

**Porter, Kevin (NIH/OD) [E]**

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**From:** Hudson, Kathy (NIH/OD) [E]  
**Sent:** Thursday, December 24, 2015 10:55 AM  
**To:** Collins, Francis (NIH/OD) [E]  
**Cc:** Burklow, John (NIH/OD) [E]  
**Subject:** Re: Congress and head injuries

**Follow Up Flag:** Follow up  
**Flag Status:** Completed

(b) (5)

Kathy Hudson, Ph.D.  
Deputy Director for Science, Outreach, and Policy  
NIH  
301 496 1455  
[kathy.hudson@nih.gov](mailto:kathy.hudson@nih.gov)

On Dec 24, 2015, at 9:12 AM, Collins, Francis (NIH/OD) [E] <[collinsf@od.nih.gov](mailto:collinsf@od.nih.gov)> wrote:

Whaddaya think?

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**From:** Burklow, John (NIH/OD) [E]  
**Sent:** Thursday, December 24, 2015 9:50 AM  
**To:** Collins, Francis (NIH/OD) [E]  
**Subject:** RE: Congress and head injuries

Hi, again, Francis—

(b) (5)  
(b) (5)

I'd like to hear KH's take on it. It would be one for the books, though.

John

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**From:** Collins, Francis (NIH/OD) [E]  
**Sent:** Thursday, December 24, 2015 8:26 AM  
**To:** Burklow, John (NIH/OD) [E] <[BurklowJ@OD.NIH.GOV](mailto:BurklowJ@OD.NIH.GOV)>  
**Subject:** FW: Congress and head injuries

(b) (5)

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**From:** Burklow, John (NIH/OD) [E]  
**Sent:** Wednesday, December 23, 2015 4:30 PM  
**To:** Collins, Francis (NIH/OD) [E]; NIH Director's Executive Committee  
**Subject:** Congress and head injuries

<http://blogs.rollcall.com/218/the-concussion-effect-congress-to-probe-head-injuries/?dcz>

**Porter, Kevin (NIH/OD) [E]**

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**From:** Burklow, John (NIH/OD) [E]  
**Sent:** Wednesday, December 23, 2015 1:08 AM  
**To:** Collins, Francis (NIH/OD) [E]; NIH Director's Executive Committee  
**Cc:** Myles, Renate (NIH/OD) [E]; Fine, Amanda (NIH/OD) [E]  
**Subject:** NIH to fund BU study on CTE | Boston Herald

**Follow Up Flag:** Follow up  
**Flag Status:** Completed

[http://www.bostonherald.com/news/local\\_coverage/2015/12/nih\\_to\\_fund\\_bu\\_study\\_on\\_cte](http://www.bostonherald.com/news/local_coverage/2015/12/nih_to_fund_bu_study_on_cte)

Sent from my iPhone

**Porter, Kevin (NIH/OD) [E]**

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**From:** Burklow, John (NIH/OD) [E]  
**Sent:** Tuesday, December 22, 2015 10:15 PM  
**To:** Collins, Francis (NIH/OD) [E]; Tabak, Lawrence (NIH/OD) [E]; Hudson, Kathy (NIH/OD) [E]  
**Cc:** Myles, Renate (NIH/OD) [E]  
**Subject:** The NFL Has Reportedly Pulled Out of A Major Concussion-Related Study - Fortune

**Follow Up Flag:** Follow up  
**Flag Status:** Completed

<http://fortune.com/2015/12/22/nfl-nih-boston-university/>

Sent from my iPhone

**Porter, Kevin (NIH/OD) [E]**

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**From:** Myles, Renate (NIH/OD) [E]  
**Sent:** Tuesday, December 22, 2015 11:05 AM  
**To:** Collins, Francis (NIH/OD) [E]; Burklow, John (NIH/OD) [E]; Tabak, Lawrence (NIH/OD) [E]; Hudson, Kathy (NIH/OD) [E]  
**Cc:** Jackson, Calvin (NIH/OD) [E]  
**Subject:** RE: ESPN article

**Follow Up Flag:** Follow up  
**Flag Status:** Completed

Hi Francis:

Yes, we're getting a number of calls (CBS News, Washington Post, USA Today) and NINDS is drafting a statement. It will be simple and straightforward. We'll share it with everyone as soon as we receive it.

Best,  
Renate

---

**From:** Collins, Francis (NIH/OD) [E]  
**Sent:** Tuesday, December 22, 2015 11:00 AM  
**To:** Burklow, John (NIH/OD) [E]; Tabak, Lawrence (NIH/OD) [E]; Hudson, Kathy (NIH/OD) [E]  
**Cc:** Jackson, Calvin (NIH/OD) [E]; Myles, Renate (NIH/OD) [E]  
**Subject:** RE: ESPN article

Is the phone ringing off the hook? Do we have plans for how to handle follow ups?

---

**From:** Burklow, John (NIH/OD) [E]  
**Sent:** Tuesday, December 22, 2015 9:31 AM  
**To:** Collins, Francis (NIH/OD) [E]; Tabak, Lawrence (NIH/OD) [E]; Hudson, Kathy (NIH/OD) [E]  
**Cc:** Jackson, Calvin (NIH/OD) [E]; Myles, Renate (NIH/OD) [E]  
**Subject:** FW: ESPN article

The story is out. WK is quoted accurately.

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** Tuesday, December 22, 2015 9:26 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E] <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Cc:** Burklow, John (NIH/OD) [E] <[BurklowJ@OD.NIH.GOV](mailto:BurklowJ@OD.NIH.GOV)>; Mott, Meghan (NIH/NINDS) [E] <[meghan.mott@nih.gov](mailto:meghan.mott@nih.gov)>  
**Subject:** ESPN article

This just in.  
Marian

The ESPN article is online: [http://espn.go.com/espn/otl/story/\\_/id/14417386/nfl-pulls-funding-boston-university-head-trauma-study-concerns-researcher](http://espn.go.com/espn/otl/story/_/id/14417386/nfl-pulls-funding-boston-university-head-trauma-study-concerns-researcher)



**From:** Burklow, John (NIH/OD) [E]  
**Sent:** 21 Dec 2015 18:12:59 -0500  
**To:** Hudson, Kathy (NIH/OD) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Re: ESPN

Hi, Kathy, Walter--

(b) (6), Kathy and I just spoke. Could you give me a call on my cell and we can close the loop? 240-478-  
Thanks!

John

Sent from my iPhone

> On Dec 21, 2015, at 5:14 PM, Hudson, Kathy (NIH/OD) [E] <Kathy.Hudson@nih.gov> wrote:  
>  
> Sounds like messages not clear to ESPN today. Can we please clarify ASAP via email from Walter to  
reporter that YES NINDS is paying this Grant and we look forward to working with nfl in new year to fund  
additional important work in this area.  
>  
> Kathy Hudson, Ph.D.  
> Deputy Director for Science, Outreach, and Policy  
> NIH  
> 301 496 1455  
> kathy.hudson@nih.gov

**From:** koroshetzw@ninds.nih.gov  
**Sent:** 21 Dec 2015 17:35:51 -0500  
**To:** Hudson, Kathy (NIH/OD) [E]  
**Subject:** Re: ESPN

Cell 617 256 (b) (6)  
Walter

Sent from my iPhone

> On Dec 21, 2015, at 5:14 PM, Hudson, Kathy (NIH/OD) [E] <Kathy.Hudson@nih.gov> wrote:  
>  
> Sounds like messages not clear to ESPN today. Can we please clarify ASAP via email from Walter to reporter that YES NINDS is paying this Grant and we look forward to working with nfl in new year to fund additional important work in this area.  
>  
> Kathy Hudson, Ph.D.  
> Deputy Director for Science, Outreach, and Policy  
> NIH  
> 301 496 1455  
> kathy.hudson@nih.gov

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 21 Dec 2015 10:38:14 -0500  
**To:** Mott, Meghan (NIH/NINDS) [E]; Walker, Paula (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Background for today's ESPN interview  
**Attachments:** CTE\_Talking Points 12.21.15.docx, CTE U01 Summary - 12-1-15.docx, Stern NINDS grant mpo--12-16-15.docx, Acta Neuropathol.Consensus Paper.pdf, NFL TBI press release\_12.13.13\_FINAL.docx  
**Importance:** High

Meghan and Paula: Walter is scheduled to speak with Steve Fainaru of ESPN on Monday at noon. We will take the call in his conference room (31/8A-52) so that John Burklow and I can sit in, as requested by Dr. Collins. Attached are some draft talking points approved by Bldg One. Also attached is some background information about the recently awarded grant, a copy of the BU release, and the paper published last week highlighting the results of the NIH-run (SHRP- funded) consensus meeting on the pathological diagnosis of CTE. In the event that Steve asks what the NFL is currently funding, I've included a copy of our 2013 press release.

By the way, Walter will remember that Fainaru wrote a story in March 2014 ([Union, NFL split over research funds](#)) which included some rather provocative quotes.

Marian

**Marian Emr**

Director, Office of Communications and Public Liaison/NINDS  
31 Center Drive MSC 2540  
Building 31, Room 8A07  
Bethesda, MD 20892-2540  
Phone: (301) 496-5924  
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[me201@nih.gov](mailto:me201@nih.gov)



National Institutes of Health  
*Turning Discovery Into Health*

#### Talking Points: CTE Media Interview

- Why is NIH/NINDS funding this work?
  - CTE is a devastating disease for those afflicted by it as well as their loved ones. Currently it can only be diagnosed after death so there is a critical need to increase our knowledge of the mechanisms underlying the disease and develop methods to diagnose the condition in living people.
  - We hope that the research we support will help answer many of the questions we have about the disease.
- Why is NFL not funding this work?
  - NFL has funded other studies in the area of traumatic brain injury, some of them are ongoing projects awarded through, and overseen by, the NIH.
  - It is my understanding that the NFL plans to fund future studies.
- How will NIH research impact policy on football and other contact sports? What is the government's role in advising amateur or professional sports organizations?
  - The NIH's mission is to improve health and reduce illness and disability through biomedical research.
  - NIH supports research on concussions and other conditions that occur in sports, but does not set policy for sports or sports organizations.
  - The NIH presents research findings to the public but does not control what professional sports or other organizations do with that information.
- What role did the NIH have in selecting the research grants?
  - The grant that was announced in December 2015 was selected through NIH's standard peer review process. In July 2014, NIH issued an RFA (request for applications) for research on chronic traumatic encephalopathy (CTE). Applications were examined through a rigorous peer-review process. The application that earned the best score was then presented to NINDS' Advisory Council for final approval.
- How will the \$30million donation and subsequent research findings help the NFL?
  - Through its donation to the Foundation for the National Institutes of Health, it is my understanding that the NFL is seeking knowledge on how to improve player safety and health, on and off the field.

# *Chronic Traumatic Encephalopathy: Detection, Diagnosis, Course, and Risk Factors*

To be funded by the National Institute of Neurological Disorders and Stroke  
U01NS093334

## Principal Investigators

Robert A. Stern, Ph.D. (Contact PI)

Jeffrey Cummings, M.D.

Eric Reiman, M.D.

Martha Shenton, Ph.D.

Summary: December 1, 2015

Chronic traumatic encephalopathy (CTE) is a neurodegenerative disease characterized by a distinct deposition of an abnormal form of the tau protein in a pattern that is unique from other diseases, including Alzheimer's disease (AD). CTE has been found most often in professional contact sport athletes (e.g., boxing, football) who have been subjected to repetitive blows to the head resulting in concussive and subconcussive trauma. Neuropathologically-confirmed CTE has been reported in individuals as young as 17 and in athletes who only played sports through high school or college. It also has been found in non-athletes who experienced repetitive head impacts, including epileptics, victims of physical abuse, and military service members. In contrast to what may be inferred by the extensive media attention on CTE, the science of CTE remains in its infancy; critical questions remain, such as whether or not it is a common disease.

Although the neuropathological features of CTE have become further clarified in recent years, the clinical presentation of CTE is still not well characterized, even though there have been case reports in the literature of "dementia pugilistica" in boxers since the early 1900's. Clinical diagnostic criteria have only recently been published and lack validation. Neuroimaging and fluid biomarkers developed for the diagnosis of other neurodegenerative diseases have only been used in preliminary studies. There is thus an urgent need to develop accurate methods for detecting and diagnosing CTE during life so that effective interventions for prevention and treatment can be developed. Moreover, though a history of repetitive head impacts is a necessary risk factor for CTE, it alone is not sufficient. There is a need to understand what specific aspects of the head impact exposure places an individual at increased risk for CTE and to examine potential genetic modifiers of that risk.

To address these needs, NINDS is funding a multidisciplinary, multicenter, longitudinal study of former athletes with high exposure to repetitive head impacts (120 former NFL players with and without symptoms) or medium exposure to repetitive head impact (60 former college football players with and without symptoms) and a control group of 60 asymptomatic same-age men without any history of repetitive head impact exposure or traumatic brain injury. The aims of the 7-year project are: (1) to collect and analyze neuroimaging and fluid biomarkers for the detection of CTE during life, including the use of a novel PET tracer to measure the amount of abnormal brain tau; (2) to characterize the clinical presentation of CTE; (3) to examine the progression of CTE over a three year period; (4) to refine and validate diagnostic criteria for the clinical diagnosis of CTE; (5) to investigate genetic and head impact exposure risk factors for CTE; and (6) to share project data with researchers across the country and abroad in order to expedite growth in our understanding and treatment of this disease.

## CTE U01 Investigator Team

CTE is a neurodegenerative disease. Although the necessary risk factor for the development of this tauopathy is a history of repetitive head impacts, CTE itself should not be confused with traumatic brain injury or considered the cumulative effect of multiple concussions. It therefore cannot be studied with the same approaches and tools used to study brain trauma. Rather, to study the clinical presentation, diagnostic criteria, biomarkers, and risk factors of CTE requires expertise across many disciplines, including neurology, neuropsychology, psychiatry, neuroimaging, molecular medicine, neuropathology, exposure science, genetics, biostatistics, bioinformatics, engineering, and others. The success of this project will be facilitated by the multiple resources available across several sites. One of the primary resources is the superb group of co-investigators, consultants, and advisors working collaboratively on this study. A primary goal of this research program is to break down typical academic "silos" in order to conduct the best science in the most efficient manner. The proposed project brings together a network of scientists and resources across major academic institutions and industry leaders, including:

- Boston University School of Medicine and School of Public Health
- Brigham and Women's Hospital, Harvard Medical School
- Cleveland Clinic Lou Ruvo Center for Brain Health
- Mayo Clinic Arizona and Banner Alzheimer's Institute
- NYU Langone Medical Center and New York University School of Medicine
- VA Puget Sound and University of Washington
- Molecular Neuroimaging
- Neuroinformatics Research Group and Central Neuroimaging Data Archive (CNDA) at Washington University School of Medicine

The groups of investigators for this project are leaders in most of the major collaborative studies of Alzheimer's disease, as well as TBI, PTSD, Sports-Related Concussion, Frontotemporal Lobar Degeneration, and Parkinson's disease. In addition, many of the principle investigators and co-investigators already have extensive experience in the study of CTE, including NIH-funded projects that have led to important preliminary data to help guide the development of this proposal and, ultimately, to expedite the initiation of the proposed work as well as the speed at which critical questions will be answered.

This project will be overseen by an Executive Committee made up of the four Project PIs (Drs. Cummings, Reiman, Shenton, and Stern), the four Clinic Site PIs (Drs. Adler, Balcer, Bernick, and Stern), the Chair of the Advisory Board (Dr. Knopman), six Team Leaders (see below), the Project Coordinator, and Dr. McKee (to assure harmonization with the findings and procedures of her NINDS-funded CTE neuropathology U01 project). The Executive Committee will meet monthly through web-conference. Each major component of the project will be overseen by multidisciplinary and multi-institutional study teams. Each team is comprised of sub-teams focusing on specific aspects of the team's activities. The teams will interact closely with one another, through informal discussions, through monthly Executive Committee meetings, and through annual Investigator Meetings that will involve all investigators across all sites. The Data Team, in particular, will work closely with all other teams, throughout the entire project, assuring that all aspects of study design, variable definitions, data collection methods, database design and entry, and data analysis, are consistent across the entire breadth of the study and throughout the duration of the project. The following pages provides a list of the project leadership.

## **Principal Investigators**

Robert A. Stern, Ph.D. (Contact PI)

Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology  
Director, Clinical Core, Boston University Alzheimer's Disease and CTE Center (BU AD&CTEC)  
Boston University School of Medicine

Jeffrey Cummings, M.D.

Director, Cleveland Clinic Lou Ruvo Center for Brain Health  
Cleveland Clinic Lou Ruvo Center for Brain Health

Eric Reiman, M.D.

Executive Director, Banner Alzheimer's Institute  
CEO, Banner Research  
Banner Sun Health Research Institute

Martha Shenton, Ph.D.

Professor, Department of Psychiatry and Radiology, Harvard Medical School  
Senior Scientist, Brigham and Women's Hospital

## **Advisory Board**

David Knopman, M.D., Advisory Board Chair

Professor of Neurology  
Mayo Clinic

Unconfirmed: Col. Dallas Hack, M.D.

Previously: Brain Health Research Program Coordinator  
U.S. Army Medical Research and Materiel Command

Brian Hainline, M.D.

Chief Medical Officer, National Collegiate Athletic Association

Mike Haynes

Special Advisor to the Commissioner, National Football League  
National Spokesperson, American Urological Association Foundation

Thomas McAllister, M.D.

Chair, Department of Psychiatry  
Albert Eugene Stern Professor of Clinical Psychiatry  
Indiana University School of Medicine

Bruce Miller, M.D.

A.W. & Mary Margaret Clausen Distinguished Professor in Neurology  
Director, Memory and Aging Center Joint Appointment in Psychiatry  
University of California, San Francisco

Arthur Toga, M.D.

Provost Professor  
Director of the Institute for Neuroimaging and Informations (INI)  
Director of the Laboratory of Neuro Imaging  
University of Southern California

Michael Weiner, M.D.

Professor of Medicine, Radiology, Psychiatry and Neurology  
University of California San Francisco

## **Performance Site Principal Investigators**

Charles Adler, M.D. Ph.D.

Professor of Neurology  
Co- Director, Arizona Parkinson's Disease Consortium  
Mayo Clinic College of Medicine, Scottsdale, Arizona

Laura Balcer, M.D.

Professor of Neurology and Population Health  
Vice Chair, Neurology  
NYU School of Medicine

Charles Bernick M.D.

Associate Director, Cleveland Clinic Lou Ruvo Center for Brain Health  
Cleveland Clinic Lou Ruvo Center for Brain Health

Robert A. Stern, Ph.D.

Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology  
Director, Clinical Core, Boston University Alzheimer's Disease and CTE Center (BU AD &CTEC)  
Boston University School of Medicine

## **Teams**

### ***Neuroimaging Team***

Eric Reiman, M.D. (Team Leader)  
Executive Director, Banner Alzheimer's Institute  
CEO, Banner Research  
Banner Sun Health Research Institute

#### Magnetic Resonance

Martha Shenton, Ph.D.

Professor, Department of Psychiatry and Radiology, Harvard Medical School  
Senior Scientist, Brigham and Women's Hospital

#### Positron Emission Tomography

Keith Johnson, Ph.D.

Professor of Radiology  
Director of Molecular Neuroimaging, Massachusetts General Hospital  
Harvard Medical School

Kenneth Marek, M.D.

Chief Executive Officer, Molecular Neuroimaging  
President and Senior Scientist, Institute for Neurodegenerative Disorders  
New Haven, Connecticut



### ***Fluid Biomarker Team***

Elaine Peskind, M.D. (Team Leader)

Associate Director, University of Washington Alzheimer's Disease Research Center, Seattle, WA

Professor Department of Psychiatry and Behavioral Sciences

University of Washington School of Medicine

#### Fluid Biomarkers

Jing Zhang, M.D., Ph.D.

Professor of Pathology

Director, University of Washington Neuropathology

University of Washington School of Medicine

#### TBN

### ***Clinical Outcomes Team***

Jeffrey Cummings, M.D. (Team Leader)

Director, Cleveland Clinic Lou Ruvo Center for Brain Health

Cleveland Clinic Lou Ruvo Center for Brain Health

#### Cognitive

Sarah Banks, Ph.D.

Head, Neuropsychology Program

Assistant Professor of Medicine

Cleveland Clinic Lerner College of Medicine of Case Western Reserve University

Robert A. Stern, Ph.D.

Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology

Director, Clinical Core, Boston University Alzheimer's Disease Center (BU ADC)

Director of Clinical Research, BU CTE Center

Boston University School of Medicine

#### Mood and Behavior

Yonas Geda, M.D.

Professor of Neurology and Psychiatry

Mayo Clinic College of Medicine

Charles Marmar, M.D.

Lucius N. Littauer Professor and Chair, Department of Psychiatry

NYU School of Medicine

#### Neurological, Motor and Headache

Robert Cantu, M.D.

Professor of Neurosurgery and Neurology

Boston University School of Medicine

James Otis, M.D.

Associate Professor of Neurology

Headache Specialist

Boston University School of Medicine

### ***Diagnostic Criteria Team***

Robert A. Stern, Ph.D. (Team Leader)

Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology  
Director, Clinical Core, Boston University Alzheimer's Disease and CTE Center  
Boston University School of Medicine

### Study Consensus Diagnostic Conferences

Charles Adler, M.D. Ph.D.

Professor of Neurology  
Co- Director, Arizona Parkinson's Disease Consortium  
Mayo Clinic College of Medicine, Scottsdale, Arizona

Jesse Mez, M.D.

Associate Professor of Neurology  
Associate Director, Clinical Core, Boston University Alzheimer's Disease Center (BU ADC)  
Boston University School of Medicine

### Diagnostic Criteria Consensus Meeting and Statement

Charles Bernick M.D.

Associate Director, Cleveland Clinic Lou Ruvo Center for Brain Health  
Cleveland Clinic Lou Ruvo Center for Brain Health

David Dodick, M.D.

Professor of Neurology  
Mayo Clinic College of Medicine, Scottsdale Arizona  
Editor-in-Chief of Cephalalgia  
President-Elect of the International Headache Society  
President of the American Migraine Foundation  
Past-President of the American Headache Society  
Chair of the American Academy of Neurology Concussion Program, 2015 annual AAN meeting

Barry Jordan, M.D.

Chief Medical Officer of the New York State Athletic Commission  
Associate Professor of Clinical Neurology  
Weill Medical College of Cornell University  
Assistant Medical Director; Director, Brain Injury Program;  
Director, Memory Evaluation and Treatment Service  
Attending Neurologist, Burke Rehabilitation Hospital

Douglas Katz, M.D.

Professor of Neurology at Boston University School of Medicine  
Member of the academic neurology staff at Boston Medical Center  
Medical Director of the Brain Injury Program at Braintree (MA) Rehabilitation Hospital  
President-Elect, American Congress of Rehabilitation Medicine (ACRM)

### ***Risk Assessment Team***

Rhoda Au, Ph.D. (Team Leader)

Professor of Neurology

Director of Neuropsychology and Senior Investigator, Framingham Heart Study

Boston University School of Medicine

### Exposure

Michael McClean, Sc.D.

Associate Professor of Environmental Health

Director, Exposure Biology Research Laboratory

Boston University School of Public Health

Laura Balcer M.D.

Professor of Neurology and Population Health

Vice Chair, Neurology

Co-Director, Concussion Center

NYU School of Medicine

Rick Greenwald, Ph.D.

President, Founder, Simbex LLC, Lebanon, New Hampshire

Executive Director, Founder, National Institute for Sports Science and Safety (NISS),

Providence, Rhode Island

### Genetics

Lindsay Farrer, Ph.D.

Professor of Medicine, Neurology, Ophthalmology, Genetics & Genomics, Epidemiology, Biostatistics

Chief, Biomedical Genetics

Boston University School of Medicine

Jesse Mez, M.D.

Associate Professor of Neurology

Associate Director, Clinical Core, Boston University Alzheimer's Disease Center (BU ADC)

Boston University School of Medicine

### ***Data Team***

Christine Chaisson, M.P.H. (Team Leader)

Director, Data Coordinating Center

Assistant Research Professor, Department of Biostatistics

Boston University School of Public Health

Director, Data Management and Biostatistics Core, BU ADC

### Biostatistics

Judith Goldberg, Sc.D.

Professor of Biostatistics, Departments of Population Health and Environmental Medicine

NYU School of Medicine

Yorghos Tripodis, Ph.D.

Assistant Professor of Biostatistics

Boston University School of Public Health

#### Data Management

Christine Chaisson, M.P.H.

Director, Data Coordinating Center

Assistant Research Professor, Department of Biostatistics

Boston University School of Public Health

#### Data Storage and Sharing

Dan Marcus, Ph.D.

Associate Professor, Radiology

Director, Neuroinformatics Research Group (NRG), Radiology Department

Washington University School of Medicine

#### ***Mechanism Team***

Thomas Wisniewski, M.D. (Team Leader)

Professor, Neurology, Pathology, Psychiatry

Director, NYU Alzheimer's Disease Center

NYU School of Medicine

#### Neurodegeneration

Neil Kowall, M.D.

Chief of Neurology, VA Boston HealthCare System

Professor, Neurology and Pathology

Director, BU Alzheimer's Disease Center

Boston University School of Medicine

#### Clinico-Pathological Correlations

Ann McKee, M.D.

Professor, Neurology, Pathology

Director, CTE Center

Director, Neuropathology Core, BU ADC

Boston University School of Medicine

DRAFT

DRAFT

DRAFT

DRAFT

**FOR IMMEDIATE RELEASE**, date

Contact: Gina DiGravio, 617-638-8480, [gjinad@bu.edu](mailto:gjinad@bu.edu)

### **NIH/NINDS Grant Awarded to Develop Methods for Diagnosing Chronic Traumatic Encephalopathy (CTE) During Life**

(Boston)—Researchers from Boston University, the Cleveland Clinic, Banner Alzheimer's Institute and Brigham and Women's Hospital in Boston, have been awarded a \$16 million grant from the National Institutes of Health/National Institute of Neurological Disorders and Stroke (NIH/NINDS). This seven-year, multi-center grant will be used to create methods for detecting and diagnosing chronic traumatic encephalopathy (CTE) during life as well as examining risk factors for CTE.

CTE is a degenerative brain disease characterized by changes in behavior, mood and cognition, including the development of dementia. Currently it can only be diagnosed post-mortem through examination of an abnormal form of tau protein. CTE has been found most often in professional contact sport athletes (e.g., boxers, football players) who have been subjected to repetitive blows to the head resulting in symptomatic concussive and asymptomatic subconcussive trauma. Neuropathologically-confirmed CTE has been reported in individuals as young as 17 and in athletes who only played sports through high school or college. It also has been found in non-athletes who experienced repetitive head impacts, including military service members.

According to the researchers, although the neuropathological features of CTE have become further clarified in recent years, the clinical presentation of CTE is still not well characterized and there remains no method to diagnose it before death. "There are so many critical unanswered questions about CTE. We are optimistic that this project will lead to many of these answers, by developing accurate methods of detecting and diagnosing CTE during life, and by examining genetic and other risk factors for this disease," explained lead principal investigator, Robert Stern, PhD, professor of neurology, neurosurgery, and anatomy & neurobiology at Boston University School of Medicine, where he is Clinical Core director of the Boston University Alzheimer's Disease and CTE Center.

Through this grant, NINDS is funding a longitudinal study of former NFL players, former college football players, and a control group of individuals without any history of contact sports or brain injury. Participants will be examined at one of four centers across the country, including Boston University School of Medicine; Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas; Mayo Clinic in Scottsdale, Ariz; and New York University Langone Medical Center, New York City.

Participants in the study will undergo extensive clinical examinations, as well as state-of-the art PET scans, advanced MRI scans, experimental blood tests and other potential methods of detecting changes in the brain associated with CTE. Researchers also will refine and validate specific criteria for clinical diagnosis of the disease and will investigate genetic and head impact exposure risk factors for CTE in order to begin to determine why some people are more prone to get CTE than others. Project data will be shared with researchers across the country and abroad to facilitate a more complete understanding of this disease, ultimately leading to successful methods of preventing and treating CTE.

The other principal investigators are Jeffrey Cummings, MD, ScD, (director, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas and Cleveland; the Camille and Larry Ruvo Chair of the Neurological Institute of Cleveland Clinic; and professor of medicine, Cleveland Clinic Lerner College of Medicine at Case Western Reserve University); Eric Reiman, MD (executive director of the Banner Alzheimer's Institute, Phoenix) and Martha Shenton, PhD (director, Psychiatry Neuroimaging Laboratory and senior scientist, Brigham and Women's Hospital; professor of psychiatry and radiology, Harvard Medical School). The project involves a group of approximately 50 investigators, representing 17 research institutions.

"There is an urgent need to clarify the clinical and biological consequences of repetitive head impacts in athletics and to use this information to find the best ways to treat and prevent those consequences," said Reiman. "It is both a great privilege and responsibility to help in that endeavor."

"This research is an exciting and important opportunity to acquire new information about the potential devastating consequences of repetitive head impact including CTE," said Shenton. "We hope that by gaining this knowledge, new avenues of treatment will emerge for those who experience debilitating symptoms from repetitive brain trauma."

"We currently have no method to diagnosis CTE during life and it is crucial to take the next steps to better understand this disease," said Cummings. "This grant will allow us to take what we know about CTE and move to the next level of research, with the end goal of diagnosing these athletes at early stages of the illness when treatments may help prevent the progression of the disease."

Editors Note:

The exact amount of this grant is \$15,859,906.

CONSENSUS PAPER

# The first NINDS/NIBIB consensus meeting to define neuropathological criteria for the diagnosis of chronic traumatic encephalopathy

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**Abstract** Chronic traumatic encephalopathy (CTE) is a neurodegeneration characterized by the abnormal accumulation of hyperphosphorylated tau protein within the brain. Like many other neurodegenerative conditions, at present, CTE can only be definitively diagnosed by post-mortem examination of brain tissue. As the first part of a series of consensus panels funded by the NINDS/NIBIB to define the neuropathological criteria for CTE, preliminary neuropathological criteria were used by 7 neuropathologists to blindly evaluate 25 cases of various tauopathies, including

CTE, Alzheimer's disease, progressive supranuclear palsy, argyrophilic grain disease, corticobasal degeneration, primary age-related tauopathy, and parkinsonism dementia complex of Guam. The results demonstrated that there was good agreement among the neuropathologists who reviewed the cases (Cohen's kappa, 0.67) and even better agreement between reviewers and the diagnosis of CTE (Cohen's kappa, 0.78). Based on these results, the panel defined the pathognomonic lesion of CTE as an accumulation of abnormal hyperphosphorylated tau (p-tau) in neurons and astroglia distributed around small blood vessels at the depths of cortical sulci and in an irregular pattern. The group also defined supportive but non-specific p-tau-immunoreactive features of CTE as: pretangles and NFTs affecting superficial layers (layers II–III) of cerebral cortex;

The members representing TBI/CTE group are listed in the Appendix.

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pretangles, NFTs or extracellular tangles in CA2 and pretangles and proximal dendritic swellings in CA4 of the hippocampus; neuronal and astrocytic aggregates in subcortical nuclei; thorn-shaped astrocytes at the glial limitans of the subpial and periventricular regions; and large grain-like and dot-like structures. Supportive non-p-tau pathologies include TDP-43 immunoreactive neuronal cytoplasmic inclusions and dot-like structures in the hippocampus, anteromedial temporal cortex and amygdala. The panel also recommended a minimum blocking and staining scheme for pathological evaluation and made recommendations for future study. This study provides the first step towards the development of validated neuropathological criteria for CTE and will pave the way towards future clinical and mechanistic studies.

**Keywords** Chronic traumatic encephalopathy · Traumatic brain injury · Tauopathy · Brain trauma · Neurodegenerative disorders

## Introduction

In 1928, the pathologist and medical examiner, Harrison Stanford Martland, introduced the term ‘punch-drunk’ to describe the clinical features of a distinct neuropsychiatric syndrome that affected boxers [26]; a condition that later came to be known as ‘dementia pugilistica’ [33]. Case reports and small series describing the neuropathologic features of the condition appeared in the 1950s and 1960s [3, 6, 16, 27, 35, 41]. Although the histological techniques varied, the most common pathological findings were cerebral atrophy, neuronal loss, gliosis and argyrophilic neurofibrillary tangles. In the seminal 1973 monograph on the clinicopathological features of dementia pugilistica in 15 former male boxers, Corsellis, Bruton, and Freeman-Browne described cerebral atrophy, enlargement of the lateral and third ventricles, thinning of the corpus callosum, cavum

septum pellucidum with fenestrations, cerebellar scarring, and argyrophilic neurofibrillary degeneration using cresyl violet and Von Braunmühl’s silver stains [5]. Subsequent re-examination of Corsellis’ original series of boxers and additional cases using beta-amyloid (A $\beta$ ) immunohistochemistry determined that 95 % of CTE cases showed widespread diffuse A $\beta$  deposits [43, 46].

Over the following decades, it was recognized that the condition affected men and women with a broad range of exposure to brain trauma, including physical abuse [42], head-banging [13, 18], poorly controlled epilepsy, “dwarf-throwing” [48], and rugby<sup>1</sup> [13]. Eventually, the term “chronic traumatic encephalopathy” or “CTE”, introduced by Critchley in 1949 [8], became the preferred designation for the condition.

Coincident with the use of more refined methodology, the early pathology of CTE was reported in several young subjects [13, 14, 18]. Hof reported a single case of repetitive head-banging in a young autistic patient with numerous perivascular clusters of thioflavin and Gallyas-positive neurofibrillary tangles (NFTs) and neurites at the depths of the cerebral sulci and in the superficial layers of the inferior temporal, entorhinal and perirhinal cortices in the absence of A $\beta$  plaques [18]. Hof and colleagues also quantitatively demonstrated the preferential distribution of the NFTs in superficial layers II and III in CTE, a laminar predilection characteristic of two other environmentally acquired tauopathies, post-encephalitic parkinsonism and Guamanian parkinsonism dementia complex (GPDC), but not found in Alzheimer’s disease (AD) [19]. Geddes and colleagues further described argyrophilic, hyperphosphorylated tau (p-tau) immunopositive neocortical NFTs and neuropil threads strikingly arranged in groups around small cortical blood vessels, in addition to diffuse granular cytoplasmic immunopositivity in some neurons [13]. Geddes also noted that the topography of the p-tau pathology principally involved the depths of sulci and that there was no A $\beta$  deposition in the 5 young cases that formed the basis of their manuscript [13].

Omaha and colleagues were the first to report CTE in a professional American football player [38, 39] and a professional wrestler [37]. Recent neuropathological studies have identified CTE in athletes who played soccer, baseball, ice hockey and rugby, as well as in military personnel exposed to explosive blast [15, 29, 31, 32, 36, 45]. P-tau pathology, with some features of CTE, has also been

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<sup>1</sup> Although often referred to as a *soccer* player, the young subject with CTE described by Geddes et al. 1999 as the “keen amateur footballer who frequently “headed” the ball while playing” [13], was an amateur *rugby* player (personal communication, T. Reeves).



described following exposure to single moderate or severe traumatic brain injury, together with A $\beta$  plaques [20, 44].

In 2013, McKee and colleagues described a spectrum of p-tau pathology in 68 male subjects with a history of exposure to repetitive brain trauma with neuropathological evidence of CTE, ranging in age from 17 to 98 years (mean 59.5 years). In young subjects with the mildest forms of CTE, focal perivascular epicenters of NFTs and astrocytic tangles (ATs) were found clustered at the depths of the cortical sulci; in subjects with severe disease, a profound tauopathy involved widespread brain regions [32]. Other abnormalities encountered in advanced disease included abnormal deposits of phosphorylated TAR DNA-binding protein of 43 kDa (TDP-43) protein that occasionally co-localized with p-tau, varying degrees of A $\beta$  pathology, axonal dystrophy and neuroinflammation [30, 32]. Based on these findings, preliminary criteria for the neuropathological diagnosis of CTE were proposed, as follows:

1. Perivascular foci of p-tau immunoreactive NFTs and ATs in the neocortex
2. Irregular distribution of p-tau immunoreactive NFTs and ATs at the depths of cerebral sulci
3. NFTs in the cerebral cortex located preferentially in the superficial layers (often most pronounced in temporal cortex)
4. Supportive, non-diagnostic features: Clusters of subpial ATs in the cerebral cortex, most pronounced at the sulcal depths.

In March 2013, the National Institutes of Health (NIH), supported by the Foundation for NIH's Sports Health Research Program with funding from the National Football League (NFL), launched a major effort to define the neuropathological characteristics of CTE. Two projects were initiated on the neuropathology of CTE and the delayed effects of traumatic brain injury. One of the initial objectives was to convene a consensus meeting to define the neuropathological criteria for the diagnosis of CTE. The primary objective for the first meeting was to determine whether CTE was a distinctive tauopathy that could be reliably distinguished from other tauopathies using the preliminary criteria. The study design was modeled after previous successful NIH-sponsored consensus conferences for other tauopathies, specifically progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD) [10, 17, 25].

## Materials and methods

Individuals not directly involved in the pathological evaluation (ACM, VEA, KFB, JFC) selected 25 cases of the various tauopathies. The selected cases were considered to

be representative of the disease and of at least moderate disease severity. The cases included 10 recently acquired cases of suspected CTE that were donated as part of the NINDS-funded traumatic brain injury (TBI) brain bank at Boston University School of Medicine (BUSM), including 7 cases with A $\beta$  plaques and 3 cases without A $\beta$  plaques. Five cases of AD, Braak stage V-VI, 2 cases of PSP and 2 cases of CBD were selected from the Alzheimer's Disease Center (ADC) brain bank at BUSM. Two cases of GPDC and 2 cases of argyrophilic grain disease (AGD) were selected from the Alzheimer's Disease Research Center (ADRC) brain bank at Mayo Clinic-Jacksonville, and 2 cases of primary age-related tauopathy (PART) were selected from the ADRC brain bank at Columbia University. Paraffin-embedded tissue blocks from 12 brain regions from each case were sent to the TBI Brain Bank at BUSM for uniform processing, staining and immunohistochemistry (IHC) (Table 1); 2 of the selected cases were missing the superior temporal block. Sections were stained with Luxol fast blue counterstained with hematoxylin and eosin (LHE) and Bielschowsky silver impregnation; IHC was performed using anti-A $\beta$ 42 (A $\beta$  1-42, EMD Millipore, 1:2000, pretreated with 88 % formic acid for 2 min; or A $\beta$ -4G8, Bio Legend, 1:100,000, pretreated with formic acid); anti-p-tau (AT8, Thermo Fisher Scientific/

**Table 1** Brain regions evaluated in the case review

Brain region	Stains/IHC				
	LHE	AT8	A $\beta$ 42	TDP43	BIEL
Superior frontal (BA 8, 9)	X	X			
Dorsolateral superior frontal (BA 45, 46)	X	X	X		
Caudate nucleus, nucleus accumbens, putamen	X	X			
Temporal pole (BA 38)	X	X			
Superior temporal gyrus (BA 20, 21, 22)	X	X		X	
Amygdala, with entorhinal cortex (BA 28)	X	X			
Hippocampus and lateral geniculate nucleus	X	X	X	X	X
Thalamus and mammillary body	X	X			
Cerebellum with dentate nucleus	X	X			

Digitized images of the following microscopic slides were provided to the evaluating neuropathologists on 25 cases of tauopathies including AD, AGD, CBD, CTE, GPDC, PART and PSP. The slides were all uniformly processed by a single laboratory

A $\beta$  Beta-amyloid, AD Alzheimer's disease, AGD Argyrophilic grain disease, BA Brodmann area, BIEL Bielschowsky's silver method, CTE Chronic traumatic encephalopathy, GPDC Guamian Parkinson's dementia complex, LHE Luxol fast blue, counterstained with hematoxylin and eosin, PART Primary age-related tauopathy, PSP Progressive supranuclear palsy

Pierce, 1:2000, pretreated with formic acid) and anti-p-TDP-43 (Anti-TDP-43, phospho, 1:2000, pretreated with formic acid) for a total of 27 slides per case (25 slides in 2 cases). An individual blinded to the origin and identity of the cases (KFB) scanned the 671 glass pathology slides into digital images at the Mayo Clinic Jacksonville using an Aperio scanner (Leica Biosystems, Buffalo Grove, IL). The digitized images were organized into folders labeled with only the case number (#1-25), brain region, stain and IHC and provided to the evaluating neuropathologists on portable hard drives as well as on an online slide-hosting website (Leica Biosystems-Aperio). No clinical or demographic information was provided to the evaluating neuropathologists—including no information regarding the subjects' age, gender, clinical symptoms, diagnosis or athletic exposure. No information was supplied regarding the gross neuropathological features of the brains. The neuropathologists were given a tauopathy criteria guide that provided the provisional criteria for CTE [32] as well as published criteria for the other tauopathies (See supplementary material for full tauopathy criteria guide) [4, 7, 11, 21, 25, 34, 40, 47]. Although the neuropathologists knew that the selected cases represented presumptive CTE, AD, PSP, CBD, AGD, PART, and GPDC, they did not know how many cases representing each diagnosis were to be evaluated.

Seven neuropathologists with experience in neurodegenerative diseases, including the tauopathies, participated in the evaluation of the digitized images (NJC, DWD, RDE, CDK, DPP, TDS, JPV). The neuropathologists evaluated the cases independently, at their own pace, and completed an evaluation form that included the pathological diagnosis and a 4-scale level of certainty (1, unsure; 2, possible; 3, probable; 4, definite). After the initial evaluations were sent to BUSM for analysis, the evaluator was provided the gross neuropathological findings and clinical summaries for each case, and asked to reevaluate the diagnosis and provide a second level of conviction. The results of all evaluations were analyzed prior to the face-to-face meeting held on February 25–26, 2015.

### Statistical analysis

To evaluate the agreement among the neuropathologists who reviewed the cases, two sets of Cohen's kappa statistics were calculated. The first kappa coefficient measured the agreement among the overall neuropathological diagnoses; the second kappa coefficient measured the agreement among neuropathologists regarding the specific diagnosis of CTE. The overall kappa coefficient combines the neuropathologist-level estimates of kappa into an overall estimate of the common agreement. Kappa values of 0.81–1.0 indicate very good agreement, kappa values of 0.61–0.80

show good agreement, while kappa values of 0.41–0.60 indicate moderate agreement [12]. All statistical analyses were done using SAS 9.4 (SAS Institute Inc., Cary, North Carolina, USA) software.

At the face-to-face consensus meeting, a larger panel that included ACM<sup>2</sup>, WS,<sup>2</sup> IL, WAG and members of the NINDs TBI/CTE group reviewed the results of the neuropathological evaluations, digitized images and glass pathology slides and discussed the cases as a group. Discussions led to refinements in the neuropathological criteria for CTE, as well as “best practice” recommendations for neuropathologists examining brains for evidence of CTE.

### Results

There was good agreement regarding the overall neuropathological diagnosis of all 25 cases (Cohen's kappa, 0.67), and even better agreement regarding the specific diagnosis of CTE (Cohen's kappa, 0.78), using the proposed criteria. In evaluating the 10 cases submitted with the presumptive diagnosis of CTE (Supplementary Table 1), 64 of the 70 reviewers responses (91.4 %) indicated CTE as the diagnosis. There was a significant decrease of errors that paralleled the sequence of cases evaluated. The log of the expected errors significantly decreased by 0.43 for each case of CTE reviewed ( $p$  value = 0.024). There were common additions to the CTE diagnosis, including “Changes of Alzheimer's disease” (ADC) and AD in the cases with AB plaques (cases #4–10). Other co-morbid diagnoses included hippocampal sclerosis (HS), AGD and PART. In the 15 other tauopathy cases (cases submitted for review with diagnoses other than CTE) (Supplementary Table 2), the reviewers generally agreed with the submission diagnoses of AD (97.1 % of responses), CBD (92.8 %), and PART (78.5 %); however, there were frequent discrepancies in cases with the presumptive diagnoses of PSP, AGD and GPDC (Supplementary Table 2). The evaluators reported a significantly increased degree of certainty ( $t$  test = 4.36,  $p$  value <0.001) in the diagnosis of CTE from an overall mean of 3.1 in a 4-point scale of conviction (1, unsure; 2, possible; 3, probable; 4, definite) to a mean of 3.7 after the gross neuropathological features and clinical features of the cases were provided to the evaluator. Three initial diagnoses of non-CTE were changed to CTE and 9 diagnoses of co-morbid CTE in non-CTE cases were changed to no CTE after revealing the clinical and gross neuropathological features.

<sup>2</sup> Neuropathologist present at the face-to-face panel discussion, but did not participate in the slide evaluations.

### Diagnostic neuropathological features of CTE

The group defined a neuropathological lesion specific to CTE that distinguished the disorder from other tauopathies. The pathognomonic lesion of CTE consists of p-tau aggregates in neurons, astrocytes, and cell processes around small vessels in an irregular pattern at the depths of the cortical sulci (Figs. 1, 2; Table 2). The group also noted that the distinctively irregular spatial pattern of p-tau in CTE was often visible with low-power inspection (Fig. 1). Although other abnormalities in p-tau were also found, especially in the more severely affected brains, the pathognomonic lesion was distinct and not found in the other degenerative tauopathies (Fig. 2). In addition, the group observed frequent evidence of other pathologies in CTE, including TDP-43-immunoreactive

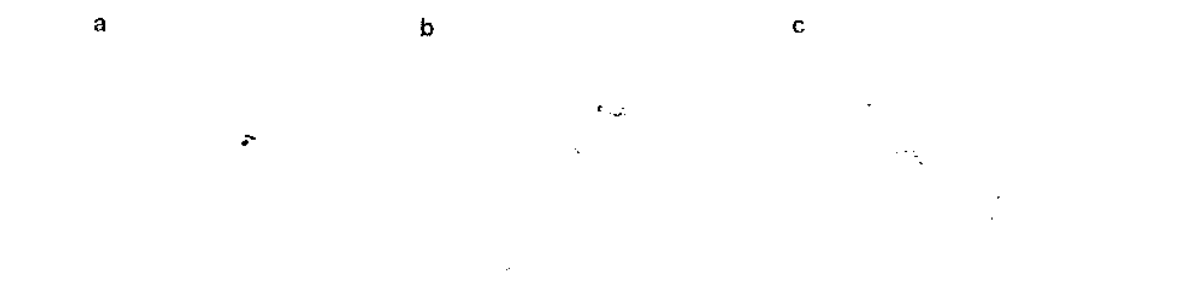
neuronal cytoplasmic inclusions, A $\beta$  plaques and amyloid angiopathy, and hippocampal neurofibrillary degeneration, including extracellular tangles best seen with silver stains.

### Supportive neuropathological features of CTE

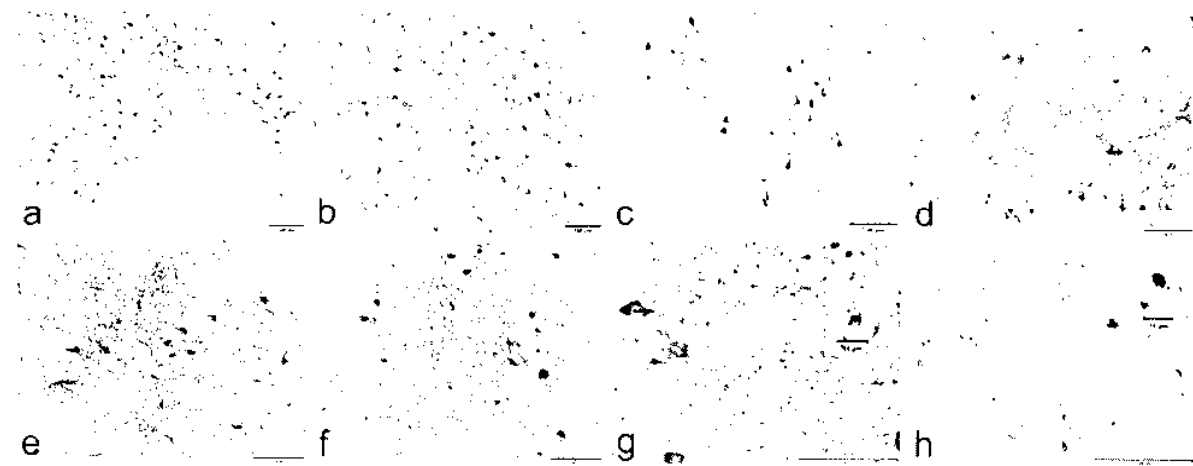
The group defined supportive pathological features for CTE. These features were commonly found in the CTE cases in addition to the required criteria, but were not considered diagnostic in isolation (Table 2).

### Exclusions to the sole diagnosis of CTE

The presence of changes compatible with the diagnosis of another neurodegenerative disease excludes CTE as a

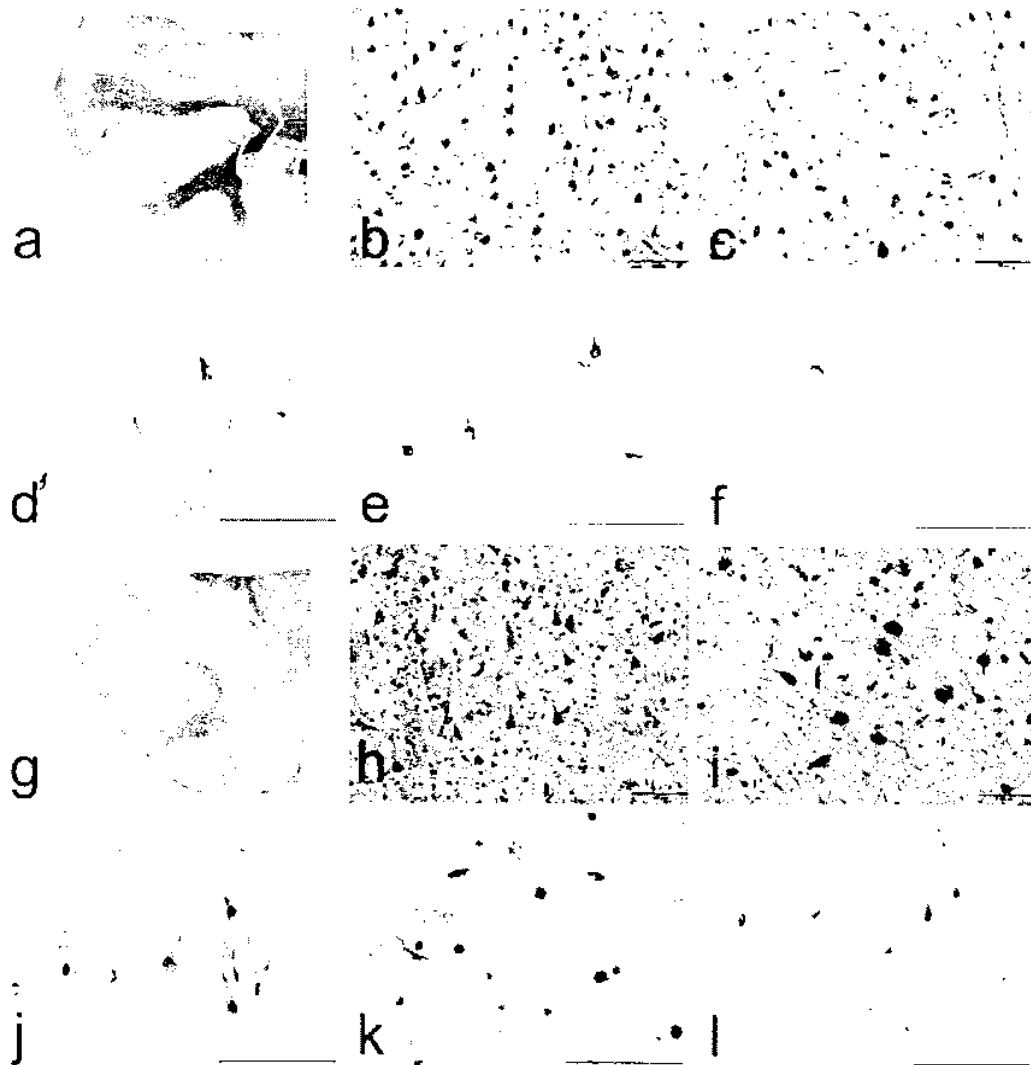


**Fig. 1** Low magnification inspection of p-tau-stained slides often revealed the irregular spatial pattern of CTE pathology. AT8-stained slides of cerebral cortex in 3 cases of CTE showing irregular patches of p-tau pathology most dense at the depths of the sulci



**Fig. 2** The microscopic features of the pathognomonic lesion of CTE. The pathognomonic feature of CTE is a perivascular accumulation of p-tau aggregates in neurons, astrocytes and cell processes in an irregular spatial pattern in the cerebral cortex and found preferentially at the depths of the sulci. **a** A large perivascular p-tau lesion is found at the sulcal depths in a subject with CTE. **b–f** Multiple perivascular foci are often found in the cortex in CTE. **g** The p-tau

aggregates in CTE include strikingly rounded structures in the neuropil that often are most dense in the areas surrounding the vessel. **h** The rounded p-tau immunoreactive cell processes are more densely distributed than those found in argyrophilic grain disease. All sections immunostained for AT8. *bars* indicate 100  $\mu$ m, except in **g** and **h** where the *small bars* indicate 10  $\mu$ m



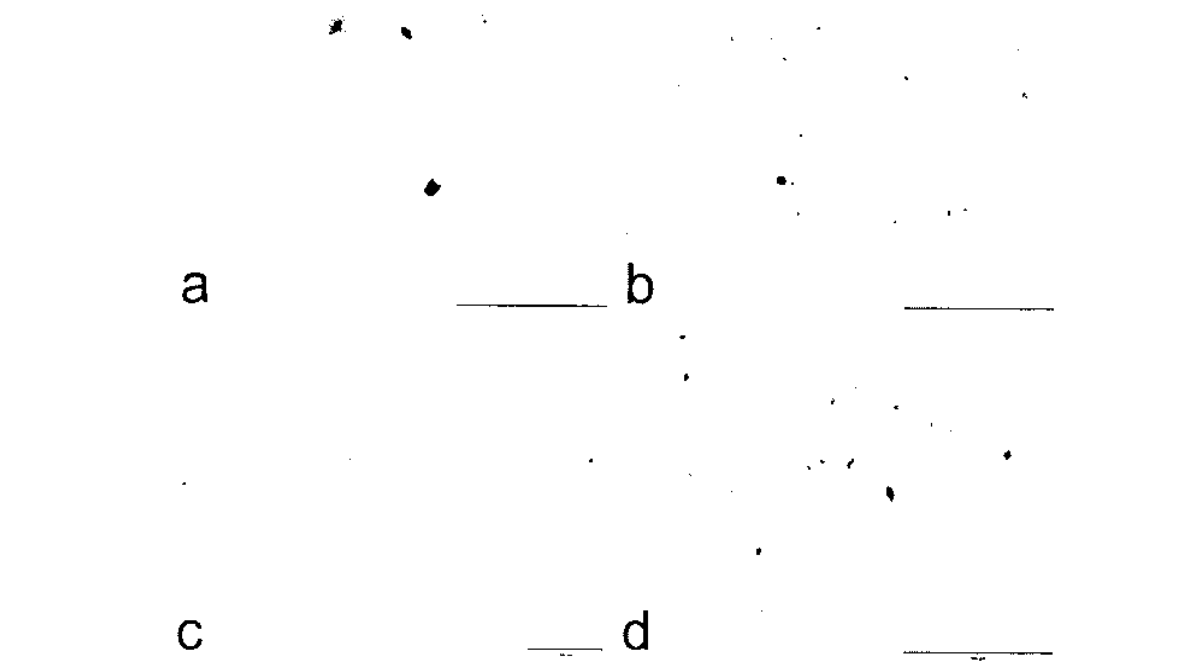
**Fig. 3** Hippocampal pathology in CTE. Examples of hippocampal pathology in 2 cases of CTE of moderate severity. In example 1 (a–f), there is **a** mild hippocampal atrophy, **b** mild neuronal loss in CA1, **c** sparse NFTs in CA1, Bielschowsky silver stain, **d** sparse NFTs in CA1, AT8 immunostain, **e** moderate numbers of diffusely immunopositive AT8-stained neurons in CA4, and **f** occasional AT8 immunopos-

sitive NFTs in the dentate gyrus. In example 2 (g–l), there is **g** more severe hippocampal atrophy, **h** clear neuronal loss in CA1, **i** moderate density of NFTs in CA1, Bielschowsky silver stain, **j** moderate density of NFTs in CA1, AT8 immunostain, **k** high numbers of AT8-stained neurons and NFTs in CA4, and **l** moderate numbers of AT8 immunopositive NFTs in the dentate gyrus. Bars indicate 100  $\mu$ m

single diagnosis, and indicates the presence of co-morbid pathology. These features include CA1-predominant neurofibrillary degeneration in the hippocampus in association with A $\beta$  plaques consistent with AD [34]; prominent cerebellar dentate nucleus cell loss, coiled bodies in oligodendroglia, and tufted astrocytes as seen in PSP [25]; severe involvement of the striatum and pallidum with extensive astrocytic plaques in cortical and subcortical structures as seen in CBD [21] or globular astrocytic inclusions of globular glial tauopathy [1].

## Discussion

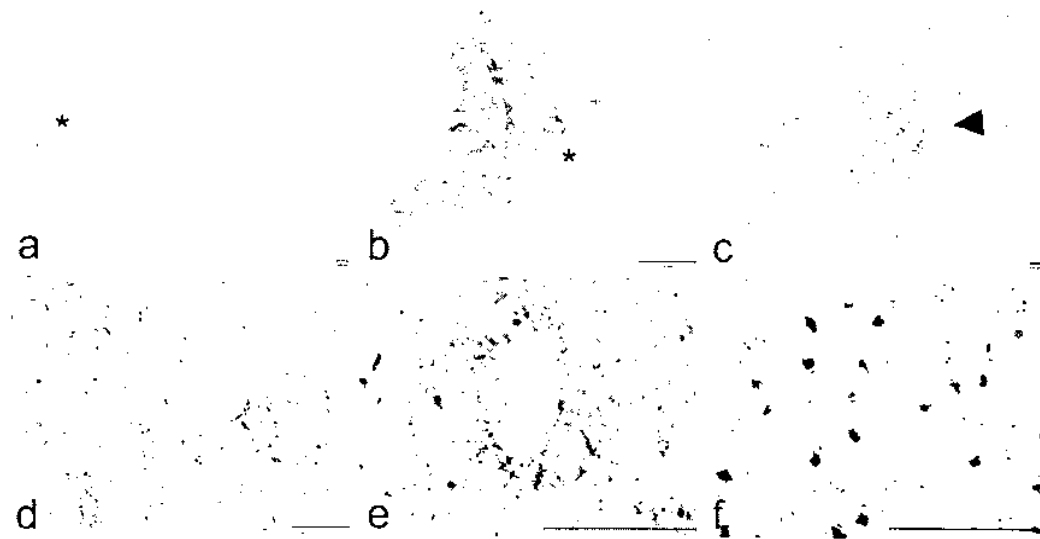
The consensus panel of neuropathologists found that the p-tau pathology of CTE is clearly distinct from other tauopathies. The panel concluded that there is a pathognomonic lesion of CTE that consists of an accumulation of abnormal tau in neurons and astroglia distributed around small blood vessels at the depths of sulci in the cortex in an irregular spatial pattern. Other supportive features of CTE include abnormal p-tau immunoreactive pretangles



**Fig. 4** pTDP-43 pathology in CTE. **a** pTDP-43 neuronal inclusions in the amygdala. **b** pTDP-43 inclusions and dot-like neurites in CA1. **c** pTDP-43 dot-like neurites in entorhinal cortex. **d** pTDP-43 inclusions and dot-like neurites in the dentate granule cell layer. All sections immunostained for p-TDP-43, bars indicate 100  $\mu$ m

**Table 2** Preliminary NINDS criteria for the pathological diagnosis of CTE

Required for diagnosis of CTE	
1. The pathognomonic lesion consists of p-tau aggregates in neurons, astrocytes, and cell processes around small vessels in an irregular pattern at the depths of the cortical sulci	
Supportive neuropathological features of CTE	
p-Tau-related pathologies:	
1.	Abnormal p-tau immunoreactive pretangles and NFTs preferentially affecting superficial layers (layers II–III), in contrast to layers III and V as in AD
2.	In the hippocampus, pretangles, NFTs or extracellular tangles preferentially affecting CA2 and pretangles and prominent proximal dendritic swellings in CA4. These regional p-tau pathologies differ from the preferential involvement of CA1 and subiculum found in AD (Fig. 3)
3.	Abnormal p-tau immunoreactive neuronal and astrocytic aggregates in subcortical nuclei, including the mammillary bodies and other hypothalamic nuclei, amygdala, nucleus accumbens, thalamus, midbrain tegmentum, and isodendritic core (nucleus basalis of Meynert, raphe nuclei, substantia nigra and locus coeruleus)
4.	p-Tau immunoreactive thorny astrocytes at the glial limitans most commonly found in the subpial and periventricular regions
5.	p-Tau immunoreactive large grain-like and dot-like structures (in addition to some threadlike neurites) (Fig. 2h)
Non-p-tau-related pathologies:	
1.	Macroscopic features: disproportionate dilatation of the third ventricle, septal abnormalities, mammillary body atrophy, and contusions or other signs of previous traumatic injury
2.	TDP-43 immunoreactive neuronal cytoplasmic inclusions and dot-like structures in the hippocampus, anteromedial temporal cortex and amygdala (Fig. 4)
Age-related p-tau astroglialopathy that may be present; non-diagnostic and non-supportive [22]	
1.	Patches of thorn-shaped astrocytes in subcortical white matter
2.	Subependymal, periventricular, and perivascular thorn-shaped astrocytes in the mediobasal regions
3.	Thorn-shaped astrocytes in amygdala or hippocampus [22]



**Fig. 5** Age-related p-tau astrogliopathy that may be present. **a** and **b**, Subpial p-tau immunopositive astrocytes may be found at the glial limitans in the sulcal depths but are non-specific and non-diagnostic for CTE (asterisks). **c** However, p-tau immunopositive subpial astrocytes accompanied by perivascular foci of p-tau positive neurons and astrocytes (arrowheads) at the depths of the sulci are diagnostic for CTE. **d** and **e** p-Tau immunopositive astrocytes surrounding small

venules in the deep white matter of the temporal lobe are not diagnostic for CTE and are often found in association with aging [22]. **f** p-Tau positive astrocytes may also be found in the crests of the white matter of the frontal and temporal lobes with aging and other conditions that are not diagnostic for CTE [22]. All sections immunostained for AT8. *bars* indicate 100  $\mu$ m

and NFTs preferentially affecting superficial layers (layers II–III), pretangles, NFTs or extracellular tangles primarily in CA2 and CA4 of the hippocampus, NFTs in subcortical nuclei, including the mammillary bodies and other hypothalamic nuclei, amygdala, nucleus accumbens, thalamus, midbrain tegmentum, isodendritic core (nucleus basalis of Meynert, raphe nuclei, substantia nigra and locus coeruleus), p-tau immunoreactive thorned astrocytes at the glial limitans in the subpial and periventricular regions, p-tau immunoreactive large grain-like and dot-like structures, and TDP-43 immunoreactive neuronal cytoplasmic inclusions and dot-like structures in the hippocampus, anteromedial temporal cortex and amygdala. While this was only the first meeting to address the neuropathological diagnosis of CTE, and more research is needed to determine the nature and degree of brain injury necessary to cause this neurodegeneration, the panel members also noted that the pathognomonic lesion of CTE has, thus far, only been found in individuals who were exposed to brain trauma, typically multiple episodes.

The panel also determined that the pathognomonic lesion of CTE is distinct from age-related tau astrogliopathy (ARTAG), a morphological spectrum of astroglial pathology detected by p-tau immunohistochemistry that may coexist in the same brain with other disorders and is of unclear etiology (Fig. 5). P-tau-immunoreactive astrocytes in ARTAG include thorn-shaped astrocytes in the subpial,

subependymal, and perivascular regions of the white and gray matter (Kovacs, in press). Changes of ARTAG may be present in CTE, but in isolation, are non-specific and non-diagnostic.

Although 9 of the 10 subjects diagnosed with CTE in this study were former American football players and only one was a former professional boxer, previous data has shown that the pathological features of CTE associated with boxing (often referred to as “dementia pugilistica”) are similar to the pathological features of CTE associated with football [28, 32]. Furthermore, the cortical areas most likely to show early focal CTE pathology in boxers are similar to American football players. While initial reports of boxers with CTE described cerebellar scarring, atrophy and loss of Purkinje cells [5], recent studies of pugilists find that cerebellar pathology is rare aside from p-tau NFTs and neurites in the dentate nucleus, Purkinje cells and roof of the 4th ventricle [28, 32].

#### Future directions

Using criteria from this consensus meeting, Bieniek and colleagues reviewed the clinical records and brains of 1721 cases donated to the Mayo Clinic Brain Bank over the past 18 years, and found CTE pathology in 32 % of contact sport athletes [2]. No cases of CTE were found in 162 control brains without a history of brain trauma or in 33

**Table 3** Recommended brain regions to be sampled and evaluated

Region	CTE
Middle frontal gyrus <sup>a</sup>	pTau <sup>a</sup> pTDP-43 Aβ <sup>c</sup>
Superior and middle temporal gyri <sup>a</sup>	pTau <sup>a</sup>
Inferior parietal lobule <sup>a</sup>	pTau <sup>a</sup> Aβ <sup>c</sup>
Hippocampus and entorhinal cortex	pTau pTDP-43 <sup>b</sup> Aβ <sup>c</sup>
Amygdala	pTau pTDP-43 <sup>b</sup>
Thalamus	pTau
Basal ganglia with basal nucleus of Meynert	pTau
Midbrain including substantia nigra	pTau
Pons including locus coeruleus	pTau
Medulla including dorsal motor nucleus of vagus	pTau
Cerebellar cortex and dentate nucleus	pTau
Additional sections if high suspicion	
Superior frontal gyrus	pTau <sup>d</sup>
Temporal pole	pTau <sup>d</sup> pTDP-43
Hypothalamus including mammillary body	pTau <sup>d</sup>

In addition to the NIA-AA recommended regions for the evaluation of Alzheimer's disease (AD) neuropathologic change and Lewy body disease (LBD) [34], we recommend wider p-tau screening to capture CTE and other tauopathies. In addition, if there is a high index of suspicion of CTE, we recommend taking extra sections of frontal and temporal cortices, and hypothalamus including the mammillary body.

Bilateral representative sections from each region are recommended if both cerebral hemispheres are available for microscopic analysis

<sup>a</sup> Most valuable for detecting CTE neuropathology

<sup>b</sup> AT8 or equivalent Tau (CP-13 or PHF-1) on all cortical sections, if positive; stain other areas and possibly sample additional areas<sup>d</sup>. We do not recommend thioflavin or silver stains for the detection of CTE lesions

<sup>c</sup> TDP-43: amygdala and hippocampus, if positive then temporal pole and frontal cortex

<sup>d</sup> Aβ: middle frontal gyrus, inferior parietal lobule and hippocampus and entorhinal cortex; if positive wider sampling is recommended

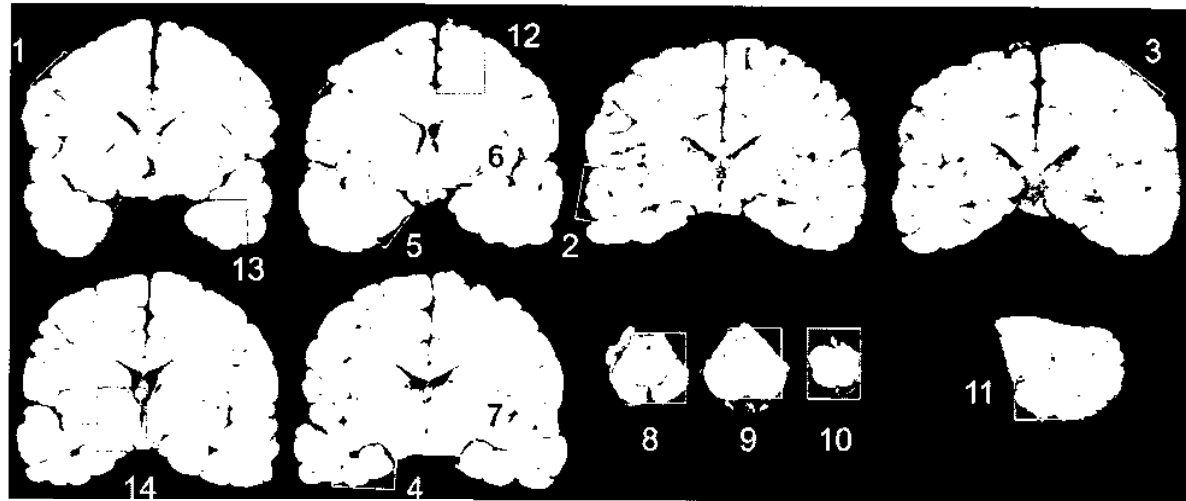
<sup>e</sup> If there is a high index of suspicion consider taking extra sections, specifically superior frontal gyrus, temporal pole, and hypothalamus including mammillary body

cases with a history of a single traumatic brain injury. Of the 21 with CTE pathology, 19 had participated in football or boxing, and many were multiple sport athletes including rugby, wrestling, basketball, and baseball. One athlete played only baseball, and another athlete only played basketball. Similarly, Ling and colleagues screened 268 cases of neurodegenerative disease and controls in the Queen Square Brain Bank for Neurological Disorders using the preliminary McKee criteria [32] and found changes of CTE in 11.9 % of neurodegenerative disorders and 12.8 % of elderly controls. Of the cases with changes of CTE, 93.8 % had a history of TBIs, 34 % had participated in high-risk sports including rugby, soccer, cricket, lacrosse, judo and squash, and 18.8 % were military veterans [24]. However,

it is unclear if all the cases with CTE changes described by Ling and colleagues would have met strict criteria for CTE using these newly defined NINDS guidelines. Furthermore, the relationship between non-diagnostic, non-specific astrocytic p-tau pathology and a history of traumatic exposure remains to be determined (Kovacs, in press).

At the present time, CTE remains a diagnosis that can only be made definitively upon neuropathological examination of the brain. Because the pathological diagnosis requires p-tau immunohistochemistry and the lesions are irregularly distributed, the detection of CTE in autopsy cohorts may require additional sampling compared to routine practices. The consensus panel's minimum recommended sampling for CTE is found in Table 3. Sampling follows the protocol recommended by Alzheimer Disease Centers (National Institute on Aging-Alzheimer's Association (NIA-AA) [34]) with the further recommendation that all cortical sections be taken to include the region at the depths of the cortical sulci. This has been shown in pilot studies to detect 80 % of CTE cases; however, 20 % of CTE cases, all early stage, would be missed by this sampling scheme [9]. Of the NIA-AA sampling guidelines, the following blocks are most valuable for detecting CTE: sulcal depths of the superior and middle frontal gyrus, superior and middle temporal gyrus and inferior parietal gyrus (Fig. 6). Of note, the Bielschowsky silver stain does not always detect the diagnostically significant focal perivascular cortical tau lesions, and the panel recommended p-tau immunohistochemistry for the diagnosis of CTE using AT8 immunostaining or equivalent p-tau antibody (CP-13 or PHF-1). The question of how extensive the sampling must be to "rule out" CTE was discussed, but no data were available to make this determination.

These criteria are the beginning of the process to fully characterize the pathology of CTE, and this is only the first of a series of consensus conferences on the subject funded by the U01 NINDS research initiative. Many important questions were not addressed in this first consensus panel, including the degree of neuronal cell loss, gliosis, inflammation, and hemosiderin deposition, and the diagnosis of CTE in the presence of comorbid pathologies, including AD. Future directions will include further validation of the neuropathological criteria for CTE, including staging of the severity of p-tau pathology and characterization of early disease. More pathological characterization will also be necessary to delineate the involvement of the other subcortical regions, including amygdala, globus pallidus, subthalamic nucleus, accumbens, neostriatum, thalamus, midbrain, cerebellum, spinal cord and white matter. It will also be important to determine the differential hippocampal p-tau pathology in CTE compared to AD, whether the TDP-43 pathology is distinctive for CTE and the contribution of hippocampal sclerosis and TDP-43 deposition to the clinical and pathological features. Population isolates



**Fig. 6** Minimum recommended brain regions for evaluation for CTE. The following sections from the NIA-AA blocking scheme are recommended for p-tau immunostaining in evaluation for CTE (*blue rectangles*). In the cortical sections (blocks 1–5, 12, 13), the depths of the cortical sulci should be included in the section. 1 Middle frontal gyrus, 2 superior and middle temporal gyri, 3 inferior parietal lobule, 4 hippocampus, 5 amygdala and entorhinal cortex, 6 basal ganglia at

level of anterior commissure with basal nucleus of Meynert, 7 thalamus, 8 midbrain with substantia nigra, 9 pons with locus coeruleus, 10 medulla oblongata, 11 cerebellar cortex and dentate nucleus; additional sections if high suspicion of CTE (*red rectangles*): 12 superior frontal gyrus, 13 temporal pole, 14 hypothalamus and mammillary body

that develop unusual p-tau pathologies will need to be distinguished from CTE pathology in addition to Guam, such as the Kii peninsula of Japan [23]. In addition, the contributions of other proteinopathies, including  $\beta$ -amyloidosis (diffuse and dense core A $\beta$  plaques and amyloid angiopathy) and alpha-synuclein will be important to determine. Similarly, the role of microvascular pathology, iron deposition, axonal injury, neuroinflammation and astrocytosis to the pathogenesis of CTE pathology needs resolution.

Future investigation will be needed to understand the relationship of the pathology to the clinical symptoms, genetics, neuroimaging and other biomarkers (including p-tau positron emission tomography (PET) imaging and cerebrospinal fluid (CSF) and blood biomarkers), metabolomics, proteomics, and epigenetics. It will also be important to determine whether specific “tau strains” are involved in the development of CTE. Furthermore, more information is needed regarding the frequency, severity, and nature of the traumatic exposures, length of survival after trauma, as well as factors such as the age at first and last exposure to trauma, and the effects of military compared to civilian brain trauma.

The limitations of the present study include the relatively small sample set, the use of digitized images, the selection of suspected CTE cases by a single source, the use of representative cases of moderate-to-late stage severity of CTE, and presence of some age-related co-morbidities. However, these limitations are offset by the fact that all evaluating neuropathologists were evaluating the exact

same digital images, the cases were all uniformly prepared by a central laboratory, and the evaluation was performed blinded to all clinical or demographical data and gross neuropathological findings. Other limitations to the present study include the lack of data regarding TBI history in the non-CTE cases under evaluation. Future studies are being designed to specifically address the contribution of TBI at all levels of severity to neurodegenerative pathologies.

## Conclusion

A consensus panel of 7 neuropathologists blinded to all clinical conditions and demographics evaluated the identical digitized images of 25 cases representing various tauopathies and concluded that the pathology of CTE is distinct from other tauopathies. In addition, the panel described the pathognomonic lesion of CTE as an accumulation of abnormal tau in neurons and astroglia distributed perivascularly at the depths of sulci in the isocortex in an irregular pattern. Future consensus meetings will address validation of the criteria among a wider group of neuropathologists using cases submitted from multiple sources. In addition, future meetings will address the identification of comorbid CTE when other neurodegenerative diseases and other diseases are present. Furthermore, additional research will be necessary to determine the contribution of p-tau and other pathologies to the development of clinical symptoms of CTE.



The incidence and prevalence of CTE remain unknown and will likely require methods of in vivo detection and diagnosis to make a clear determination. This first consensus conference on the pathological criteria for CTE represents the first step along the path to standardizing the neuropathology of CTE and paving the way for future determinations of specific clinical symptomatology and refinements in clinical diagnosis.

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#### Compliance with ethical standards

**Conflict of interest** ACM, NJC, DWD, RDF, CDK, IL, DPP, TDS, JPVS, WS, YT, JFC, KFB, KDO, VEA and WAG have no conflicts of interest to disclose.

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#### Appendix: TBI/CTE group

Elissa Flannery, Daniel H. Daneshvar, Patrick T. Kiernan, Jesse Mez, Lauren Murphy, Todd M. Solomon, Debra Babcock, Patrick S. F. Bellgowan, and Walter J. Koroshetz.

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**Porter, Kevin (NIH/OD) [E]**

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**From:** Myles, Renate (NIH/OD) [E]  
**Sent:** Monday, December 21, 2015 8:39 AM  
**To:** Collins, Francis (NIH/OD) [E]; NIH Director's Executive Committee  
**Cc:** Jackson, Calvin (NIH/OD) [E]; Fine, Amanda (NIH/OD) [E]; Wojtowicz, Emma (NIH/OD) [E]  
**Subject:** Boston Globe -- Head games: The story of 'Concussion'  
  
**Follow Up Flag:** Follow up  
**Flag Status:** Completed

Boston Globe

Movies

## **Head games: The story of 'Concussion'**

By Ed Symkus Globe Correspondent December 19, 2015



Nick Veasey/Getty Images

Hollywood has long had a fascination with movies about someone uncovering a wrongdoing, then setting out to right it. Sometimes the hero is a cop trying to root out corruption on the force (1973's "Serpico"), sometimes she is a legal assistant getting to the bottom of a utility company poisoning its customers' drinking water ("Erin Brokovich," 2000), and sometimes he is an immigrant doctor who takes on the all-powerful National Football League, which might be looking the other way while evidence mounts that head injuries on the field can lead to dementia and death down the line.

The doctor-turned-crusader of the latter is Bennet Omalu, played by Will Smith in the new film "Concussion," opening Friday. He's a forensic neuropathologist who connected the degenerative brain condition chronic traumatic encephalopathy (CTE) to repeated concussions suffered by football players. Omalu first noted the problem in 2002, during his autopsy of retired Pittsburgh Steelers center and Football Hall of Fame member Mike Webster (David Morse) who, suffering from CTE, abandoned his family, started living in his truck, fell into a spiral of drug addiction and physical self-abuse, and died of a heart attack at 50.

With its roots in the 2009 GQ article “Game Brain” by Jeanne Marie Laskas, the film was written and directed by Peter Landesman, who previously adapted “Kill the Messenger” (2014) and wrote and directed “Parkland” (2013).

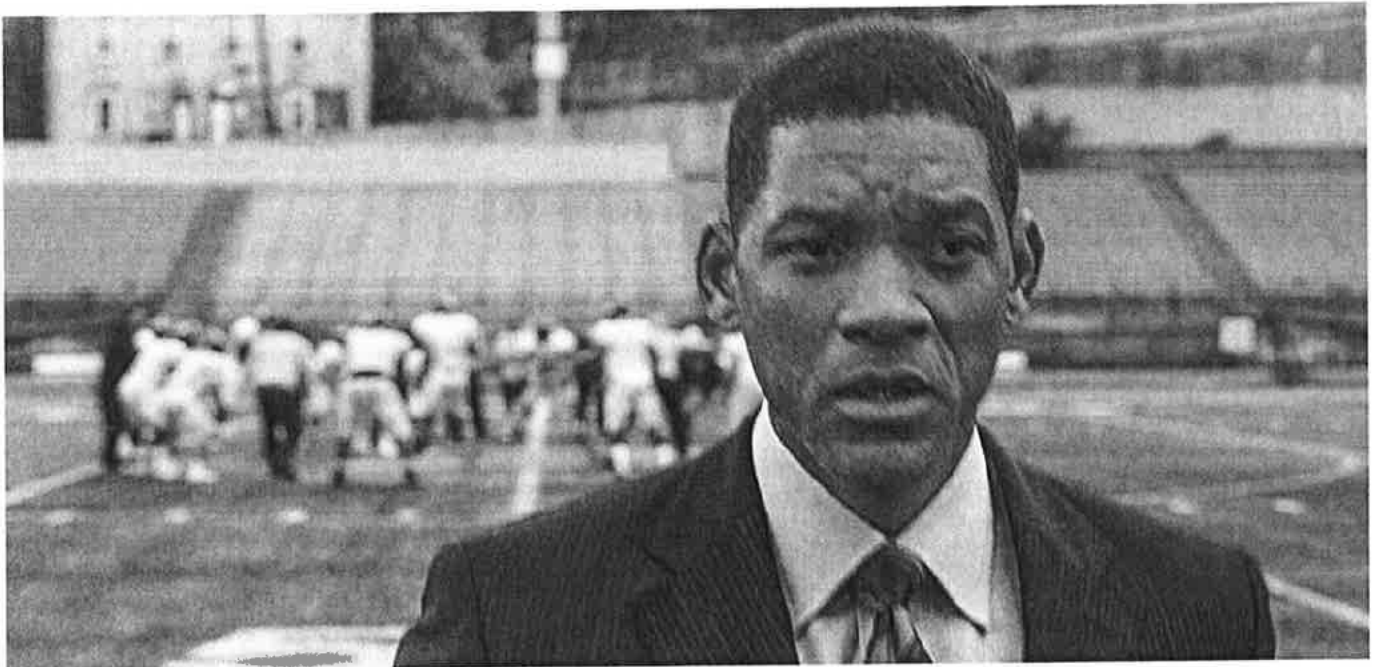
Even though football is by far the most popular televised spectator sport in America, and the film is fraught with fingerpointing — not at the game but at the NFL — neither Landesman nor Morse is concerned about negative reactions from passionate fans.

“If a filmmaker or storyteller is concerned about alienating people by telling a truthful, powerful story, then he should give up his day job,” said Landesman by phone from New York. “I was never afraid of the consequences; I was never afraid of alienating anybody, because I believe that an audience respects the truth, and respects having an emotional, authentic experience in a movie theater.”

Morse, a native of Beverly who grew up in nearby Hamilton, started his acting career at Boston Repertory Theatre, and is best known for his role as the beleaguered Jack Morrison on “St. Elsewhere,” had a slightly different take. Also speaking from New York, he said, “I thought if we did our job right, some people would be alienated, and that would be great! If you’re going to tell this kind of story, and if you’re telling the truth, you’re going to alienate people; you can’t back away from that. Of course, other people will be thrilled and grateful about the film.”

Landesman, who played football for a year in college, was a fan of Mike Webster. Morse, who tried out for his high school football team “but they wouldn’t have me,” had heard about a player on the Steelers who was living in his truck and had died. But neither of them suspected there was a larger story to be told.

“I had followed, in a peripheral way, the deaths and disappearances of these football players,” said Landesman. “But they were strange, disconnected stories. Mike Webster dies, [Cincinnati Bengals receiver] Chris Henry dies, [Chicago Bears safety] Dave Duerson shoots himself. Some part of me was thinking, ‘What’s going on here?’ But none of it was synthesized until I saw the GQ piece.”



Columbia Pictures

Will Smith as Dr. Bennet Omalu in “Concussion.”

Because of Landesman’s former career as an investigative reporter with The New York Times Magazine, he was determined to get everything right in his movie.

“Before I even started writing the script I told the studio I wanted them to hire an objective third-party fact-checker,” he said. “I knew that the NFL would be combing through this film and trying to find some way to discredit us. I didn’t want to leave room for critics to come after us and weaken our narrative by finding trivial mistakes.”

He insists that there was no meddling from the NFL, nor was there any contact between the league and Landesman — or Sony Pictures — beyond a single e-mail.

“It was a one-e-mail exchange between me and someone at the NFL, just wondering if it was a good idea to have a meeting,” said Landesman. “But I decided, and the studio decided, that I didn’t need them, that they had nothing to offer me. So I canceled the meeting.”

When it came time to assemble his actors, Landesman, whose mantra is that the success of a film is “all in the casting,” scored with his first choice of Will Smith, then got Alec Baldwin for some gravitas as former Steelers’ team physician Julian Bailes, along with Albert Brooks, who added subtle comic relief in his delivery of the role of Omalu’s mentor. And then there was Morse, who turned out to be exactly what Landesman was looking for, even though the role of Mike Webster was first offered to another actor.

“The other [unnamed] actor’s schedule didn’t work out,” said Landesman. “I had offered David the role of the assistant in the morgue. But when the role of Webster became open, I realized I actually had Webster all along. It was just another guy. I asked David if he would consider it, and he jumped at it.”

‘I had followed, in a peripheral way, the deaths and disappearances of these football players. But they were strange, disconnected stories. . . . Some part of me was thinking, “What’s going on here?”’

“

Morse, who played George Washington in HBO’s “John Adams” a few years ago, was as determined as Landesman about getting things right.

“Everybody has an idea of who Washington is, so I felt a real responsibility to that part,” said Morse. “But it was a very different thing with Mike Webster because he means so much to his family, and he was such an important figure in the game. It was really hard to do those scenes [of him homeless] in the truck. Nobody wants to remember him that way.

“For legal reasons, I wasn’t allowed to talk to Mike’s family. But I did get to spend a lot of time with his lawyer. And a couple of doctors introduced me to people with head trauma and dementia. And I watched Mike’s Hall of Fame speech over and over again.”

Morse also admits to being conflicted about football after making the film.

“It’s hard for me to watch the game now, knowing what I know about what’s happening to those people on the field. Sure, the protocols are changing, but it’s still a really brutal sport.”

He was silent for a moment, then added, “But, like so many people, I’m totally fascinated by the game and, living in Philadelphia, I don’t want to miss watching the Eagles play.”

Another pause, then, “Yes, I’m from Boston, but I have to say I took some pleasure a couple of weeks ago when the Eagles beat the Patriots.”

Ed Symkus can be reached at [esymkus@rcn.com](mailto:esymkus@rcn.com).

**From:** Stern, Robert A  
**Sent:** 18 Dec 2015 19:12:13 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** FW: UO1 press release

Hi Walter,  
Just checking in to make sure this plan is good for you.  
Bob

**From:** Ober, Maria Pantages  
**Sent:** Friday, December 18, 2015 1:49 PM  
**To:** McMakin, Barbara (NIH/NINDS) [E] <mcmakinbi@ninds.nih.gov>  
**Cc:** Stern, Robert A <bobstern@bu.edu>; Wilczewski, Gina Maria <ginad@bu.edu>; Emr, Marian (NIH/NINDS) [E] <emrm@ninds.nih.gov>  
**Subject:** RE: UO1 press release

Thank you, Marian...we will move forward as outlined below.

**From:** McMakin, Barbara (NIH/NINDS) [E] [mailto:mcmakinbi@ninds.nih.gov]  
**Sent:** Friday, December 18, 2015 1:47 PM  
**To:** Ober, Maria Pantages <mpober@bu.edu>  
**Cc:** Stern, Robert A <bobstern@bu.edu>; Wilczewski, Gina Maria <ginad@bu.edu>; Emr, Marian (NIH/NINDS) [E] <emrm@ninds.nih.gov>  
**Subject:** RE: UO1 press release

Hi Maria.

Thank you for honoring our request to push back the embargo on the release.

Other than the grant number, we have no additional changes to your release.

Best,  
Barbara

**From:** Ober, Maria Pantages [mailto:mpober@bu.edu]  
**Sent:** Friday, December 18, 2015 1:34 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Cc:** Stern, Robert A; Wilczewski, Gina Maria; McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: UO1 press release

Marian, Barbara:  
Totally understand things from your perspective. We will embargo the announcement for **9 a.m. EST Tuesday, Dec. 22.**  
How does that sound?  
If you're fine with that, please let me know and we will notify the PIs and communications colleagues (and the Fainaru bros).

We've added the grant number to the release in the editor's note; other than that, I would like your confirmation that you had no other content suggestions.



Thank you,  
maria

**From:** Emr, Marian (NIH/NINDS) [E] [<mailto:emrm@ninds.nih.gov>]  
**Sent:** Friday, December 18, 2015 11:06 AM  
**To:** Ober, Maria Pantages <[mpober@bu.edu](mailto:mpober@bu.edu)>  
**Cc:** Stern, Robert A <[robstern@bu.edu](mailto:robstern@bu.edu)>; Wilczewski, Gina Maria <[ginad@bu.edu](mailto:ginad@bu.edu)>; McMakin, Barbara (NIH/NINDS) [E] <[mcmakinbi@ninds.nih.gov](mailto:mcmakinbi@ninds.nih.gov)>  
**Subject:** RE: UO1 press release

Your release is very well written. We would only ask that you include the grant number somewhere in the release (a footnote will do) so that it is picked up by the NIH RePORTER search algorithm. Hoping you will consider our request to allow time for Dr. Koroshetz to speak with Steve before you release. I wouldn't be surprised if you receive the same request for consideration from him.  
Marian

**From:** Ober, Maria Pantages [<mailto:mpober@bu.edu>]  
**Sent:** Friday, December 18, 2015 10:57 AM  
**To:** McMakin, Barbara (NIH/NINDS) [E]; Wilczewski, Gina Maria  
**Cc:** Emr, Marian (NIH/NINDS) [E]; Stern, Robert A  
**Subject:** UO1 press release

Barbara  
We will confer on our end and get back to you this afternoon.

Meanwhile, any feedback on the release or is that good to go? Please send the grant number so that we can include that.

Thank you,  
maria

**From:** McMakin, Barbara (NIH/NINDS) [E] [<mailto:mcmakinbi@ninds.nih.gov>]  
**Sent:** Friday, December 18, 2015 10:52 AM  
**To:** Wilczewski, Gina Maria <[ginad@bu.edu](mailto:ginad@bu.edu)>  
**Cc:** Emr, Marian (NIH/NINDS) [E] <[emrm@ninds.nih.gov](mailto:emrm@ninds.nih.gov)>; Ober, Maria Pantages <[mpober@bu.edu](mailto:mpober@bu.edu)>; Stern, Robert A <[robstern@bu.edu](mailto:robstern@bu.edu)>  
**Subject:** RE: UO1 press release

Hi Gina,

I just spoke with Marian. We're dealing with pressure on our end regarding the timing of your statement and Dr. Koroshetz's interview with the Fainaru brothers. Dr. Koroshetz is scheduled to speak with them at noon on Monday. Would you reconsider delaying your release until Monday afternoon or Tuesday morning?

Best,  
Barbara

**From:** Wilczewski, Gina Maria [<mailto:ginad@bu.edu>]  
**Sent:** Thursday, December 17, 2015 3:58 PM  
**To:** Emr, Marian (NIH/NINDS) [E]; Ober, Maria Pantages; Stern, Robert A

**Cc:** McMakin, Barbara (NIH/NINDS) [E]

**Subject:** RE: UO1 press release

Marian,

We need to go forward with the dissemination of the release on Monday (12/21) morning as planned. As Dr. Stern and Maria have both explained we are feeling pressure to proceed with the announcement.

Gina DiGravio-Wilczewski  
Media Relations Manager  
Boston University School of Medicine  
617-638-8480 (O)  
617-224-(b) (6) 1)  
[glnad@bu.edu](mailto:glnad@bu.edu)

**From:** Emr, Marian (NIH/NINDS) [E] [<mailto:emrm@ninds.nih.gov>]

**Sent:** Thursday, December 17, 2015 2:42 PM

**To:** Ober, Maria Pantages; Stern, Robert A

**Cc:** McMakin, Barbara (NIH/NINDS) [E]; Wilczewski, Gina Maria

**Subject:** RE: UO1 press release

Steve has contacted us, as well, but I can't get him time to speak with Walter until noon on Monday which is why I was asking for some leeway in the release time.

Marian

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** Ober, Maria Pantages [<mailto:mpober@bu.edu>]

**Sent:** Thursday, December 17, 2015 2:39 PM

**To:** Stern, Robert A; Emr, Marian (NIH/NINDS) [E]; Wilczewski, Gina Maria

**Cc:** McMakin, Barbara (NIH/NINDS) [E]

**Subject:** RE: UO1 press release

Thank you, Bob... I'll respond from our communications point of view and echo what you are saying. We are getting pressure to announce with adequate time before the holidays so that PIs are available to do interviews. Monday morning works for everyone.

Regarding ESPN, we are dealing with the Fainaru brothers, Steve and Mark.

maria

**From:** Stern, Robert A

**Sent:** Thursday, December 17, 2015 2:35 PM

**To:** Emr, Marian (NIH/NINDS) [E] <[emrm@ninds.nih.gov](mailto:emrm@ninds.nih.gov)>; Wilczewski, Gina Maria <[glnad@bu.edu](mailto:glnad@bu.edu)>

**Cc:** Ober, Maria Pantages <[mpober@bu.edu](mailto:mpober@bu.edu)>; McMakin, Barbara (NIH/NINDS) [E]

<[mcmakinbi@ninds.nih.gov](mailto:mcmakinbi@ninds.nih.gov)>

**Subject:** RE: UO1 press release

Thanks Marian. I'm not sure if Gina has responded yet, but I wanted to give my input about the timing. My co-PIs and their teams are really wanting to move forward with the announcement; a combination of pressure from their institutions, a desire to get the word out quickly, and also with the holidays coming up, they would like to make sure that the announcement is widely disseminated before people go on vacation. For me personally, I will be going out of the country for a week starting on the 24<sup>th</sup>, and so I want to make sure I am available for interviews following the release. For all these reasons, I would very much like to keep to the Monday morning release. I hope you understand.

Regards,

Bob

**From:** Emr, Marian (NIH/NINDS) [E] [<mailto:emrm@ninds.nih.gov>]  
**Sent:** Thursday, December 17, 2015 2:09 PM  
**To:** Wilczewski, Gina Maria <[ginad@bu.edu](mailto:ginad@bu.edu)>  
**Cc:** Ober, Maria Pantages <[mpober@bu.edu](mailto:mpober@bu.edu)>; Stern, Robert A <[robstern@bu.edu](mailto:robstern@bu.edu)>; McMakin, Barbara (NIH/NINDS) [E] <[mcmakinb@ninds.nih.gov](mailto:mcmakinb@ninds.nih.gov)>  
**Subject:** RE: UO1 press release

Gina: Thanks for sharing your draft with us. We've asked a few people to take a look at it (on very close hold, of course) and will get back to you by tomorrow. One thing that we will need you to do is to add the grant number somewhere on the release. A footnote will do.

I wonder if you would be willing to hold on your release until Tuesday morning since we're trying to find availability for Dr. Koroshetz to speak with reporters who have questions about the grant. Also, can you tell us who you've spoken with at ESPN?

Marian

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** Wilczewski, Gina Maria [<mailto:ginad@bu.edu>]  
**Sent:** Wednesday, December 16, 2015 4:30 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Cc:** Ober, Maria Pantages; Stern, Robert A; McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** ACTION: UO1 press release

Marian,

As per Dr. Stern's discussion with Dr. Koroshetz last week, we are taking the lead on issuing a press release announcing the receipt of this grant. We understand the NIH will not be issuing anything.

The attached release was collaboratively developed with the four PIs and their public information officers.

We feel it is ready for release but are sending it to you for your review.

We would appreciate receiving your feedback by this Friday (12/18) morning.

Our current plan is to distribute it widely on Monday (12/21) morning.

In anticipation of this announcement, we shared an earlier draft version of the release with two ESPN reporters, with whom we have had a longstanding relationship, to allow them the opportunity to include the other PIs in their story.

Look forward to hearing from you.

Thank you

Gina DiGravio-Wilczewski  
Media Relations Manager  
Boston University School of Medicine  
617-638-8480 (O)  
617-224-(b) (M)  
[ginad@bu.edu](mailto:ginad@bu.edu)

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 17 Dec 2015 23:59:57 +0000  
**To:** Walker, Paula (NIH/NINDS) [E]  
**Subject:** RE: CONFIRMATION: Meeting Request on Behalf of Director Collins - Decision on NFL

I am pretty sure this is the same meeting that was called as emergency yesterday?  
walter

**From:** Walker, Paula (NIH/NINDS) [E]  
**Sent:** Thursday, December 17, 2015 6:09 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Fw: CONFIRMATION: Meeting Request on Behalf of Director Collins - Decision on NFL

Hi Walter:

This meeting has been confirmed for Monday. See confirmation below.

Thanks.

Paula

Sent from my BlackBerry 10 smartphone.

**From:** McManus, Ayanna (NIH/OD) [E] <[amcmanus@od.nih.gov](mailto:amcmanus@od.nih.gov)>  
**Sent:** Thursday, December 17, 2015 3:30 PM  
**To:** Simon, Dina (NIH/OD) [C]; Schulke, Hilda (NIH/OD) [E]; Gray, Felicia (FNIH) [T]; Walker, Paula (NIH/NINDS) [E]  
**Cc:** Burrus-Shaw, Cyndi (NIH/OD) [E]  
**Subject:** CONFIRMATION: Meeting Request on Behalf of Director Collins - Decision on NFL

Good Afternoon,

This note confirms the meeting as follows:

DATE:	Monday, December 21, 2015
TIME:	3:45 p.m. – 4:15 p.m.
PLACE:	Bldg. 1, Room 116
PURPOSE:	Decision on NFL
PARTICIPANTS:	Francis Collins Lawrence Tabak Kathy Hudson Maria Freire

	Stephanie James Walter Koroshetz
--	-------------------------------------

Thank you,  
Ayanna

**From:** McManus, Ayanna (NIH/OD) [E]  
**Sent:** Wednesday, December 16, 2015 12:53 PM  
**To:** Simon, Dina (NIH/OD) [C] <dina.simon@nih.gov>; Schulke, Hilda (NIH/OD) [E] <schulkeh@od.nih.gov>; Gray, Felicia (FNIH) [T] <fgray@fnih.org>; Walker, Paula (NIH/NINDS) [E] <walkerp@ninds.nih.gov>  
**Subject:** RE: Meeting Request on Behalf of Director Collins - Decision on NFL

Unfortunately, the proposed time does not work. Can we please consider 3:45PM to 4:15PM?

Thanks,  
Ayanna

**From:** McManus, Ayanna (NIH/OD) [E]  
**Sent:** Wednesday, December 16, 2015 12:44 PM  
**To:** Simon, Dina (NIH/OD) [C] <dina.simon@nih.gov>; Schulke, Hilda (NIH/OD) [E] <schulkeh@od.nih.gov>; Gray, Felicia (FNIH) [T] <fgray@fnih.org>; Walker, Paula (NIH/NINDS) [E] <walkerp@ninds.nih.gov>  
**Cc:** Burrus-Shaw, Cyndi (NIH/OD) [E] <Cyndi.Burrus-Shaw@nih.gov>; Dougenik, Theodore (NIH/OD) [E] <theodore.dougenik@nih.gov>  
**Subject:** Meeting Request on Behalf of Director Collins - Decision on NFL

Good Afternoon,

Dr. Collins requests your principals' attendance to the following meeting:

DATE:	Monday, December 21, 2015
TIME:	3:00 p.m. – 3:30 p.m.
PLACE:	Bldg. 1, Room 116
PURPOSE:	Decision on NFL
PARTICIPANTS:	Francis Collins Lawrence Tabak Kathy Hudson Maria Freire Stephanie James Walter Koroshetz

By reply to this email, please confirm participation in this meeting.

Many thanks,  
Ayanna

**Ayanna McManus**

Immediate Office of the Director  
National Institutes of Health  
Bldg. 1, Room 126  
One Center Drive  
Bethesda, MD 20892  
Voice: 301.496.2433  
Fax: 301.402.2700  
Email: [amcmanus@od.nih.gov](mailto:amcmanus@od.nih.gov)

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**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 17 Dec 2015 21:09:26 +0000  
**To:** 'Mckee, Ann C'  
**Subject:** RE: Your article in Acta Neuropathologica is now online

Thanks Ann, and the manuscript looks great. We'll try to get an NIH highlight of your paper.

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Mckee, Ann C [<mailto:amckee@bu.edu>]  
**Sent:** Wednesday, December 16, 2015 6:46 PM  
**To:** Cairns, Nigel; Dennis Dickson; Folkerth, Rebecca Dunn, M.D.; Keene, Dirk ([cdkeene@uw.edu](mailto:cdkeene@uw.edu)); irene Litvan; daniel Perl; Stein, Thor; Jean Paul Vonsattel; William Stewart; Tripodis, Yorghos; John Crary; Bieniek, Kevin F.; Dams-O'Connor, Kristen; Alvarez, Victor E; Gordon, Wayne; Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Kiernan, Patrick; Murphy, Lauren Elizabeth; Mez, Jesse; Solomon, Todd M; Daneshvar, Daniel, Hamed  
**Subject:** Fwd: Your article in Acta Neuropathologica is now online

All,

I am writing to let you know that the next consensus meeting is planned for May 25-27. Also, the manuscript is now available online, see below.

Thank you for all your help in getting this manuscript out! and best wishes for a happy holiday season and a wonderful new year.

Cheers,

Ann

Begin forwarded message:

**From:** Springer <[SpringerAlerts@springeronline.com](mailto:SpringerAlerts@springeronline.com)>  
**Subject:** Your article in Acta Neuropathologica is now online  
**Date:** December 16, 2015 at 6:32:31 PM EST  
**To:** <[amckee@bu.edu](mailto:amckee@bu.edu)>  
**Reply-To:** Springer <[springeralerts@springeronline.com](mailto:springeralerts@springeronline.com)>



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We are pleased to inform you that your article has just been published:

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The first NINDS/NIBIB consensus meeting to define neuropathological criteria for the diagnosis of chronic traumatic encephalopathy

**Journal**

Acta Neuropathologica, (), 1-12

**DOI**

10.1007/s00401-015-1515-z



Your article is available as 'Online First':

<http://link.springer.com/doi/10.1007/s00401-015-1515-z>

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Managing Director Springer Research Group

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Tel: +1 212 462 1400, Fax: +1 212 462 1700  
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**From:** Walker, Paula (NIH/NINDS) [E]  
**Sent:** 17 Dec 2015 18:08:38 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Fw: CONFIRMATION: Meeting Request on Behalf of Director Collins - Decision on NFL

Hi Walter;

This meeting has been confirmed for Monday. See confirmation below.

Thanks.

Paula

Sent from my BlackBerry 10 smartphone.

**From:** McManus, Ayanna (NIH/OD) [E] <amcmanus@od.nih.gov>  
**Sent:** Thursday, December 17, 2015 3:30 PM  
**To:** Simon, Dina (NIH/OD) [C]; Schulke, Hilda (NIH/OD) [E]; Gray, Felicia (FNIH) [T]; Walker, Paula (NIH/NINDS) [E]  
**Cc:** Burrus-Shaw, Cyndi (NIH/OD) [E]  
**Subject:** CONFIRMATION: Meeting Request on Behalf of Director Collins - Decision on NFL

Good Afternoon,

This note confirms the meeting as follows:

DATE:	Monday, December 21, 2015
TIME:	3:45 p.m. – 4:15 p.m.
PLACE:	Bldg. 1, Room 116
PURPOSE:	Decision on NFL
PARTICIPANTS:	Francis Collins Lawrence Tabak Kathy Hudson Maria Freire Stephanie James Walter Koroshetz

Thank you,  
Ayanna

**From:** McManus, Ayanna (NIH/OD) [E]  
**Sent:** Wednesday, December 16, 2015 12:53 PM  
**To:** Simon, Dina (NIH/OD) [C] <dina.simon@nih.gov>; Schulke, Hilda (NIH/OD) [E] <schulkeh@od.nih.gov>; Gray, Felicia (FNIH) [T] <fgray@fnihi.org>; Walker, Paula (NIH/NINDS) [E] <walkerp@ninds.nih.gov>  
**Subject:** RE: Meeting Request on Behalf of Director Collins - Decision on NFL

Unfortunately, the proposed time does not work. Can we please consider 3:45PM to 4:15PM?

Thanks,  
Ayanna

**From:** McManus, Ayanna (NIH/OD) [E]  
**Sent:** Wednesday, December 16, 2015 12:44 PM  
**To:** Simon, Dina (NIH/OD) [C] <dina.simon@nih.gov>; Schulke, Hilda (NIH/OD) [E] <schulkeh@od.nih.gov>; Gray, Felicia (FNIH) [T] <fgray@fnih.org>; Walker, Paula (NIH/NINDS) [E] <walkerp@ninds.nih.gov>  
**Cc:** Burrus-Shaw, Cyndi (NIH/OD) [E] <Cyndi.Burrus-Shaw@nih.gov>; Dougenik, Theodore (NIH/OD) [E] <theodore.dougenik@nih.gov>  
**Subject:** Meeting Request on Behalf of Director Collins - Decision on NFL

Good Afternoon,

Dr. Collins requests your principals' attendance to the following meeting:

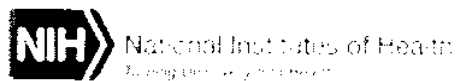
DATE:	Monday, December 21, 2015
TIME:	3:00 p.m. – 3:30 p.m.
PLACE:	Bldg. 1, Room 116
PURPOSE:	Decision on NFL
PARTICIPANTS:	Francis Collins Lawrence Tabak Kathy Hudson Maria Freire Stephanie James Walter Koroshetz

By reply to this email, please confirm participation in this meeting.

Many thanks,  
Ayanna

**Ayanna McManus**  
Immediate Office of the Director  
National Institutes of Health  
Bldg. 1, Room 126  
One Center Drive  
Bethesda, MD 20892  
Voice: 301.496.2433  
Fax: 301.402.2700  
Email: [amcmanus@od.nih.gov](mailto:amcmanus@od.nih.gov)

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**From:** koroshetzw@ninds.nih.gov  
**Sent:** 17 Dec 2015 17:11:10 -0500  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** Re: U01 press release

Thanks Marian  
W

Sent from my iPhone

On Dec 17, 2015, at 2:19 PM, Emr, Marian (NIH/NINDS) [E] <[emrm@ninds.nih.gov](mailto:emrm@ninds.nih.gov)> wrote:

Attached is BU's draft release announcing the new CTE grant. Their plan is to distribute it to the press on Monday morning. I think the draft looks quite good but please take a look at it and let me know if you have any comments or suggestions for changes. I have already asked them to add the grant number in accordance with NIH policy.

BU has already shared the draft with two trusted ESPN reporters (on an embargoed basis). We are trying to arrange a time on Monday at noon for Walter to speak with Steve Fainaru.

**Walter: Do you have 5 minutes to discuss before you head over to the DIR holiday party?**

Marian

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

<Stern NINDS grant mpo--12-16-15.docx>

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 17 Dec 2015 16:38:45 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/NINDS) [E]  
**Bcc:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** Clearance request for CDC statement on "Head Injuries, Sports Culture"  
**Attachments:** ASPA\_1324\_20151215\_CDC\_OpEd\_Head Injuries, Sports Culture\_v01.docx  
**Importance:** High

Attached is a blog message that CDC plans to post timed to the release of Will Smith's film, *Concussion*. As a courtesy, HHS has sent a copy of the message to NIH for review and comment. Please let me know if you wish to submit any comments before 3 pm today.

Thank you.

Marian

*Marian Emr  
Director, Office of Communications and Public Liaison; NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*







**From:** Belligowan, Patrick (NIH/NINDS) [E]  
**Sent:** 17 Dec 2015 12:01:19 -0500  
**To:** Emr, Marian (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** FYI: Sports Illustrate article  
**Attachments:** CTE-December 12-14-15.pdf

**Filed → I:\OCPL\PRESS\TBI\Sports Illustrated.CTE\CTE-December 12-14-15.pdf**

Hi Walter and Marian,

Just wanted to forward you this article that Wayne Gordon sent us. It looks like both he and Ann's study got extensive coverage in this Sports Illustrated article.

Pat

Patrick SF Belligowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-495-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Gordon, Wayne [<mailto:wayne.gordon@mountsinai.org>]  
**Sent:** Wednesday, December 16, 2015 11:49 AM  
**To:** Belligowan, Patrick (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]; Michel, Mary Ellen (NIH/NICHD) [E]  
**Subject:** FW: Sports Illustrate article

Hi:

Attached are two articles for the current issue of Sports Illustrated. The first covers Ann McKee's territory. The second summarizes (pretty well) our grant.

Wayne A. Gordon, Ph.D., ABPP/Cn  
Jack Nash Professor,  
Vice Chair, Department of Rehabilitation Medicine  
Icahn School of Medicine at Mount Sinai  
3 East 101 Street,  
First Floor, Room 118  
Box 1240  
New York, New York 10029  
Voice: 212-824-8372  
Fax: 212-348-5901  
Fax: 212-731-7269 (fax to computer)



**Mount Sinai** *Brain Injury  
Research Center*

**BIG**



**From:** Brouard, Chantal  
**Sent:** Wednesday, December 16, 2015 10:56 AM  
**To:** Gordon, Wayne  
**Subject:** Sports Illustrate article

Please see attached.

Thank you.  
Chantal



**Leahn  
School of  
Medicine at  
Mount  
Sinai**

Chantal Brouard  
Administrative Assistant to  
Wayne A. Gordon, Ph.D.  
Jack Nash Professor & Vice Chair  
Department of Rehabilitation Medicine  
Leahn School of Medicine at Mount Sinai  
Phone: (212) 304-8377  
Fax: (212) 348-5901

NFL BRAIN RESEARCH:

\$30 Million Later, What Do We Know? By Tom Taylor

# SPILTS

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After his five TDs in  
the ACC title game,  
Clemson's Watson  
went to the front  
of the line in the  
championship game.

COLLEGE  
FOOTBALL  
PLAYERS  
PROFILE

## Dashaun Watson

Makes Clemson  
The Team To Beat

By PETE THAMEL

SPECIAL REPORT

# BRAN AND B

TO ADDRESS THE PERCEPTION THAT BRAIN INJURIES ARE EPIDEMIC  
IN THE NFL, THE LEAGUE DONATED MILLIONS TO FUND  
RESEARCH ON THE SUBJECT. SCIENTISTS HAVE LEARNED

A LOT SINCE, BUT WE STILL CAN'T DIAGNOSE  
CHRONIC TRAUMATIC ENCEPHALOPATHY IN LIVING PEOPLE,  
AND SOME PLAYERS ARE GIVING UP THE GAME IN FEAR

OF A DISORDER THAT MIGHT NEVER AFFECT THEM  
BY TOM TAYLOR

BY 2012, THE NFL had a brain problem. Five days before Super Bowl XLIII, in 2009, Boston University neuropathologist Ann McKee held a press conference across the street from Tampa's Raymond James Stadium to discuss chronic traumatic encephalopathy (CTE). Nine months later McKee testified at a congressional hearing, and in February 2010, TIME magazine did a cover story on football calling it "The Most Dangerous Game." Beginning in August 2011 more than 4,500 former players sued the NFL, accusing the league of hiding the dangers of concussions. In May 2012, Hall of Fame linebacker Junior Seau fatally shot himself, and an autopsy showed he had CTE.

The NFL settled the lawsuit for \$765 million in April 2015. That October, PBS aired *League of Denial*, a documentary based on the book of the same name by Steve Fainaru and Mark Fainaru-Wada, who detailed what they called the league's "concussion crisis." Across America parents were pulling their kids off the field, concerned that the children's brains and psyches would be permanently damaged. From 2010 to '12, participation in Pop Warner football dropped 9.5%.

Every day, it seemed, another retired player (or his family) came forward to discuss depression that the player attributed to years of absorbing blows to the head. CTE went from an obscure degenerative brain disease diagnosed posthumously in prizefighters to a household acronym that threatened the very existence of football. Never mind that no causal link had been demonstrated between CTE and depression. Or that researchers hadn't shown that playing football causes CTE. Players—and the public—became convinced that NFL veterans were destined to suffer debilitating depression or dementia.

PHOTOGRAPH BY STEVE GRANITZ FOR TIME



CTE: LLOYD GUNY-SIRENCA

## SPECIAL REPORT

NIH would distribute the money; the NFL would have no say in where it went. In December 2013 the NIH announced that there would be two recipients of the NFL's largesse: The first group, led by McKee, was awarded \$6 million to define a set of criteria for the stages of CTE; the other team, led by Wayne Gordon, a professor of rehabilitation medicine at Mount Sinai Hospital in New York City, would also receive \$6 million to research traumatic brain injury (*page 80*).

If the NFL was trying to push CTE from the front page, the strategy appeared to have worked (with assistance from the NFL's mismanagement of domestic violence cases and Deflategate). Since 2010 participation in high school football has fallen by just 2.2%, according to the National Federation of State High School Associations. Over the same period, the NFL's annual revenue increased by more than 20%, to \$11.1 billion. Eight of the 10 top-rated TV broadcasts of 2012-13 were NFL games. Football's role in brain injury seems to have receded from public consciousness (at least until the release of the movie *Concussion* later this month).

Meanwhile research continues, in part thanks to NFL money. So what do we really know about CTE? Or concussions? Or, for that matter, how football or soccer or any other sport contributes to them?

JOSH PLESCE'S head still ached. On Sept. 18, 2013, the 16-year-old sophomore at John Champe High School in Aldie, Va., had gone to the ER with a suspected concussion after hitting his head on the ground during soccer practice. He missed the rest of that week of school, then gradually returned to classes. Earlier, in the spring, he'd been kicked in the head while playing goalie and was diagnosed with his first concussion. That time the pain had been sharper but had dissipated in three weeks.

A month after the second injury, though, Josh's pain lingered. Loud noises were excruciating; the alarm during a school fire drill set him back just when his headaches seemed to be subsiding. He couldn't focus in class, and he couldn't sleep. Maybe the time before hadn't really been a concussion, he thought. Maybe this is what a concussion is really like. Or perhaps this isn't a concussion at all.

Josh's parents, Angie and George, took him to his pediatrician, then to a concussion clinic in nearby Leesburg and finally to a neurologist. On the recommendation of Josh's pediatrician and school nurse, his diet was changed to low-carb and high-protein. He drank lots of water and got regular exercise and plenty of rest. Josh tried to hide how much he was suffering; he didn't want to worry his parents.

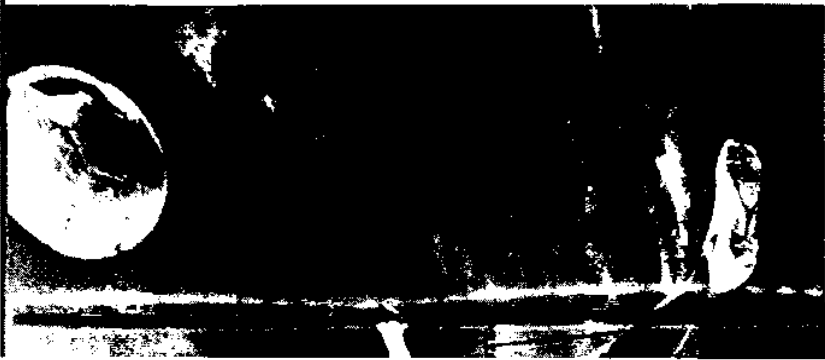


## CONCUSSION IS A TRAUMATIC BUT—IF TREATED CORRECTLY—NOT NECESSARILY A DANGEROUS CONDITION, WHILE CTE CAN BE

Josh says, "I wanted to commit suicide. It was just never-ending pain."

Josh started seeing a psychiatrist and a neuro-psychologist. He was prescribed a barbiturate (Phrenilin), antiseizure medication (Neurontin), an antidepressant (Cymbalta) and ADHD medication (Clonidine). At one point he was taking 15 pills a day, and when he didn't take them he got more headaches from withdrawal. He had Botox injections in his scalp and was prescribed opioid patches (Fentanyl) but quit using them because they made him throw up.

Nothing seemed to work, so Josh's neurologist suggested he get a PET-CT scan of his brain. The results showed that his brain was not normal, but the



#### BACK KICKING

After being told erroneously that he had CTE, Plesce was treated for a concussion and has returned to the soccer field.

## ATEC CORRECTLY—RECOVERABLE

## TEI AN INCURABLE DEGENERATIVE DISEASE.

Four days later Angie, George and Josh sat in the neurologist's office. Josh can't remember anything from that meeting—he was in a daze much of the time—but his parents can. "It was the worst day of my life," George says. Angie broke down in tears. "I'm sorry to tell you," the doctor said, "your son has CTE."

It was a catastrophic diagnosis. Or would have been, had it been true.

**HARRISON MANTLAND**, a forensic pathologist and the chief medical examiner of Essex County, N.J., called CTE "punch drunk" when he first identified it in boxers during autopsies in 1928. *Dementia pugilistica*,

Concussion is a traumatic but—if treated correctly—recoverable condition, while CTE is an incurable degenerative disease. When someone suffers head impact, the brain can shift and twist inside the skull. Shearing forces stretch the membranes of the nerve fibers (axons) that connect the nerve cells (neurons) and, through a process that is not fully understood, trigger an energy crisis: Blood flow, which delivers glucose, is restricted at precisely the same time as the neurons' demand for energy spikes. The brain responds by powering down functions in the affected area, causing the symptoms of concussion, which can last for weeks or longer.

Though CTE, like concussion, is associated with head trauma, its physiological changes are irreversible and develop over years. Similar to Alzheimer's disease, CTE is a tauopathy, characterized by the presence of deposits of a protein called tau throughout the brain. While this protein is present in healthy neurons—it forms the scaffolding of microtubules that run the length of axons—in tauopathies it clumps together. Over time these fibrous tangles spread throughout the brain. According to a review article in August by William Meekhan III, director of the Mitchell Center for Sports Injury Prevention in Waltham, Mass., in the journal *Neurology*, "Early symptoms [of CTE] include memory problems and confusion, depressive symptoms, suicidal ideation, headaches, and behavior changes."

Josh's prognosis looked bleak. His father worried, *Is he going to start to degenerate right away? Is he going to be able to finish high school? To hold down a job? To have a relationship?*

Angie Plesce, who works as a substitute teacher, already had experience caring for children with special needs and knew how demanding that could be. *I do it on an eight-hour basis and I struggle*, she thought. *I can't imagine having to do this all the time for the rest of my son's life.*

**JOSH PLESCE** does not have CTE. "There is no test or biomarker or anything out there that would allow us to reach that diagnosis without postmortem analysis," says Micky Collins, director of the University of Pittsburgh Medical Center Sports Medicine Concussion Program, to whom Angie and George turned for a second opinion. Josh simply had a poorly treated concussion, which cleared up after four months of treatment at UPMC, where doctors slowly reduced the medications he had been taking and gave him exercises to work out his vestibular and ocular systems. He had to relearn how to coordinate his head and eye movements, and used a computer program to retrain his eyes how to track together. He got back to school and started working out again. When an activity became too easy, the doctors made it harder. Josh still suffers from occasional migraines, but he's back playing soccer and has mostly caught up academically.

Even cutting-edge science cannot yet definitively diagnose Alzheimer's disease in living patients, let alone the far less common CTE. The only

way to do that is at autopsy, when the brain can be examined under a



## SPECIAL REPORT

symptoms of a degenerative brain disease, the fact that almost all have such an illness is unsurprising. "But," Bailes says, "the findings are real."

According to figures released in September, Boston University's CTE Center has found CTE in 87 of the 91 brains of deceased NFL players it has studied—95.6%. That came two years after McKee said, "I'm really wondering if, on some level, every single football player doesn't have [CTE]."

The problem with McKee's approach is that her group looks for degenerative brain disease in football players who clearly had degenerative brain disease. "There's certainly a bias," McKee concedes. "We take a brain based only on exposure. If the family contacts us, our criteria for admission into the brain bank are: Were they exposed to [brain injury]? How long did they play? At what level did they play? But families who are concerned about their loved ones are much more likely to go to the trouble of donation because they want an answer."

To understand with any certainty what the effect of football might be on the brain, researchers need to study both the brains of former players who had no symptoms of dementia and the brains of people with symptoms of dementia who never stepped on a football field.

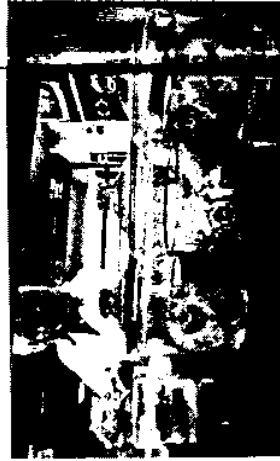
**WE KNOW** that some football players have developed a disease that appears different from other degenerative brain conditions, but we don't know why or how. How many blows to the head increase the risk of CTE? Why do some athletes develop this disease and others don't? Does genetics make some people more susceptible to injury than others? Most important, how can we identify and track the disease in living patients? Without being able to monitor the development of CTE, how will we be able to evaluate the effectiveness of potential therapies?

Last March, 49ers star linebacker Chris Borland quit football after his rookie season, citing fears of the long-term risk of brain damage. But did he jump ship too early or too late? He might have hit a genetic jackpot and not be susceptible to CTE at all. Or the accumulation of hits from youth, college and his single year of pro football might already be causing rogue tau protein to clump inside his brain.

Several NFL veterans have come forward saying that they have been clinically diagnosed with CTE based on symptoms of dementia, including Brent Boyd, a guard with the Vikings, who claims to be the first person alive to have been diagnosed with the disease, and former Vikings linebacker Fred McNeill. McNeill was originally diagnosed with dementia in 2009, then CTE by Omalu in 2010, and finally with amyotrophic lateral sclerosis (ALS), a degenerative disease of

vast majority of ALS patients have normal thinking, they don't have any dementia of any type, but there's a subgroup, I'll just say 5%, that do have dementia." The NIH held its first consensus conference to attempt to agree on a clinical definition for the diagnosis of CTE last February. Omalu, though, strongly believes McNeill had chronic traumatic encephalopathy, meaning that tau tangles were building up in both his brain and spinal cord. "[McNeill's] brain damage manifested with both cognitive and motor symptoms resembling dementia and ALS," says Omalu. The true test of that hypothesis will come in the next couple of weeks. After McNeill died on Nov. 3, his family gave his brain to Omalu for analysis, and according to Omalu the results will be ready soon.

There are signs of progress in understanding CTE. Bailes and Omalu have had success in detecting tau deposits in retired football players by injecting a chemical marker that binds to the neurofibril-



### RACKED BRAINS

McKee (right), who got a grant from Goodell (far right) and the NFL, has found CTE in dead players, but for more meaningful results she must study brain tissue from a greater variety of people.

## HOW MANY BLOWS TO THE HEAD INCREASE THE RISK OF CTE? WHY

## DISEASE AND OTHERS DON'T? DOES GENETICS MAKE SOME PEOPLE

lary tangles and by using PET scans to depict the distribution of the marker. McNeill was one of the former players who took part in that research, and results showed evidence of tau protein buildup. If

PHOTO BY AP/WIDEWORLD FOR THE NEW YORK TIMES

## ON THE LOOKOUT

CONCERNED ABOUT CONCUSSION RATES, LEAGUES HAVE ADOPTED THE FOLLOWING PROTOCOLS TO DETECT BRAIN INJURIES

<b>NFL</b> League-employed spotters sit in a sky box monitoring the action. When they suspect a concussion, they are now authorized to call a medical timeout, stopping the game so medical personnel can attend to a player. The spotters relay any concerns to the team physician, an unaffiliated "neurotrauma consultant" and a trainer, who then evaluate the player. There have been three medical timeouts so far this season.	takes over further evaluation.
<b>NCAA FOOTBALL</b> The NCAA's process is similar to the NFL's. Spotters stationed in the replay booth can stop a game when they suspect a concussion and relay information to trainers and physicians.	
<b>NBA</b> If a potential concussion occurs, the player is removed from the game by trainers to undergo evaluation by team doctors.	
<b>NASCAR</b> When a driver is involved in a crash and his car can no longer roll, he must be taken to the infield, where doctors evaluate him. If his car is not immobilized, the infield doctors can decide whether to evaluate him.	
<b>NHL</b> It too uses spotters. Before this season each club had its own trained concussion spotter. Now teams can use a spotter supplied by the league, who takes mandated online seminars and studies written materials	<b>MLS</b> After a

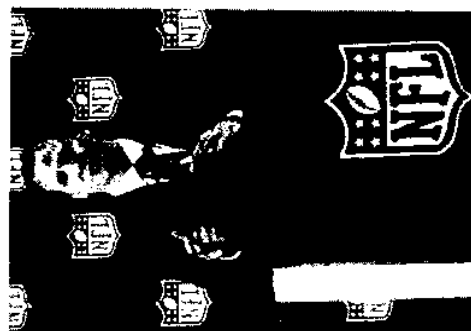
intervention to halt CTE's progress. But the results of these studies might take decades to reach patients, in part because of the long gestation period of the illness, and also because proof still requires an autopsy.

This isn't to say that football can't be made safer. The major sports all have policies, developed in the last few years, to assess concussions (*right*). According to Bailes, there is consensus among experts that CTE is a result of repetitive head trauma, with or without diagnosis of concussion, and there is agreement that reducing exposure to and improving treatment of head impacts will be beneficial.

The key to reducing exposure to head impacts may lie in improving detection of damage. "We desperately need a way of measuring the amount of minor brain trauma that occurs on the field," McKee says, "even in the absence of concussions." That would allow researchers to evaluate ideas

intended to decrease exposure, and also help prevent players from sustaining successive subconcussive blows without time for healing and recovery in between. A whole industry touting helmet- or head-mounted accelerometers has sprung up, and Gary Strangman, associate professor of psychology at Harvard Medical School, is working to develop a near-infrared system that could be worn and would give live feedback of how the brain is moving within the skull.

Keep in mind that it is certainly more dangerous for humans to avoid all physical risks—i.e., not engage in athletic activity—than



TE: WHY DO SOME ATHLETES DEVELOP THIS

OMI PEOPLE MORE SUSCEPTIBLE TO INJURY THAN OTHERS?

to play football or soccer or any other sport in which the head could suffer a blow. "America's problem is not that it plays football," says Uzma Samiadian, an associate professor of neurosurgery at the University of Minnesota and a neurotrauma consultant to the NFL, "but that it watches football." Ac-



# WHEELS OF DESTRUCTION

AFTER DOUG MARKGRAF WAS HIT BY A TRUCK  
WHILE RIDING HIS BIKE, HE WASN'T  
EXPECTED TO LIVE, LET ALONE RECOVER.  
BUT HE DID, AND NOW HIS TYPE OF  
TRAUMATIC BRAIN INJURY IS BEING  
STUDIED. THANKS TO NFL MONEY

BY MATT MCCARTHY

IN THE EARLY EVENING of May 31, 2006, Doug Markgraf, a sophomore materials engineering major at Drexel, put on his training gear and helmet and hopped on his bicycle for a ride across West Philadelphia to meet a landlord. The apartment for rent turned out to be just what Markgraf had hoped for—cheap and spacious—so after speaking with the owner, he got back on his bike to report the good news to his roommate, Andy Evenson. Approaching the intersection of 55th Street and Lancaster Avenue, Markgraf was wondering where in the new place he and Evenson would store the equipment for their engineering project: a chain-mail shirt like the ones medieval knights wore into battle. But Markgraf never finished that thought. At the busy intersection a white Dodge Quad Cab struck him and sped off. Markgraf, thrown several feet, lay unconscious on the side of the road.

Moments later emergency responders transported him three miles to the emergency room at the Hospital of the University of Pennsylvania (HUP); he was then moved to the hospital's Neurologic Intensive Care Unit. The impact of his head hitting the ground had caused bleeding in

the words, but they're just not registering." Within hours the hospital hallways were lined with Doug's friends and relatives. "It was like a nonstop vigil," Jen says. "We were never alone."

About five days after the accident Jen started to lose hope. "A few doctors [were] saying there's no brain activity, and I thought, Oh, my God, my son isn't going to make it."

Nine days later, Doug Markgraf woke up.

ON SEPT. 5, 2012, Roger Goodell said that the NFL was donating \$30 million to the National Institutes of Health to support research on injuries, with a focus on brain trauma. Fifteen months later the NFL announced the recipients of the NFL grants: two groups that had each pooled resources from

McKee's group was a primary grant recipient. But the other team favored by the NIH, led by Wayne Gordon, a rehabilitation medicine professor at Mount Sinai Hospital in New York City, was unexpected. Many neurologists had never heard of Gordon or his work. And the NIH was handing him \$6 million of NFL money to fund research that seemed largely unrelated to football or to concussions.

Gordon had teamed up with scientists at Mass General, Oregon Health Sciences University and the University of Washington to create a proposal to evaluate brain tissue from hundreds of patients living with moderate to severe traumatic brain injury (TBI), of which concussion is a mild form. Unlike CTE, whose symptoms develop over years, TBI occurs immediately after a distinct dramatic event such as an automobile accident, an explosion or, in football, a high-speed collision. Partly because of car crashes, TBI is the leading cause of death in North America for people ages one to 45. But it's shockingly misunderstood.

"Our means of classification of traumatic brain injury is terrible," says Gordon, 69. "We currently divide folks into three groups: mild, moderate and severe traumatic brain injury. But a mild injury can act like a severe injury and vice versa, and we don't know why." TBI appears to reduce life expectancy by seven years for those who survive the injury, but that too, says Gordon, is "something we don't yet understand."

Gordon and his team are studying the general population to discover ways to better classify patients who have suffered a TBI. But to accomplish that—to understand how the brain changes after a dramatic injury—Gordon needs access to damaged brains that have recovered.

After Markgraf was broadsided by the truck, the force of his head's collision with the ground caused widespread tearing of the neurons and blood vessels in his brain, resulting in a form of TBI called diffuse axonal injury. For him to regain consciousness after two weeks was very unlikely. The first person to notice a hopeful sign was Brian Edlow, a 26-year-old medical student

Markgraf suffered a host of complicated medical problems, including depression and post-traumatic amnesia. "Brain injury is really frightening," he says. "You wake up and gain awareness, only to realize you can't trust yourself the way you used to. Nothing works the same way." But with aggressive physical therapy and rehabilitation, things slowly began to make sense to him. "It wasn't until doctors prescribed serious antidepressants that I realized that this horrible thing really happened," he says.

Markgraf also had a vestibular disturbance, which disrupted his sense of balance. If he reached for something, he missed his target. If he stood up, he fell over. A frontal-lobe injury caused other impairments: "I had the physical ability to move my legs, but I couldn't control them," he says. "I could move my arms, but they wouldn't go where I wanted. I couldn't make a complete sentence, but in my brain I thought I was fine."

After several weeks at HUP, Markgraf was transferred to MossRehab in Elkins Park, Pa., one of the premier facilities for patients recovering from TBI. As he recuperated, he became fixated on one thing: getting back on his bike. "Cycling was my avenue to do everything," he says. "It's the reason I studied engineering—I wanted to put better materials in a bike—and it became the driving force behind my rehab."

When Markgraf arrived at MossRehab, he was in a wheelchair and told he'd be lucky to walk again. "I've never done well with someone telling me I can't do something," he says. During weeks of inpatient rehab and about a year as an outpatient, he regained enough strength and coordination to ride a bike again. On June 27, 2011, about a month after the fifth anniversary of his accident, he began a cross-country ride.

Markgraf cycled 3,200 miles from San Francisco to Toms River, N.J., making stops to speak to patients recovering from TBI. It took him two months. "I did it to show everyone what was possible," he says. He also started Project Mend the Mind to increase awareness of TBI and inspire victims to have achieved such functional independence after so severe an injury.

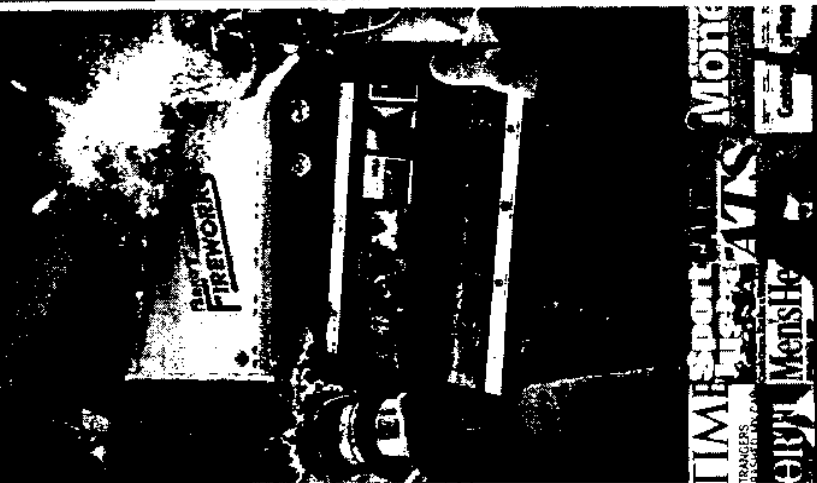
ONE YEAR after Markgraf's accident, Brian Edlow graduated at the top of his class at the University of Pennsylvania Medical School. He did his residency in neurology and a fellowship in neurocritical care at Mass General and Boston's Brigham and Women's Hospital. He is now a victim advocate in

## HANDS ON

Edlow (below), the neurologist who noted the first sign of Markgraf's recovery, is now a leading researcher into traumatic brain injury.



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patients were healthy volunteers, who would serve as a control group. When he needed to look at a previously damaged brain, one that had recovered from a devastating injury, he knew whom to call.

Six years and seven months after his bike accident, Markgraf underwent a scan at Harvard. By mapping the connectivity of Markgraf's brain, Edlow and his team saw disruptions within neural networks that likely caused his coma, as well as the intact connections that might have enabled him to recover. These networks were previously undetectable by MRI scanners. Markgraf was, essentially, Patient Zero, and his brain provided crucial information for Gordon's grant proposal to the NFL.

"There are few tools that help physicians predict which patients in traumatic coma will make a recovery like Markgraf's," says Edlow, "and which will be like his neighbor in the neurocritical care unit. That patient had the same type of brain injury but died one month later, never having regained consciousness. And we don't really know why."

Gordon, Edlow and their collaborators are using the NFL's grant to analyze hundreds of living patients who have a history of mild, moderate or severe TBI. Participants undergo a neurobehavioral assessment as well as a genomic analysis. When they die, their brains will be shipped to Edlow and his colleagues at the Martinos Center for the same type of high-resolution MRI performed on Markgraf. Each brain will then undergo a detailed microscopic evaluation by pathologists.

The combination of state-of-the-art imaging and microscopic analysis is expected to yield insights into how TBI causes long-term problems with memory, attention, emotional regulation and other functions. Researchers hope the study will lead to the identification of a biomarker (or markers) that will allow for the diagnosis of traumatic brain disease or CTE while people are still alive, providing a foundation for better treatment.

**WHAT TIES** the two largest grant proposals together is a quest to understand how the brain responds to injury, whether from a series of concussive or subconcussive blows or from a single massive event. What has become clear from the initial work is that there is a wide variability in response to head trauma, from concussion to coma. "A concussion is a response of the brain to head trauma," says Daniel Perl, head of the Center for Neuroscience and Regenerative Medicine's Brain Repository at Uniformed Services University of the Health Sciences in Bethesda, Md., and one of Gordon's collaborators. "It doesn't define the head trauma; it's a response."

This is a subtle and crucial point, and it has significant implications for the NFL's concussion protocol. If a concussion doesn't properly quantify the severity of a blow to the brain, then the NFL, using its current protocol, might be allowing players to remain on the field who shouldn't—players who have a higher threshold before they exhibit concussion symptoms. Absence of concussion does not equal absence of injury. There were 123 documented concussions and head injuries in the NFL in 2014, but that number might represent only a fraction of significant head injuries.

**From:** Burklow, John (NIH/OD) [E]  
**Sent:** 16 Dec 2015 14:29:07 -0500  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** PRIORITY ACTION: Emergency phone call this afternoon  
**Attachments:** image001.png

If you'd like to discuss, pls give me a call. Thx!

Sent from my iPhone

Begin forwarded message:

**From:** "Wood, Gretchen (NIH/OD) [E]" <[woodgs@od.nih.gov](mailto:woodgs@od.nih.gov)>  
**Date:** December 16, 2015 at 2:22:58 PM EST  
**To:** "Freire, Maria (FNIH) [T]" <[mfreire@fnihi.org](mailto:mfreire@fnihi.org)>, "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetz@ninds.nih.gov](mailto:koroshetz@ninds.nih.gov)>, "Burklow, John (NIH/OD) [E]" <[Burklow.J@OD.NIH.GOV](mailto:Burklow.J@OD.NIH.GOV)>  
**Cc:** "Walker, Paula (NIH/NINDS) [E]" <[walkerp@ninds.nih.gov](mailto:walkerp@ninds.nih.gov)>, "Gray, Felicia (FNIH) [T]" <[fgray@fnihi.org](mailto:fgray@fnihi.org)>, "Schulke, Hilda (NIH/OD) [E]" <[schulsh@od.nih.gov](mailto:schulsh@od.nih.gov)>, "Daugenik, Theodore (NIH/OD) [E]" <[theodore.daugenik@nih.gov](mailto:theodore.daugenik@nih.gov)>, "Burrus-Shaw, Cyndi (NIH/OD) [E]" <[Cyndi.Burrus-Shaw@nih.gov](mailto:Cyndi.Burrus-Shaw@nih.gov)>, "Simon, Dina (NIH/OD) [C]" <[dina.simon@nih.gov](mailto:dina.simon@nih.gov)>, "Harris, Melissa (NIH/OD) [E]" <[mjharris@od.nih.gov](mailto:mjharris@od.nih.gov)>  
**Subject:** Emergency phone call this afternoon

Good afternoon,

Drs. Collins, Tabak, and Hudson would like for you to join them on an emergency phone call this afternoon re. NFL. Can you please advise your availability for a 15 minute phone call between 3:00 PM and 4:30 PM today? Many thanks.

Best wishes,

Gretchen

Gretchen S. Wood  
Staff Assistant  
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**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 14 Dec 2015 22:42:49 +0000  
**To:** Wolf-Rodda, Julie (FNIH) [T]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** James, Stephanie (FNIH) [T]; Wiener, Susan (FNIH) [T]; Sanghrajka, Anisa (FNIH) [T]; Coyne, Eva (FNIH) [T]  
**Subject:** RE: \$2,500,000 wire transferred to NINDS for SHRP Research Plan #2

Thank you Julie.  
Walter

**From:** Wolf-Rodda, Julie (FNIH) [T]  
**Sent:** Monday, December 14, 2015 2:41 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** James, Stephanie (FNIH) [T]; Wiener, Susan (FNIH) [T]; Sanghrajka, Anisa (FNIH) [T]; Coyne, Eva (FNIH) [T]  
**Subject:** \$2,500,000 wire transferred to NINDS for SHRP Research Plan #2

Dear Walter and Pat,

Today, the FNIH wire transferred \$2,500,000 to NINDS CAN #8017234. These funds represent payment 3 of 4 from the NFL's contribution to the FNIH for the CTE neuropathology study, as outlined in SHRP Research Plan #2. Please let me know if you have questions.

Best,  
Julie

Julie Wolf-Rodda  
Director of Development  
Foundation for the National Institutes of Health  
9650 Rockville Pike | Bethesda, MD 20814 | [fnih.org](http://fnih.org)  
Direct (301) 402-6027 | [jwolf-rodga@fnih.org](mailto:jwolf-rodga@fnih.org)

REDISCOVER THE FNIH AT [fnih.org](http://fnih.org)



**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 14 Dec 2015 19:52:15 +0000  
**To:** Warren, Margo (NIH/NINDS) [E]  
**Bcc:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** FW: PRIORITY ACTION: Concussions

Margo: See the correspondence below. I told Meghan I thought it best if OCPL responds, particularly if Walter doesn't know the reporter. She agreed, so it's all yours.  
...and so it begins...  
Marian

**From:** Mott, Meghan (NIH/NINDS) [E]  
**Sent:** Monday, December 14, 2015 1:50 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** PRIORITY ACTION: Concussions

Hi Marian,

Walter wanted to send the following response but just wanted to clear it with you first. Look ok to send?


Thanks,  
Meghan

---

(b) (5)



Thank you,  
Meghan

Meghan C. Mott, Ph.D.  
Chief of Staff  
Office of the Director  
National Institute of Neurological Disorders and Stroke  
Office: (301) 594-7470  
Cell: (301) 221-



National Institutes of Health  
*Turning Discovery Into Health*



**From:** Golen, Jimmy [mailto:jgolen@ap.org]  
**Sent:** Monday, December 14, 2015 1:08 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Concussions

Walter,

I'm writing a story about CTE research before 2002, and how it didn't really begin with the Mike Webster autopsy.

I was wondering if you would have a chance to talk to me about it.

Jimmy Golen  
Associated Press, Boston

The information contained in this communication is intended for the use of the designated recipients named above. If the reader of this communication is not the intended recipient, you are hereby notified that you have received this communication in error, and that any review, dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify The Associated Press immediately by telephone at +1-212-621-1898 and delete this email. Thank you.

[IP US DISC]

msk dccc60c6d2c3a6438f0cf467d9a4938

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 14 Dec 2015 19:28:23 +0000  
**To:** Mott, Meghan (NIH/NINDS) [E]  
**Subject:** RE: PRIORITY ACTION: Concussions

Consider it done.  
Marian

**From:** Mott, Meghan (NIH/NINDS) [E]  
**Sent:** Monday, December 14, 2015 2:24 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** PRIORITY ACTION: Concussions

No, he does not. Please feel free to respond on his behalf!

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** Monday, December 14, 2015 2:22 PM  
**To:** Mott, Meghan (NIH/NINDS) [E]  
**Subject:** RE: Concussions

It would probably be best if OCPL responds unless, of course, he knows the reporter personally.  
Marian

**From:** Mott, Meghan (NIH/NINDS) [E]  
**Sent:** Monday, December 14, 2015 1:50 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** Concussions

Hi Marian,

Walter wanted to send the following response but just wanted to clear it with you first. Look ok to send?

Thanks,  
Meghan

---

Dear Jimmy,

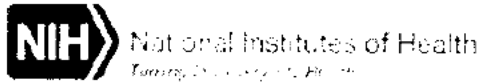
(b) (5)



Thank you,  
Meghan

Meghan C. Mott, Ph.D.

Chief of Staff  
Office of the Director  
National Institute of Neurological Disorders and Stroke  
Office: (301) 594-4470  
Cell: (301) 221-(b) (6)



**From:** Golen, Jimmy [mailto:ggolen@ap.org]  
**Sent:** Monday, December 14, 2015 1:08 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Concussions

Walter,

I'm writing a story about CTE research before 2002, and how it didn't really begin with the Mike Webster autopsy.

I was wondering if you would have a chance to talk to me about it.

Jimmy Golen  
Associated Press, Boston

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[IP\_US\_DISC]

msk dccc60c6d2c3a6438f0cf467d9a4938

**From:** Stern, Robert A  
**Sent:** 11 Dec 2015 20:37:51 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Fwd: Checking in re: U01 Press Release

Walter,

I hope all is well. Sorry to bug you on a Friday afternoon. Please see below emails. Is there anything I should know that may be related to the lack of info I am receiving from Marian, et al?? Knowing how sensitive this topic is with the media, I just want to make sure I am "in the loop." Thanks.

Bob

Begin forwarded message:

**From:** "Stern, Robert A" <[robstern@bu.edu](mailto:robstern@bu.edu)>  
**Date:** December 11, 2015 at 1:58:41 PM EST  
**To:** "Emr, Marian (NIH/NINDS) [E]" <[emrmar@ninds.nih.gov](mailto:emrmar@ninds.nih.gov)>  
**Cc:** "Wilczewski, Gina Maria" <[ginad@bu.edu](mailto:ginad@bu.edu)>, "McMakin, Barbara (NIH/NINDS) [E]" <[mcmakinb@ninds.nih.gov](mailto:mcmakinb@ninds.nih.gov)>  
**Subject:** RE: Checking in re: U01 Press Release

Hi Marian,

Thanks for the response. I would really prefer that BU (or any other institution) not release individual releases if NINDS will, indeed be having its own release. Is there a reason for the hold up? And, can you possibly provide a timeline so we can make a decision about the timing of any individual releases. I look forward to hearing back from you. Thanks.

Bob

**From:** Emr, Marian (NIH/NINDS) [E] [[maritorenyn@ninds.nih.gov](mailto:maritorenyn@ninds.nih.gov)]  
**Sent:** Friday, December 11, 2015 12:45 PM  
**To:** Stern, Robert A <[robstern@bu.edu](mailto:robstern@bu.edu)>  
**Cc:** Wilczewski, Gina Maria <[ginad@bu.edu](mailto:ginad@bu.edu)>; McMakin, Barbara (NIH/NINDS) [E] <[mcmakinb@ninds.nih.gov](mailto:mcmakinb@ninds.nih.gov)>  
**Subject:** RE: Checking in re: U01 Press Release

Hi, Bob. Marian Emr, here. I understand your desire to make a statement as soon as possible so it's probably best if you go ahead with your own release and not wait for us. Please ask your folks to observe the NIH requirement that you wait 72 hours after receiving the NGA. Also, I'd appreciate it if Gina could send me a copy of her draft once you clear it. Congratulations on your new grant. We look forward to working with you and your team going forward to announce your research results.  
Marian

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
Building 31, Room 8A07  
Bethesda, MD 20892-2540  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** Stern, Robert A [mailto:[robertstern@bu.edu](mailto:robertstern@bu.edu)]  
**Sent:** Friday, December 11, 2015 11:32 AM  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Cc:** Emr, Marian (NIH/NINDS) [E]; Wilczewski, Gina Maria  
**Subject:** ACTION: Checking in re: U01 Press Release

Thanks, Barbara. Would it be possible for you to provide me with the reasoning behind waiting so long after the NoGA to even have an update on the plans. My colleagues and I will be letting all of the co-investigators, consultants, and advisory board members know about the receipt of the NoGA immediately since everyone has been waiting for this for approximately six months and are eager to get to work. It seems to me that it would be helpful to have the PR come out pretty soon since word will quickly spread once the team is informed of the NoGA. Obviously, I am not a communications/media expert, but I do know that this area of research is the focus of tremendous media attention and I always feel more comfortable when the dissemination of the information is controlled by the communications experts and not the individual investigators. I apologize if I am being a pest. I just would really like to have a sense of the plans. I hope you understand. Thanks very much.

Bob

**From:** McMakin, Barbara (NIH/NINDS) [E] [mailto:[barbarmcmakin@ninds.nih.gov](mailto:barbarmcmakin@ninds.nih.gov)]  
**Sent:** Friday, December 11, 2015 11:21 AM  
**To:** Stern, Robert A <[robertstern@bu.edu](mailto:robertstern@bu.edu)>  
**Cc:** Emr, Marian (NIH/NINDS) [E] <[emrm@ninds.nih.gov](mailto:emrm@ninds.nih.gov)>; Wilczewski, Gina Maria <[ginad@bu.edu](mailto:ginad@bu.edu)>  
**Subject:** RE: Checking in re: U01 Press Release

Hi Dr. Stern,

Thank you for your email. We should have an update regarding our plans sometime next week.

Best,  
Barbara

**From:** Stern, Robert A [mailto:[robertstern@bu.edu](mailto:robertstern@bu.edu)]  
**Sent:** Friday, December 11, 2015 11:04 AM  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Cc:** Emr, Marian (NIH/NINDS) [E]; Wilczewski, Gina Maria  
**Subject:** Checking in re: U01 Press Release

Hi Barbara,

I am checking in about the status of the CTE U01 Press Release. My understanding is that the Notice of Grant Award is expected to be released tomorrow (12/12/15). When do you anticipate to release the PR? I know you have been working with Gina (cc'd) from our place, as well as the communications folks at the other three institutions. Please let me know if you have any questions or if there is anything I can do to assist.

Regards,

Bob

Robert A. Stern, Ph.D.

Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology  
Clinical Core Director, BU Alzheimer's Disease and CTE Center  
Boston University School of Medicine

72 East Concord Street, B7800  
Boston, MA 02118

Dir. Tel: 617-638-5678 \* Nicole Gullotti (Admin. Asst.): 617-414-1195  
Fax: 617-638-5679

Email: [robstern@bu.edu](mailto:robstern@bu.edu)

Web: [www.sternneurolab.org](http://www.sternneurolab.org)

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 9 Dec 2015 15:58:36 +0000  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]; McMakin, Barbara (NIH/NINDS) [E]  
**Bcc:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** RE: U01 NS093334-01

As you probably know, we are in a holding pattern awaiting further instructions from Dr. Collins about any press activity. Before hearing from Dr. Collins, we notified the PR staff from BU and the co-PI institutions to hold their publicity so that NIH could take the lead. When the final decision is made by Dr. Collins, we will send an appropriate updated message to each.  
Marian

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Wednesday, December 09, 2015 10:49 AM  
**To:** Emr, Marian (NIH/NINDS) [E]; McMakin, Barbara (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: U01 NS093334-01

Hi Barbara,

Tia in GMB just informed us that Dr. Stern's U01 will be released on Dec. 12<sup>th</sup>. Will you be contacting the various organizations PR people?

Thanks  
Pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Decoster, Tijuanna (NIH/NINDS) [E]  
**Sent:** Wednesday, December 09, 2015 10:21 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** FW: U01 NS093334-01

The grant has been released with an issue date of 12/12/15. The issue date is when the grantee will be notified.

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 9 Dec 2015 15:57:46 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/NINDS) [E]; McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: U01 NS093334-01

Can we do this on a conference call number?

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Wednesday, December 09, 2015 10:57 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Emr, Marian (NIH/NINDS) [E]; McMakin, Barbara (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/NINDS) [E]  
**Subject:** RE: U01 NS093334-01

Thanks Pat. Will give a call. If free can call now.  
310 496 3167  
walter

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Wednesday, December 09, 2015 10:49 AM  
**To:** Emr, Marian (NIH/NINDS) [E]; McMakin, Barbara (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: U01 NS093334-01

Hi Barbara,

Tia in GMB just informed us that Dr. