restored along with behavioral deficits. Taken together, these results support the hypothesis and demonstrate that the chronic inflammation that follows brain injury drives neuroplasticity and disrupts neurotransmission that contribute to the emergence of behavioral deficits. By modulating post-injury inflammatory processes, behavioral morbidity may be minimized.

POSTER PRESENTATION

Insulin-Like Growth Factor -1 Overexpression Provides Regional Neuroprotection Dependent on Injury Severity

Presenter:

Sindhu Kizhakke Madathil

Collaborators:

Heather Foozer, B.S., Kathryn Saatman, Ph.D.¹

Departmental Affiliations:

University of Kentucky, Spinal Cord and Brain Injury Research Center (SCoBIRC)

Abstract Text:

Insulin-like growth factor 1 (IGF-1) is a potent neurotrophic factor that is essential for cell survival, synaptogenesis, and myelination. In traumatic brain injury (TBI) clinical trials, patients receiving IGF-1 showed improved metabolic status. We have previously shown that administration of IGF-1 improved neurobehavioral function following TBI in rats. However, the neuroprotective potential of IGF-1 treatment in brain injury has not been determined. In this study we investigated the histological effects of astrocytic overexpression of IGF-1 after moderate and severe TBI using transgenic mice (IGF-1Tg) which conditionally express IGF-1 under the control of the GFAP promoter regulated by a 'tet-off' system. Both C57BL/6 wildtype (WT) and IGF-1Tg mice received a controlled cortical impact (CCI) injury of either 0.5mm or 1.0mm depth or sham injury. Augmented astrocytosis concomitant with IGF-1 expression was observed in the cortex and hippocampus of IGF-1Tg mice 72h after both moderate and severe injuries. However, cortical neuroprotection was observed only for the moderate injury whereas hippocampal neuroprotection was observed following both injury severities. Interestingly, at 24h after severe CCI, astrocytosis accompanied by increased IGF-1 was observed in the hippocampus but not in the cortex of IGF-1Tg mice. More rapid astrocytosis in the hippocampus compared to the cortex provided an earlier upregulation of IGF-1 which may have contributed to effective neuroprotection in the hippocampus. The current findings suggest that non-neuronal IGF-1 overexpression promotes neuronal survival following TBI and endorses the usefulness of IGF-1 as a therapeutic agent in brain-injured patients.

Supported in part by NIH NS045131, NS051220 and KSCHIRT 7-20

Key Words:

Controlled Cortical Impact, Traumatic Brain Injury, IGF-1

POSTER PRESENTATION

Investigation of the Effect of Hindlimb Exercise on Adult Rat Spinal Cord cAMP following Contusion Thoracic Injury

Presenter:

Stephen M. Onifer

Collaborators: Ryan K. Morgan¹⁻⁴, Kashif Raza³, Stephanie N. Thompson³, Esther Dupont-Versteegden^{3,5}, Stephen M. Onifer^{3,4}

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Abstract Text:

The functional deficits and limits on recovery occurring after traumatic spinal cord injury (SCI) result from the primary mechanical insult and a cascade of secondary events. These occur within minutes and can last for months and years. Clinical and experimental evidence indicate that it is possible for applied interventions to attenuate and prevent secondary events after SCI as well as to promote neuroprotection, neurorepair, and recovery. Adenosine 3', 5' cyclic monophosphate (cAMP) decreases in adult rat thoracic spinal cord and supraspinal brain regions after contusion injury. This can be attenuated by rolipram, an inhibitor of phosphodiesterase IV which hydrolyzes cAMP, and result in neuroprotection. Rolipram and dibutyryl-cAMP, an analog of cAMP, also lead to axonal regeneration after SCI. All of the known effects of cAMP result from the downstream activation of nuclear cAMP response element binding protein (CREB), which controls transcription of various genes. Rehabilitation exercise after hemisection thoracic SCI has been shown to increase CREB mRNA and protein in the adult rat lumbar spinal cord. Compared to adult rats after contusion thoracic SCI, it was recently reported that similarly injured rats had significantly better locomotion in the open field when their hindlimbs were exercised on a bike device. Collectively, these findings led us to hypothesize that exercise's therapeutic effects involve alterations of the cAMP response to SCI. In this project, we began testing this hypothesis by performing contusion thoracic SCI in adult rats, exercising their hindlimbs with a bike device, and measuring cAMP in their spinal cords.

