DIDACTIC SESSION: RESEARCH II

STATE OF THE SCIENCE OF mTBI IN SPORTS

PROGRAM SYLLABUS
2015 AAN Sports Concussion Conference
July 24-26, 2015

Didactic Session: Research II
Saturday, July 25, 2015
1:00 p.m. – 2:50 p.m.

Program Directors
Jeffrey S. Kutcher, MD, FAAN – Ann Arbor, MI
Christopher Giza, MD – Los Angeles, CA

Program Schedule and Faculty
1:00 PM – 1:30 PM Challenges of Blood-Based Biomarkers of Mild TBI and a Novel Marker Panel
   Ina B. Wanner, PhD
   Los Angeles, CA
1:30 PM – 2:00 PM Prospective Cohort Research in Sports mTBI
   Steven Broglio, PhD
   Ann Arbor, MI
2:00 PM – 2:30 PM State of Science of mTBI in Sports
   Walter J. Koroshetz, MD, FAAN
   Bethesda, MD
2:30 PM – 2:50 PM Panel Q&A

Program Description:
This three-day conference will focus on the science behind concussion. The conference will follow a new programming model to include five half-day sessions, each with its own general theme, faculty presentations, and a panel discussion. Poster presentations will occur on the first two days of the conference. The five half-day topics are: concussion, concussion research (epidemiology, biomechanics, and imaging), post-concussive syndrome, research (mTBI), and chronic Sequelae. In addition, there will be lunchtime breakout sessions targeted to the following audiences: professional sports, collegiate sports, high school sports, and youth sports.

Learning Objectives:
Participants should be able to accurately and appropriately diagnose concussion; institute appropriate and clinically useful diagnostic tests when indicated; provide state-of-the-art management of concussed athletes and individuals; make safe and appropriate return to play, school, work, and life decisions; and educate athletes, non-health care professionals, and other health care practitioners on key issues related to concussion.

Recommended Audience:
Neurologists, Athletic Trainers, Primary Care Physicians, Neuropsychologists, and Sports Medicine Professionals.

Accreditation
The American Academy of Neurology is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

AMA PRA Credit
The AAN designates these educational activities for a maximum number of hours in category 1 credit toward the AMA Physician's Recognition Award. The number of credits assigned to each individual program is outlined in the

General Information:
- Attendees must be registered and badged to attend the individual programs.
- CME Category 1 Credit is awarded to persons registering for and participating in the AAN Regional Programs and submitting an evaluation form. Program evaluations are online and a link to access them will be emailed to you at the end of each day. Evaluations are due within two weeks of the program.
- An email will be sent to all attendees on how to access your CME credits earned approximately six weeks after the conference.
program's description. Each physician should only claim those hours of credit that he/she actually spent in the activity.

Certificates for Non-Physicians
Non-physician participating in the programs will receive a certificate of attendance indicating attendance at an activity designated for AMA PRA category 1 credit.

Education/Posters Disclaimer
The primary purpose of the AAN Sports Concussion Conference is to provide educational programs and information. Information presented, as well as publications, posters, technologies, products and/or services discussed, are intended to inform attendees about the knowledge, techniques, and experiences of physicians and other professionals who are willing to share such information with colleagues. A diversity of opinions exists in the medical field, and the view of the conference’s faculty and other presenters is offered solely for educational purposes. Faculty members’ and presenters’ views represent neither those of the AAN nor constitute endorsement by the AAN. The AAN disclaims any and all liability for all claims which may result from the use of information, posters, publications, products, and/or services discussed at the AAN Sports Concussion Conference.

Faculty's Disclosure of Commercial Relationships
Consistent with the AAN and ACCME policies, faculty must disclose any significant financial or other relationship with the manufacture(s) of any commercial product(s) or service(s) discussed in their course. This policy is intended to make participants aware of all speakers' financial or other relationship(s), so that attendees may form their own judgments about material discussed during the educational activity. Full disclosure of faculty's commercial relationships will appear in the individual program materials. All faculty must sign a letter of agreement stating explicitly that they understand and will adhere to AAN and ACCME guidelines that require full disclosure of commercial relationships, unlabeled use of products, and identification of data sources.

