KEYNOTE SPEAKER: WALTER J. KOROSHEZT, MD, FAAN

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

Program Schedule and Faculty
4:15 PM – 5:15 PM     Keynote Speech
                        Walter J. Koroshetz, MD, FAAN
                        Bethesda, MD

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 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.
- 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. Koroshetz will not include any information on unlabeled use of products or investigational uses during the presentation.
Presentation Overview

- TBI and concussion research at NINDS
- NIH-NFL Collaboration
- NIH-DOD Collaboration
- International Collaborations

What is Traumatic Brain Injury (TBI)?

“TBI is defined as an acute alteration in brain function, or other evidence of brain pathology, caused by an external force.”
The Burden of TBI

- Leading cause of death in children and young adults in industrialized countries
- Leading cause of disability worldwide
- Recently the advisability of contact sports has become a societal issue due to the concern for long term effects of concussion.
- Lots of failed clinical trials of acute neuroprotection strategies.

Common Disabling Injuries

- Diffuse Axonal Injury
- Contusion
- Hemorrhage
- Ischemia
- Edema and high intracranial pressure

TBI Neuroscience: The Big Questions

How to protect the brain from secondary injury post TBI- edema, cell death, hemorrhage?

What are the key biologic mechanisms triggered by concussive and repetitive concussive?

How to protect the brain in individuals involved in activities at high risk for TBI?

What is the nature of progressive brain atrophy in years post TBI? Is there a long term inflammatory process that is harmful?

How does the brain recover from TBI? How can this process be enhanced?
IOM Report

SPORTS-RELATED CONCUSSIONS IN YOUTH

Improving the science, changing the culture

- Surveillance
- Neuroscience and Biomechanics
- Diagnosis and Management
- Short- and Long-term Consequences
- Age-appropriate Rules and Standards
- Biomechanics, Equipment, Safety Standards
- Culture change

Sponsors: NINDS, NICHD, NIMH, CDC, DoD, HHS, NASA, NFL


What Do We Know About Sports Concussion?

- ~ 3.8 million/year in the USA
- Recovery generally good, but not always
  - Though rare, acute symptoms can be life-threatening
  - Post-concussive syndrome (PCS)
  - Chronic or late onset symptoms – chronic traumatic encephalopathy (CTE)
    - Punch drunk syndrome first reported in boxers in 1928
    - Recent reports of CTE in youths who played football has raised awareness and concern
    - Reports of neurobehavioral problems and increased suicide rates in veterans has added to the concerns

Degenerative change

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
What Are Critical Gaps in Scientific Knowledge?

- What is the “dose” required to cause a concussion? To cause PCS? To cause CTE?
- How does a concussion affect the brain in the short and long-term?
- How can we reliably and objectively detect when the brain is injured and when it is fully recovered?
- How does the brain recover from TBI? How can we harness discoveries in neuroplasticity to improve recovery?

The National Institute of Neurological Disorders and Stroke (NINDS)

The mission of NINDS is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease.

Strategies:
- Invest across the full spectrum of basic, translational, and clinical research
- Establish a data-driven process to identify unmet scientific opportunities and public health needs within and across neurological diseases
- Support research resources and technical advances that catalyze new discoveries
- Communicate and collaborate with the public and with others involved in biomedical research
- Train a robust and diverse neuroscience research workforce
- Adopt a culture of evaluation and continuous improvement across all NINDS programs

http://www.ninds.nih.gov/about_ninds/plans/NINDS_strategic_plan.htm

TBI Research is Supported by Many NIH Institutes and Centers

<table>
<thead>
<tr>
<th>Funding</th>
<th>FY 2011</th>
<th>FY 2012</th>
<th>FY 2013</th>
<th>FY 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall NIH</td>
<td>$81.33</td>
<td>$79.40</td>
<td>$88.48</td>
<td>$87.30</td>
</tr>
<tr>
<td>NINDS</td>
<td>$54.55</td>
<td>$53.09</td>
<td>$52.14</td>
<td>$62.40</td>
</tr>
<tr>
<td>NICHD</td>
<td>$11.36</td>
<td>$11.32</td>
<td>$8.48</td>
<td>$9.38</td>
</tr>
<tr>
<td>RMAP</td>
<td>$0.17</td>
<td>$0.17</td>
<td>$4.76</td>
<td>$3.69</td>
</tr>
<tr>
<td>NINR</td>
<td>$0.42</td>
<td>$1.22</td>
<td>$1.82</td>
<td>$3.57</td>
</tr>
<tr>
<td>NIA</td>
<td>$2.18</td>
<td>$1.91</td>
<td>$3.11</td>
<td>$2.27</td>
</tr>
</tbody>
</table>
Decline in NINDS Purchasing Power