Keywords:

Mechanism, Neuroplasticity, Rehabilitation

POSTER PRESENTATION

Proliferation in the Hippocampal Subgranular Zone after Traumatic Brain Injury of IGF-1 Overexpressing Mice

Presenter:

Shaun Carlson

Collaborators:

Sindhu K. Madathil¹, Xiang Gao², Jinhui Chen², and Kathryn E. Saatman¹

Departmental Affiliations:

¹Spinal Cord and Brain Injury Research Center, Department of Physiology, University of Kentucky

²Stark Neurosciences Research Institute, School of Medicine, Indiana University

Abstract Text:

Traumatic brain injury (TBI) increases hippocampal progenitor cell proliferation and alters neurogenesis in the subgranular zone (SGZ). Insulin-like growth factor-1 (IGF-1) is a potent neurotrophic factor that promotes CNS progenitor cell proliferation and drives neuronal differentiation of precursor cells in the rodent brain. IGF-1 administration attenuates neurological motor and cognitive deficits following TBI in rats, but the effect of IGF-1 on neurogenesis after TBI is unknown. We hypothesized that elevating levels of IGF-1 would increase proliferation and neurogenesis within the SGZ following moderate controlled cortical impact (CCI) brain injury. To this end, we subjected IGF-1 conditionally overexpressing (n=4) and wild-type (n=5) mice to 0.5mm CCI or sham injury (n=3 wild-type). Mice were injected with bromodeoxyuridine (BrdU) daily for 12 days beginning 1h post-injury. At 14 days immunohistochemistry was performed for BrdU, a thymidine analog incorporated into DNA, as a marker of replicating cells, and doublecortin (DCX) as a marker for immature neurons. DCX positive, BrdU positive and DCX/BrdU double-labeled cells were manually counted in the ipsilateral and contralateral SGZ (14-18 sections per animal). Across all groups, numbers of BrdU, DCX, and BrdU/DCX positive cells were significantly higher in ipsilateral SGZ compared to the contralateral SGZ ($p < 0.05$). Both IGF-1 overexpressing and wild-type brain-injured mice exhibited increased proliferation relative to sham animals ($p < 0.05$). However, there was no significant difference between the brain-injured groups. These data indicate that moderate CCI brain injury results in comparable increases in proliferation within the hippocampal SGZ in wild-type and IGF-1 overexpressing mice at 14 days.

POSTER PRESENTATION

Effects of the Lipid Peroxidation Inhibitor U-83836E on Mitochondrial Dysfunction in the Mouse TBI Model

Presenter:

Ayman G. Mustafa

Collaborators:

Indrapal N. Singh, Kimberly M. Carrico and Edward D. Hall

Departmental Affiliations:

University of Kentucky, Spinal Cord and Brain Injury Research Center (SCoBIRC)

Abstract Text:

After traumatic brain injury (TBI) brain mitochondrial function is severely compromised which plays a major role in post-traumatic secondary damage (Sullivan et al., 2000). Isolated mitochondria from the injured brain tissue display a significant increase in mitochondrial lipid peroxidation together with marked reduction in complex I-driven mitochondrial respiration (Singh et al., 2006). Lipid peroxidation of mitochondrial membranes is believed to cause an irreversible loss of mitochondrial respiration, oxidative phosphorylation and ion transport (Kowaltowski and Vercesi 1999) which is implicated in neuronal cell death (Sullivan et al. 1999). The aim of this study was to pharmacologically validate the cause and effect relationship of mitochondrial lipid peroxidation and loss of mitochondrial bioenergetics after TBI using the potent and selective lipid peroxidation inhibitor U-83836E (Hall, et al. 1991). Male CF1 mice were randomized into sham, saline treated and U-83836E treated (3.0 mg/kg) groups. The sham group received only craniotomy with no further treatment, whereas both saline- and U-83836E-treated groups received craniotomy and were subjected to severe (1.0 mm impact depth) controlled cortical impact (CCI)-TBI followed by I.V (tail vein) injection of the assigned treatment 15 minutes post injury. The injury caused a significant increase in lipid peroxidation and a marked reduction in mitochondrial state III respiration rate (ATP synthesis capacity) in cortical mitochondria harvested at 12 hrs post-injury. U-83836E treatment was able to significantly attenuate levels of 4-hydroxynonenal (4-HNE) which is a specific marker of lipid peroxidation and partially salvage mitochondrial respiratory function. The findings help to validate lipid peroxidation as an important mediator of post-traumatic mitochondrial dysfunction. Currently we are using the drug U83836E to investigate the role of lipid peroxidation in neurodegeneration after CCI-TBI (supported by 5R01 NS046566 and 5P30 NS051220).

POSTER PRESENTATION

Impactor Tip Geometry Influences Rates of Cell Death Following Controlled Cortical Impact

Presenter:

Jennifer Pleasant

Collaborators:

Shaun W. Carlson¹, Stephen W. Scheff^{1,2}, and Kathryn E Saatman¹

Departmental Affiliations:

¹University of Kentucky, Spinal Cord and Brain Injury Research Center (SCoBIRC)

²University of Kentucky, Sanders-Brown Center for Aging

Abstract Text:

Controlled cortical impact (CCI) results in progressive cortical and hippocampal cell death. The rate at which cells die is a key parameter in determining the therapeutic window for neuroprotective interventions. We hypothesized that impactor tip geometry alters the rate of cell death, with the commonly used beveled tip resulting in an accelerated rate of cell death compared to a rounded tip. C57BL/6 mice were subjected to 1.0mm CCI using a beveled or rounded tip, and euthanized at 1, 4, or 24hr post-injury (4-5 per group). Quantification of the volume of cortical tissue damage in the ipsilateral hemisphere as a percentage of the contralateral cortex showed that the beveled tip resulted in rapid damage to 16.5±5.9% (mean±SD) of the cortex at 4 hr and 16.4±2.4% at 24 hr. In contrast, the rounded tip resulted in a slower rate of damage, involving -2.2±3.8% at 4 hr and 16.4±2.6% at 24 hr. Impact with either tip resulted in Fluor Jade-C positive neurons in the dentate gyrus granule layer at 1 hr, but onset of CA3 and CA1 staining was more rapid for injury with the beveled tip as. These data demonstrate that the rate of cortical and hippocampal neurodegeneration was decreased by using a rounded tip as compared to the beveled tip. Slowing the rate of posttraumatic cell death should not only increase the ability to identify injury mechanisms and relative time courses, but also afford a more practical and clinically relevant therapeutic window for the administration of putative neuroprotective agents.

NOTES

KEYNOTE SPEAKER PRESENTATION

“Constraint Induced Movement Therapy in the Treatment of Upper Extremities Post-Stroke: Findings and Mechanisms”



STEVEN L. WOLF, Ph.D., PT, FAPTA, FAHA

Dr. Steve Wolf is a Professor in the Department of Rehabilitation Medicine at Emory University, Atlanta, and also holds appointments as Professor of Geriatrics, Associate Professor of the Department of Cell Biology, and Research Health Scientist at the Atlanta VA Medical Center.

Dr. Wolf has more than 100 peer-reviewed publications that reflect his interest and expertise in areas such as motor learning, upper extremity motor recovery, neuroimaging, biofeedback, neuromuscular re-education, postural control and gait in older adults who undergo novel treatment interventions such as Tai Chi, and treatment of patients with chronic pain. He was the principal investigator of the first-ever large scale multicenter randomized clinical trial, Extremity Constraint Induced Therapy Evaluation, widely known as the EXCITE trial. This study explored the effects of constraint-induced movement therapy on recovery of motor function among patients who have sustained stroke. Over his career, he has been a part of 35 funded peer-reviewed grant proposals, of which he is listed in more than half as either the principal or co-principal investigator. Currently, he is evaluating the mechanisms underlying possible massed practice cortical reorganization using constraint-induced therapy.

NOTES: Steven L. Wolf, Ph.D., PT, FAPTA, FAHA

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