Faculty Commercial Relationship Disclosures
- Jeffrey S. Kutcher, MD – Dr. Kutcher has received personal compensation for activities with the National Basketball Association Concussion Program as a director, with National Hockey League Players Association and ElMindA, Ltd. As a consultant. Dr. Kutcher has received research support from ElMindA, Ltd. For a research grant.
- Christopher Giza, MD – Dr. Giza has received personal compensation for activities with the Medical Education Speakers Bureau and for medicolegal consultation with Alcobra and Pearson TLC.
- Ina B. Wanner, PhD – Dr. Wanner has received research support from Abott Diagnostics.
- Steven Broglio, PhD – Dr. Broglio has received research support from ElMindA.
- Walter J. Koroshetz, MD, FAAN – Dr. Koroshetz has nothing to disclose.

Unlabeled Use of Product Disclosure
The AAN, as an ACCME accredited provider, requires all faculty members to disclose if a product is not labeled for the use being discussed or that the product is still investigational.

Faculty Unlabeled Use of Product Disclosures
- Dr. Wanner will not include any information on unlabeled use of products or investigational uses during the presentation.
- Dr. Broglio will not include any information on unlabeled use of products or investigational uses during the presentation.
- Dr. Koroshetz will not include any information on unlabeled use of products or investigational uses during the presentation.
Concussion Research: Brief State of the Science

Walter J. Koroshetz, M.D.
Acting Director, National Institute of Neurological Disorders and Stroke, NIH

SHRP Stakeholders Board Meeting
March 31, 2015

Military and Athletes:
Long History of Trying to Protect the Brain

CEREBRAL CONCUSSION
D. DENNY-BROWN
Neurological Unit, Boston City Hospital, and the Department of Neurology, Harvard Medical School

The practical importance of the subject is twofold. First, there is lack of clear understanding of common sequelae to head injury, namely: liability to headaches and dizziness, inability to concentrate, nervousness or unwarrented fears, various degrees of change in personality (irritability, aggressiveness, euphoria), and intellectual impairment. These symptoms have often loosely been called "the post-concussion syndrome." Secondly, the efforts of exposure to violent explosion particularly common in war include persistent anxiety, loss of memory, and difficulty in concentration with or without headache and dizziness similar or identical with the "post-concussion syndrome," without outward sign of direct injury to the head. It is therefore pertinent to inquire whether any of the phenomena of concussion can be associated with a persistent structural disorder, what is the relationship between "post-concussion syndrome" and concussion, and whether the blast of explosive produces concussion or some other related state. It should be made clear that there is already a

1/25/2015
Concussion: Scope of the Issue

I

II

III

IV

V

PCS: Post-concussive syndrome
H: Sub-concussive hits
Long period of time

State of Concussion Science: Predicting Clinical Consequences

- Dose-response relationship between biomechanical force and neurologic deficits
  - Measuring the relevant biomechanical force
  - Measuring the relevant neuropathology/pathophysiology
    - Biomarkers of concussion pathophysiology
- Acute to post-concussive syndrome
  - Characteristics of the injury/person
- Risk of "second hit" fatal outcome
- Long term consequences:
  - Alzheimer's type dementia
  - CTE
Chronic Traumatic Encephalopathy (CTE)

- Progressive degenerative disease
- Dementia pugilistica “punch-drunk syndrome”
- Post-mortem diagnosis
  - Nerve cell loss
  - Accumulation of tau protein/neurofibrillary tangles
- Repetitive brain injury raises the risk

Pathology Associated with Compression Injury: McGavern and Latour/NINDS

Image: http://www.bumc.bu.edu/supportingbusm/research/brain/cte/
SHRP 2 Funding

- Multi-Center Research on CTE and delayed effects of TBI: Focus on Neuropathology and Neuroimaging Correlation
- 6 Pilot Projects on Sports-related concussion
- *Longitudinal study of symptomatic individuals.

Punctate Cortical Regions with Phosphorylated Tau Proteins in Neurons

- 45 y.o. veteran with blast exposure 2 yrs ago and prior concussion
- 34 y.o. veteran with 2 blast exposures 6 yrs ago.
- 18 y.o. amateur football player with multiple concussions.
- 21 y.o. amateur football player with multiple concussions.

Criteria for Pathological Diagnosis of CTE

- NIH Consensus Conference (Boston, Feb 2015)
- In CTE, the tau lesion considered pathognomonic was an abnormal perivascular accumulation of tau in neurons, astrocytes, and cell processes in an irregular pattern at the depths of the cortical sulci.

[Image of tau antibody staining of neurons and neurites in perivascular pattern (arrow pointing to blood vessel).]
Cavum Septum Pellucidum in retired American Pro-football Players--Gardner R et. Al. J of Neurotrauma

Published in Journal of Neurotrauma Ahead of Print DOI: 10.1089/neu.2014.3805 © Mary Ann Liebert, Inc.

Criteria for Pathological Diagnosis of CTE

Supportive criteria for a diagnosis of CTE:

To complement the required criteria, the group also defined supportive pathological features that were frequent in CTE brains, especially in the more severely affected cases. These include:

1. Macroscopic abnormalities in the septum pellucidum (cavum, fenestration), disproportionate dilatation of the IIIrd ventricle or signs of previous brain injury;
2. Abnormal tau immunoreactive neuronal lesions affecting the neocortex predominantly in superficial layers 2 and 3 as opposed to layers 3 and 5 as in AD;
3. Abnormal tau (or silver-positive) neurofibrillary lesions in the hippocampus, especially in CA2 and CA4 regions, which differ from preferential involvement of CA1 and subiculum in AD;
4. Abnormal tau immunoreactive neuronal and astrocytic lesions in subcortical nuclei, including the mammillary bodies and other hypothalamic nuclei, amygdala, nucleus accumbens, thalamus, midbrain tegmentum and substantia nigra;
5. Tau immunoreactive in thorny astrocytes in subpial periventricular and perivascular locations.

Chronic Traumatic Encephalopathy (CTE)

Pathology

- Foci of tau deposition in neurons
- Confluent tau deposition in multiple brain regions
- Brain atrophy

Clinical Syndrome

- Memory/Limbic System Dysfunction?
- Dementia

No change over time?
New PET Imaging Agent Shows Promise for Detecting a Biomarker of Alzheimer’s Disease

Early Clinical PET Imaging Results with the Novel PHF-Tau Radioligand [F18]-T808

- A novel PET imaging agent, [F18]-T808, has been reported to aid in identifying the presence of PHF-tau, a structural component of the amyloid protein whose aggregation leads to the formation of toxic neurofibrillary tangles (NFTs).
- Since the formation of aggregates of PHF-tau may precede the cognitive symptoms of AD, a method for imaging this protein may provide the first reliable pre-symptomatic biomarker of the devastating neurological disease.
- A reliable biomarker for AD could enable the diagnosis of AD years prior to symptom onset, objectively quantify disease progression, and accelerate the discovery of effective treatments.


Tau PET radioligands in Alzheimers

Acta Neuropath Commun 2015;3:40
Lemoine et. Al.


PET tau imaging in CTE

- In vivo characterization of CTE with FDDNP PET. 2015, PNAS 112: 2039
- 14 American Football players with suspected CTE compared to normal controls and persons with Alzheimers
**Tau PET Radioligands**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Requirement</th>
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<tbody>
<tr>
<td>High binding affinity</td>
<td>Kat or Kd&lt;3hM for normal brain samples</td>
</tr>
<tr>
<td>High binding affinity</td>
<td>&lt;25 fold selectivity for P301L over AD</td>
</tr>
<tr>
<td>Radioligand exposure</td>
<td>2-4×10¹⁹ for 2-4×10¹⁸ 2×10¹⁸ 1×10¹⁸ and 2×10¹⁷ 7×10¹⁷ 2×10¹⁷ 8×10¹⁷ 4×10¹⁷</td>
</tr>
<tr>
<td>Metabolite stability</td>
<td>LogD=9.34</td>
</tr>
<tr>
<td>Low nonspecific binding</td>
<td>Low or no binding to substantial white matter</td>
</tr>
<tr>
<td>Low sensitivity</td>
<td>Metabolites should not enter into the brain</td>
</tr>
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**Radioligand Pros Cons**

- **[18F]FDDNP**
  - Abnormal in CTE and AD and PSP
  - Binds to senile plaques as well as tangles
  - Lowest sensitivity to tau.
  - High white matter binding?

- **[11C]PBB3**
  - Abnormal in AD, CBD
  - Very low nonspecific binding to white matter
  - Defluorination?

- **[18F]T807, 808**
  - Strong and selective binding to PHF-tau
  - Abnormal in AD
  - Very low nonspecific binding to white matter
  - Defluorination?

- **THK 5117**
  - High sensitivity to tau over Abeta
  - Low nonspecific binding to white matter
  - Abnormal in AD

**BIG Questions Remain**

1. What are the underlying mechanisms of post-concussive syndrome? How can these be targeted therapeutically.
2. What are the underlying mechanisms of increased vulnerability to prolonged post concussive syndrome with repeated concussion? How to ID those to inform return to play?

1. What are the net effects on quality of life of participation in sport with risk of concussion.
2. What dose of TBI (e.g., number, intensity, temporal pattern, regional factors) is associated with foci of tau deposits?
3. How does tau deposition evolve to affect widespread brain regions. (e.g., spread vs. different regional rates of neurodegeneration)?
4. Given similar exposures, how can we predict an individual’s risk for CTE? (e.g., genetics, environmental influences, lifestyle, etc.)

**Measuring brain deformation in humans. Dzung Pham CNRM-NIH**

![Image](http://example.com/image.jpg)
NIH-Funded Concussion Research

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Principle Investigator /Institution</th>
<th>Funding IC</th>
<th>Abstract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging and Biomarkers in Adolescents Treated for Return to Play After Concussion</td>
<td>Harvey Levin, Baylor College of Medicine</td>
<td>NINDS</td>
<td>This prospective, international study addresses the overarching hypothesis that brain biomarkers and structural changes observed in trauma-exposed and healthy children and adults are highly associated. The study will recruit a total of 400 high school athletes who have been cleared for return to play. Data will be collected before the injury, during the return to play period, and up to six months after injury. The hypothesis that biomarker measured from meninges will vary with the age of the injury is tested.</td>
</tr>
<tr>
<td>ISATL: Imaging Sensitivity and Use in Youth Football</td>
<td>Joseph Maljian, Wake Forest University</td>
<td>NINDS</td>
<td>This study will evaluate biomarkers related to fluid dynamics during a head impact. It examines how fluid dynamics changes in the brain in response to subconcussive impacts, and the brain response to cognitively enhanced brain imaging. The study is designed to test the hypothesis that biomarkers measured from the meninges will vary with the age of the injury.</td>
</tr>
<tr>
<td>Sports Related Subconcussive Impacts in Children: MRI &amp; Biomechanical Correlates</td>
<td>Joseph Maljian, Wake Forest University</td>
<td>NINDS</td>
<td>This study will evaluate biomarkers related to brain function and structural changes observed in trauma-exposed and healthy children and adults. The study will recruit a total of 400 high school athletes who have been cleared for return to play. Data will be collected before the injury, during the return to play period, and up to six months after injury. The hypothesis that biomarker measured from meninges will vary with the age of the injury is tested.</td>
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Adolescent Brain Cognitive Development Study

- 10 year study of 10,000 youth starting at age 9
- Multi-Institute focus is effects of substance/alcohol use
- NINDS interested in the impact of concussion on the developing brain?
- 3 FOAs: Coordinating center (U24), Research project sites (U01), Data analysis & informatics center (U24)

State of the Science in Concussion: Big Questions in Pathophysiology

What is the dose-response relationship between force and:

- neural depolarization - amplitude, duration, geography
- lactate elevation -
- axonal stretch - degree, location
- altered CBF - autoregulation, O2 deliver
- altered BBB - degree, duration, geography

What is the physiologic basis of the post-concussive syndrome?
**Intelligent Mouthguard for Measuring Head Impacts in Youth Athletes**

- **Goal:**
  - Short-term: reduce the incidence and consequences of sport-related concussion and sub-concussive impacts in young athletes via commercialization of a low-cost wireless “Intelligent Mouthguard” head impact dosimeter.
  - Long-term: define the relationship between cumulative sub-concussive head impacts and risks of decline in brain health

- Provides frontline caregivers with a low-cost, accurate tool to identify all at-risk athletes in real-time in helmeted and non-helmeted sports so they may be removed from play for further assessment.

**SPORTSGUARD LABORATORIES, INC**

**BARTSCH, ADAM JESSE**

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**NIH-Funded Concussion Research**

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<tr>
<td>Intelligent Mouthguard for Measuring Head Impacts in Youth Athletes</td>
<td>Adam Jesse Bartsch, Sportsguard Laboratories Inc.</td>
<td>NICHHD</td>
<td>This goal of this project is to reduce the incidence and consequences of sport-related concussion and sub-concussive impacts in young athletes via commercialization of a low-cost wireless “Intelligent Mouthguard” head impact dosimeter. This technology will provide frontline coaches with a non-invasive, accurate tool to identify at-risk athletes in real-time so they may be removed from play for further assessment.</td>
</tr>
<tr>
<td>Investigation of an Instrumented Mouthguard for Measuring Head Impact Exposure</td>
<td>David Camarillo, Stanford University</td>
<td>NIBIB</td>
<td>This proposed project centers on the use of a mouth-concentrated excitability that will be worn by collegiate football players in practice and in games to measure brainwave activity. As a non-invasive, non-invasive tool, it may be used to identify and prevent further concussive injuries and to provide real-time monitoring of sub-concussive impacts.</td>
</tr>
<tr>
<td>Low Cost Head Impact Alert System for Helmeted Sports</td>
<td>Richard Greenland, SIMBEX, LLC</td>
<td>NICHHD</td>
<td>The Principal Objective of this NIH Phase II SBIR project is to expand the utility of the mouthguard, and non-concussive mild TBI, and non-invasive, non-invasive tool. We hypothesize that this technology will be a valuable tool in the detection of sub-concussive impacts and to provide real-time monitoring of sub-concussive impacts in real-time and to identify at-risk athletes in real-time so they may be removed from play for further assessment.</td>
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**The Role of Microglia in Acute Pathology of Repeated Concussion and CTE**

- **Advance:** a closed head injury (CHI) mouse model of concussion in which repeated concussive impacts, but not a single impact, result in acute microglial activation that is associated with greater neuron death and astrogliosis.
- **Goal:** To better understand the role of microglia in the pathology of repeated concussion, posttraumatic microgliosis will be amplified or attenuated

**OLTON, AMANDA/UNIVERSITY OF KENTUCKY**
The Impact of Concussive and Sub-concussive Blows on Brain Network Activity

- **Problem:**
  - Highly variable clinical presentation of concussion makes an accurate diagnosis and return to play decision difficult
  - Many of the common clinical assessments are not sensitive to post-concussion changes in performance
  - Need for more sensitive measure of cognitive functioning

- **Goal:** implement a novel evaluation of electroencephalogram (EEG) recordings and standard clinical assessments in high school football athletes to evaluate concussive and sub-concussive impacts

Steve Broglio/UNIVERSITY OF MICHIGAN

The Persistent Influence of Concussive Injuries on Cognitive Control and Neuroelectric Function

Robert D. Moore, MS,*, Charles H. Hillman, PhD,,* and Steven P. Broglio, PhD, ATC?

NIH-Funded Concussion Research

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<tr>
<td>Eye Movement Dynamic: A Rapid Objective Sensory</td>
<td>Nicholas Port, Indiana University</td>
<td>NICHD</td>
<td>The first aim of the study is to build and validate a calibration matrix broken that would be portable, free-cost, and suitable for everyday life assessment of cognitive control. We will validate the clinical utility of eye movement performance as a rapid, objective, and potentially sensitive measure of CTE among female and male high school and college level athletes.</td>
</tr>
<tr>
<td>Sensory Processing: Assessing Youth Sport-Related</td>
<td>Stacy Miller, Marcus Sukauer,</td>
<td>NICHD</td>
<td>The overall goal of this project is to evaluate the utility of a novel, cheap, robust measure of sensory processing (aCFT) as a biomarker for youth and young adults for evaluating the neurological risk of SRC and recovery from SRC. The aCFT measures sensory processing and evaluates the overall risk of SRC. The study will confirm validity of aCFT and improve performance, making it useful for early detection of SRC.</td>
</tr>
<tr>
<td>Neuroimaging Assessments: Concussion</td>
<td>Mark Tommerdahl, UNC Chapel Hill</td>
<td>NINDS</td>
<td>We developed a neural approach to measure brain injury. The approach was designed and validated in a model, which is a novel and applicable computer simulation that enables high-resolution bedside sensory testing. The approach is used to measure and report the severity of injury, and individual risk of neurodegeneration can be determined rapidly (3-5 minutes per test).</td>
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<tr>
<td>Evaluation of Spontaneous Concussion Injury Management App for Youth Sports</td>
<td>Lara Beth Triffitt, McKernan, Nationwide Children’s Hospital</td>
<td>NICH</td>
<td>The overall objective of this application, which is the first of its kind, is to provide a non-invasive management application to detect concussions in children and adolescents. The application will use machine learning algorithms to identify concussions based on sensor data collected from the app. It will alert caregivers and healthcare providers to potential concussions, allowing for timely intervention and management. This project will evaluate the effectiveness of the app in detecting concussions and improving outcomes.</td>
</tr>
<tr>
<td>Field-side Mobile Device OcularMotor Function Assessment</td>
<td>Nathan Richards, Barron Associates, Inc.</td>
<td>NINDS</td>
<td>This proposed research program aims to protect athletes against the risk of concussions by developing a portable device that measures oculomotor function. The device will be designed to be easy to use and compatible with mobile devices. The objective is to determine if oculomotor function can be used as a predictor of concussion severity and recovery.</td>
</tr>
<tr>
<td>Objective &amp; Portable Balance &amp; Gait Measures to Document Recovery After Concussion</td>
<td>Laurie King, Oregon Health &amp; Science University</td>
<td>NICH</td>
<td>The objective of this proposal is to use portable sensors to quantify and determine patterns of recovery for both single and dynamic balance after an injury to the brain. This will be accomplished by developing a sensitive and objective tool that can be used to assess recovery and inform rehabilitation.</td>
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**Instrumenting the Balance Error Scoring System for Use With Patients Reporting Persistent Balance Problems After Mild Traumatic Brain Injury**

**Title:** Instrumenting the Balance Error Scoring System for Use With Patients Reporting Persistent Balance Problems After Mild Traumatic Brain Injury

**Authors:** Chapman, King, Hall, Brown, et al.

**Abstract:**

The Balance Error Scoring System (BESS) is a widely used tool for assessing balance in patients with concussion. However, it is not designed to be used in a clinical setting. This project aims to develop a portable and user-friendly BESS to be used in clinical settings. The BESS will be instrumented with accelerometers and gyroscopes to measure balance in real-time. The project will involve the development of algorithms to interpret the sensor data and generate a score. The effectiveness of the instrumented BESS will be evaluated in a clinical trial involving patients with persistent balance problems after mild traumatic brain injury. The results will be compared to the traditional BESS to determine if the instrumented BESS can accurately and efficiently assess balance in clinical settings.

**Figure:**

![Balance Error Scoring System](image)

**References:**


**NIH-Funded Concussion Research**

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<tbody>
<tr>
<td>Identification of Persistent Impairments in Postural Control Following Concussion</td>
<td>Barry Munkasy, Georgia Southern University</td>
<td>NINDS</td>
<td>This project aims to identify persistent impairments in postural control following concussion. The proposed methodology will use a combination of sensor data and traditional clinical assessments to determine the presence and severity of these impairments. The objectives include developing a sensitive and objective tool to detect and quantify these impairments.</td>
</tr>
<tr>
<td>Cortical GABA in Pediatric Sports Concussion</td>
<td>Jeffrey Qemani, Seattle Children’s Hospital</td>
<td>NINDS</td>
<td>This project will investigate the role of GABA in pediatric sports concussion. The proposed methodology will involve the use of functional magnetic resonance spectroscopy (fMRS) to measure GABA levels in the brain of children with concussions. The objectives include determining if changes in GABA levels correlate with clinical outcomes and recovery.</td>
</tr>
<tr>
<td>Using Transcranial Brain Stimulation to Prevent Cortical Spreading Depression</td>
<td>Richard Rushmore, Boston University</td>
<td>NINDS</td>
<td>The goal of this project is to investigate the potential of using transcranial brain stimulation to prevent cortical spreading depression (CSD). The proposed methodology will involve the use of transcranial magnetic stimulation (TMS) to disrupt CSD. The objectives include determining if TMS can prevent or reduce CSD and improve clinical outcomes.</td>
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**7/25/2015**
Let’s get started!

Walter J. Koroshetz, M.D.
Acting Director
National Institute of Neurological Disorders and Stroke
Email: koroshetzw@ninds.nih.gov
Website: http://www.ninds.nih.gov/
Follow me @NINDSdirector

NINDS
Seeking Knowledge about the Brain,
Reducing the Burden of Disease

McGavern Lab/NINDS
Continuous monitoring of brain surface after the most mild compression injury shows leakage of BBB, generation of damaging reactive oxygen species, microglia response, leak of CSF into brain, and glial cell death.
Figure 1. Composite Z scores of the 7 quantitative electroencephalographic features in the multivariate analysis of variance between groups, shown at BL, injury/retest, day 8, and day 45 after injury. Standard error of the mean shown for each group average point. Clear differences between the groups at point of injury and day 8 can be seen. BL, baseline; INJ, time of injury.