FY 2014 Taxpayer Investment in Neuroscience Exceeds Other Science Areas

Industry is Moving to Later Stage Clinical Development and Out of CNS Disorders


Choi DW et al. Neuron 2014 84:554

China Now Has Largest Science and Technology Workforce in the World

Top 10 countries by size of science and technology workforce, 1996-2011

China Now Leads in the Number of Global Life Science Patent Applications

Global life science patent applications by country of origin, 1981 – 2011

Budget

- NINDS budget $1.6b in 2015
- NINDS did receive increase of ~$25million for BRAIN Initiative.
- Pretty strong support for NIH on both sides of the legislature.
- Main issue is whether Congress can see through the cap on spending and put together a budget.
- NIH has been asked to submit a "bypass budget" for the National Action Plan for Alzheimers (NAPA)
  - Plan includes research on Alzheimer related dementias named as dementias related to Lewy Body, Fronto-temporal, vascular disease.
NIH Funds a Broad Range of TBI Research

Annual funding by research topic ($millions)

- BIOMARKERS AND RISK FACTORS: 15.5
- DIAGNOSTICS: 3.6
- MECHANISMS OF ACUTE INJURY: 9.1
- MECHANISMS OF RECOVERY: 7.4
- TREATMENT - ACUTE PHASE: 5.1
- TREATMENT - RECOVERY PHASE: 1.3
- TBI and CHRONIC DISEASE: 3.0

NIH Supports Foundational Research & Resources

NIH Toolbox for Neuroimaging and Neurobehavioral Research

Figs. 8 & 9. Streamline/deterministic versus probabilistic tractography. (A) Illustration of the FACT algorithm. Stationary time seed points, i.e., 5 samples in a square, yield a 3D streamline using the principal eigenvectors, shown by the yellow line. (B) Highly Deployable Head Only MRI Scanner.

The Human Connectome Project (HCP)

HCP aims to provide:
- an unparalleled compilation of neural data
- an interface to graphically navigate this data
- the opportunity to achieve new conclusions about the living human brain

Study Aims:
1) develop tools to process high-angular diffusion (HARD) and diffusion-spectrum imaging (DSI)
2) optimize advanced high-field imaging technologies and neurocognitive tools to map the human connectome
3) design and deploy a novel, web-based, relational database infrastructure to disseminate materials

Approach:
- Scan brains of ≥1200 healthy adults
- Ages 18–94
- Male and female
- Collected genotypic, behavioral, and phenotypic data

Disconnection of the Ascending Arousal System in Traumatic Coma.

Disconnection of the Ascending Arousal System in Traumatic Coma.

Traumatic Brain Injury Research at NINDS

NINDS leads TBI research at NIH, which encompasses the full range of TBI severity, from mild (concussion) through severe TBI (car crash or serious fall).
- NIH funded $87 million of research on TBI in FY 2014
- NICHD supports research on pediatric TBI and coordinates NIH rehabilitation research through the National Center for Medical Rehabilitation Research
- International Collaborations in Clinical Trials
  - NIH is currently funding 2 large TBI clinical studies to understand which treatments are associated with the best outcomes in adults and children. These studies are coordinated with studies in Europe and Canada through the International Initiative for TBI Research (InTBIR).
- Interagency Resources: Federal Interagency TBI Research Interagency Collaboration: Center for Neuroscience and Regenerative Medicine (CNRM)
**TRACK-TBI, ADAPT**

**Goal:** Personalized medicine for TBI

**Study Arms:**
- Establish novel preventive methods for TBI diagnosis and prognosis (WAVE Long Term Follow-Up)
- Validate imaging, fluid, and genetic biomarkers
- Validate NIH Tool Kit for TBI and APH MS TBI
- Assess the effectiveness and costs of tests, treatments, and services

**Approach:**
- 3,000 children and adults
- All injury severities
- 11 hospitals and rehab centers in the USA
- CCTEs and standardized protocol for CT and MRI; bio specimens and outcome assessments
- Coordinated with 3 other large observational TBI studies

**Accomplishments:**
- Aligning CCTEs with 3 other major TBI studies
- Recruitment to begin in Fall 2014
- Timeline and Cost:
  - Sept 2013 – August 2016
  - $2.5M/year

---

**International TBI Collaboration**

- Comparative Effectiveness Research between EU, Canada, and NIH to prospectively collect data on 10,000 children and adults with TBI to examine which therapies are associated with best outcomes.
- Utilize common data elements for collection of TBI data
- US data is deposited and shared in the FITBIR TBI data repository, a collaboration between NIH and DOD.

---

**NIH-funded Research on Sports Concussion**

**Concussion Case Study:**
- Head injuries: TBI, concussions, sports concussions
- Greenwald HD40473; HD48538

**Funding:**
- NINDS NS55020
- **McAllister NS55020**
Concussion Research at NINDS

Sports and Health Research Program

- Launched in 2012 with $30M investment from NFL
- Public-private partnership among NIH, NFL, and FNIH
- Focus on TBI
- 2 collaborative agreements on CTE and delayed effects of TBI: neuropathology and neuroimaging correlation
- 6 pilot projects on sports-related brain injury: developing new ways to diagnose and treat athletes who suffer concussions
- Stakeholder meeting March 31, 2015 is online http://www.ninds.nih.gov/news_and_events/proceedings/shrp_report_03312015.htm

FNIH-NFL Collaboration

- Sports and Health Research Program (2012)
  - Foundation for the NIH (FNIH)
  - An NIH-NFL Partnership to advance research, $30M
- To answer some of today’s most important questions about TBI.
- Effects of concussion in school age athletes
- Chronic pathologic effects of neurotrauma
- Clinical diagnosis and natural history of chronic effects of neurotrauma

1 CTE
2 ALS
3 Lewy Body + CTE
4 CTE
5 Alzheimers
6 Lewy Body
Sources for Brain Examination

- NIH Neurobiobank
- ACT study - Seattle Washington
- TBI model systems - Mt Sinai
- Center for study of traumatic encephalopathy - Boston University

Adult Changes in Thought Study

- Study of aging in Group Health patients with $12 million grant from NIH's National Institute of Aging in 2009. In continuous operation for 23 years, it is the longest-running study of its kind.
- Collaboration with University of Washington aims to prevent dementia, including Alzheimer's
- Every two years, 2,000 senior Group Health patients check in with the Adult Changes in Thought (ACT) study and volunteer as brain donors
- 15% of participants report history of TBI with loss of consciousness
- >500 brains already collected

NIH Neurobiobank Gives Researchers One-stop access to post-mortem brains

- To expedite research on brain disorders, the National Institutes of Health is shifting from a limited funding role to coordinating a Web-based resource for sharing post-mortem brain tissue.
- Under a NIH NeuroBioBank initiative, five brain banks will begin collaborating in a tissue sharing network for the neuroscience community.
- Contracts totaling about $4.7 million for the 2013 fiscal year were awarded to brain banks
  - Mount Sinai School of Medicine, New York City
  - Harvard University, Cambridge Mass.
  - University of Miami
  - Sepulveda Research Corporation, Los Angeles
  - University of Pittsburgh
**Coming: Longitudinal Study of Chronic Effects of Neurotrauma**

- Multi year study of persons at high risk for CTE
  - Neurologic symptoms 15-20 years post exposure
  - Neuropsychiatric symptoms 5-10 years post exposure
    - Repeat neurocognitive and neurologic examination
    - Repeat MRI
    - Tau-PET if radioligand found to bind tau in CTE
- Multi year study of persons at lower risk.
  - College contact athletes vs. non contact athletes

**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.

*Journal of Alzheimer’s Disease, 2014, 38: 171-184. DOI: 10.3233/JAD-132098*

**Longitudinal Study Deliverables**

- Estimates of the number of high risk individuals and the numbers of controls who demonstrate a progressive decline in neurobehavioral function within 2 - 3 years.
- Characterization of which neurobehavioral functions decline.
- Determination of whether neurobehavioral function correlates with fluid biomarkers, neuroimaging and/or postconcussive syndrome.
- Identification of the most probable diagnosis in subjects with progressive neurobehavioral declines, e.g. AD, CTE, ALS, PD, or other.
- Valid clinical tools for making a probable diagnosis of CTE.
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)

DoD Numbers for Traumatic Brain Injury Worldwide - Totals

2000-2014 (Q1 - Q3)

- Penetrating: 4,577
- Severe: 3,126
- Moderate: 25,953
- Mild: 258,816
- Not Classifiable: 21,344

Total - All Severeities: 312,816

NIH-DOD Collaboration

Shared Leadership on Committees

Joint committees: US MRMC leadership and NINDS leadership are in almost weekly communication.

2007
- Original NICCe planning
- US MRMC IP6 has NINDS representation

2009
- US Army Medical Command integrated program team (IPT) committee
- US MRMC concussion definition project

2010
- NFL - Foundation for NIH (FNIH) Sports Health Research Program (SHRP) with US MRMC representation
- FL-NFL sports concussion project
- DOD Secretary's conference on TBI
- National Research Action Plan

2014
- DOD- NCAA sports concussion project

*DOD always has an appointed member on the NINDS Council
Federal Interagency TBI Research (FITBIR) Informatics System

- Established in 2006, work began in 2008
- Interagency group: NINDS, VA, NIDRR, US Army Medical Research and Material Command, Defense and Veterans Brain Injury Center (DVBiC), and NiCOE
- Established common data elements (CDEs) in 2010 to be used in TBI research

FITBIR Database

- Established in 2011
- Data repository for NIH and DOD clinical TBI research built at CIT by NIH staff, MOU signed between US Army Medical Research and Materiel Command and NIH.
- $~10 million from USMRC and DMRDP. Expired March 2015.

Data Sharing: Informatics and Policies
NIH-DOD Intramural Research

A collaborative effort, involving Intramural NIH/Uniformed Services University/WRNMC to advance the knowledge and treatment of TBI with a special focus on forms of TBI relevant to military
- Diagnostics & Imaging
- Biomarkers
- Neuroprotection & Modeling
- Neuroregeneration
- Neuroplasticity
- Rehabilitation & Evaluation

National Research Action Plan (NRAP)

National Research Action Plan: 2013
- Responding to the Executive Order: Improving access to mental health services for veterans, service members and military families.
- DOD, HHS, Dept of Education reviewed activities and made comprehensive recommendations for future research.
- Tracking milestones on regular basis.


NINDS Office of Translational Research (OTR) Launches New Programs

- Goal – advance promising therapies to hand off to biotech/pharma companies
  - Innovation Grants to Nurture Initial Translational Efforts (IGNITE)
    - Early-stage therapy development
  - Four separate opportunities from assay development to platform technology development
  - Blueprint Neurotherapeutics Network (BPN) for small molecules
    - Development of small molecules
    - Provides investigators with access to consultants and contracts that provide discovery, preclinical development, and clinical trial support
  - Cooperative Research to Enable and Advance Translational Enterprises (CREATE) Bio and Devices
    - Development of biologics (including proteins, peptides, nucleic acids, gene and cell therapies)
    - Development of devices (including implants, stents, and prosthetics)

- These programs:
  - Are milestone driven
  - Offer multiple entry points and seamless path of support across the therapy development pipeline

http://www.ninds.nih.gov/funding/areas/translational_research/
The NeuroNEXT program aims to:

- Provide a robust, standardized, and accessible infrastructure to conduct studies of treatments for neurological diseases
- Create and leverage partnerships with academia, private foundations, and industry
- Increase the efficiency of clinical trials
- Support scientifically sound, possibly biomarker-informed, exploratory clinical trials that provide data for clear go/no-go decisions
- Expand the pool of experienced clinical investigators and research staff

“The Next Great American Project”

“So there is this enormous mystery waiting to be unlocked, and the BRAIN Initiative will change that by giving scientists the tools they need to get a dynamic picture of the brain in action and better understand how we think and how we learn and how we remember. And that knowledge could be – will be – transformative.”

~President Obama, April 2, 2013

“A Focus on Circuits and Networks”

To map the circuits of the brain, measure the fluctuating patterns of electrical and chemical activity flowing within those circuits, and understand how their interplay creates our unique cognitive and behavioral capabilities.
The disability that patients with TBI suffer is a direct result of disordered brain circuits.

We need to be able to see the circuits in action to:
- Diagnose concussion
- Understand the circuit abnormality underlying post-concussive syndrome
- Determine how to therapeutically modulate brain activity for improved recovery after concussion and more severe forms of TBI.

Goal: do this with the precision of individual circuits and at the speed of thought.

Where Does Scientific Progress Come From?

"New directions in science are launched by new tools much more often than by new concepts. The effect of a concept-driven revolution is to explain old things in new ways. The effect of a tool-driven revolution is to discover new things that have to be explained."

Freeman Dyson (1997) *Imagined Worlds*
Harvard University Press, Cambridge, MA

What Is Next?

1974

Original axial CT image form Siretom CT scanner circa 1975. Physicians were fascinated by the ability to see the brain and ventricles.

2012

5T susceptibility MRI imaging by Jeff Duyn, NIH

7/24/2015
Tremendous Progress in Defining Structure of Connections.

Exciting New Discoveries

Dr. Lihong Wang

- Nature Methods publication on photo-acoustic microscopy
  - uses pressure waves to measure biological structures/function
  - brain tissue minimally scatters pressure waves, allowing for deep imaging penetration
- Awarded BRAIN funding for related photoacoustic tomography
  - Measure activity of large groups of neurons
- Advantages:
  - non-invasive
  - targets defined subpopulations of neurons
  - deep penetration enables measurements of whole brain activity
NINDS
Seeking Knowledge about the Brain, Reducing the Burden of Disease

NIH-DOD Collaboration: Integration of Major Research Projects

Neuropathology of chronic effects of TBI

- NIH-NFL $12 million study of neuropathology/post mortem imaging of chronic effects of neurotrauma and planned longitudinal study of persons suffering from likely chronic traumatic encephalopathy (civilians)
- MRMC/VA Chronic effects of neurotrauma consortia (CENC) (active military and veterans).
- NIH NeuroBiobank set (https://neurobiobank.nih.gov/pages/discoveries/#toc6) to collect brain tissue from individuals who suffered repetitive TBI in past
- DOD Brain tissue repository/CNRM neuropathology core.

News Release

NIH NeuroBiobank

NIH NeuroBiobank

NIH NeuroBiobank

NIH NeuroBiobank

NIH NeuroBiobank

NIH NeuroBiobank
NIH-DOD Collaboration: Integration of Major Research Projects

Comparative Effectiveness Research
• NIH prospective data collection study in TBI (TRACK-TBI) is linked with similar European Union study (http://ec.europa.eu/research/health/medical-research/brain-research/international-initiative_en.html) to understand prognostic factors, identify best therapy for well identified patient subgroups (N=13,000).
• TRACK TBI will be integrated (both grants to same PI, Dr. Geoff Manley UCSF) with a new MRMC project, TBI Endpoint Development (TED), to develop a much improved outcome measure for TBI research and patient classification.
• DOD’s TED grant will also tie TRACK TBI data with data from the DOD-NCAA study of concussion in sports.

NIH-DOD Collaboration

Joint Scientific Workshops
• 2007 Classification of TBI
• 2008 Combination therapies for traumatic brain injury
• 2010 Advancing integrated research in psychological health and TBI: Common data elements.
• 2010 Mild TBI diagnostic workshop
• 2011 Therapy development for diffuse axonal injury
• 2012 The neuropathology of chronic traumatic encephalopathy
• 2013 Brain trauma related neurodegeneration. Strategies to define, detect, predict.
• 2014 International TBI Research (InTBIR) conference on ongoing comparative effectiveness research projects.

Center for Neuroscience and Regenerative Medicine (CNRM): A Catalyst for Brain Injury Research

CNRM Goal:
Improve Recovery from TBI in Military Service Members

CNRM
• Collaborative intramural federal research program involving DoD and NIH
• Developed to bring together the expertise of clinicians and scientists across disciplines
• Aim: to catalyze innovative approaches to traumatic brain injury (TBI) research
Center for Neuroscience and Regenerative Medicine (CNRM): A Catalyst for Brain Injury Research

Capabilities Developed as a Center That Catalyze Integrated TBI Research:

- 11 research cores to support interdisciplinary collaborative research
- Over 130 publications since 2009
- State-of-the-art neuropathology center, brain tissue and specimen biorepository infrastructure for specimen acquisition, evaluation, and distribution
- Natural history studies, including:
  - Identify effective outcome measures for TBI and co-morbid psychological health issues.
  - Addressing the progression from hyperacute through chronic stages post-injury.
  - Patient phenotyping (note: consent to re-contact for other CNRM studies has produced a robust patient registry for recruitment into ongoing and future clinical studies).
- Advanced neuroimaging capabilities, including: human MRI and PET, improved clinical diffusion imaging, development of novel MR diffusion techniques and PET ligands for inflammation and neurodegeneration.
- Complementary set of civilian and DoD clinical sites in the National Capital Area for clinical trials of novel pharmacological and rehabilitative interventions.
- Facilitated pre-clinical through clinical translational studies use CNRM scientific cores to gain expertise and sustainability of interdisciplinary research efforts.

Pathology Associated with Compression Injury

McGavern Lab/NINDS
Facilitate coordination of portfolio analysis and collaboration on research projects of shared interest by exploring the possibility of participation of the DoD and NIDDR in the NIH Electronic Research Administration system, which provides support for the full life cycle of grants administration functions for the NIH, VA, and several other agencies.

**Responsible Departments:** DoD, HHS, ED

**Progress:**
- All departments are exploring the use of the Federal and/or NIH RePORTER systems and the processes for data transfer.
- VA has been successfully using the NIH Reporter for several years.
- CNIC has recently uploaded grant abstracts to NIH RePORTER.
- ED/NIDRR has verbally agreed to use the Federal Reporter and is waiting to obtain an MOU from NIH.
- DoD and CDC are exploring the feasibility of using the Federal RePORTER.

**Upcoming Actions/Dates:**
- DoD to develop long-term MOA for DoD and hosting of DoD data in NIH IT systems (4th Quarter 2014).
- DoD to develop real-time data transfer mechanism (4th Quarter 2014).
- Test 2014 NIH and NIDRR MOA completion.

**Barriers/Challenges:**
- Budget and financial reporting varies significantly across agencies.
- DoD needs to address information assurance concerns before migrating data to the Federal RePORTER.

**C-C Immed. 1.5 New Tools/Technologies for Mechanism Studies**

Build new tools and technologies to understand the underlying mechanisms of PTSD, TBI, suicide and other conditions. Appropriate NRAP-participating agencies will continue to fund innovative research for the BRAIN Initiative. The DoD will leverage the BRAIN initiative efforts and continue to fund complementary work.

**Responsible Departments:** DoD, HHS, ED

**Progress:**
- NIH has established a high-level working group of the Advisory Committee to the NIH Director (ACD) to help shape this initiative, articulate the scientific goals of the BRAIN initiative and develop a multi-year scientific plan for achieving these goals, including timetables, milestones, and cost estimates. The final report was delivered to the NIH Director in June 2014 (http://www.nih.gov/science/brain/2025/).
- NIH released a funding opportunity in 2013 for $40 million in awards, and other federal and private funds are planned for other aspects of the BRAIN initiative.
- OARPA hosted a Collaborative BRAIN Data Exploration workshop in 2013. One NINDS Neurosurgery PI on a DARPA team.

**Upcoming Actions/Dates:**
- The BRAIN initiative is focused on development of new technologies, which may take several years to develop.
- Communication between the BRAIN initiative and TD OARPA program directors.

**Barriers/Challenges:**
- None identified.
Summary of NIH-DOD Collaborations

- DOD has become the major steward of taxpayer funds for TBI research.
- NIH-DOD collaboration on TBI has been robust since 2007 and growing.
- NRAP and FITBIR are the convergence points for coordination of multi-agency TBI research. They are primarily informational, not strategic partnerships.
- Direct line relationships between NIH and MRMC staff, and NIH-USUHS staff have been most effective means of collaboration.

Unlocking Treatments for CTE

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

Follow me @NINDSdirector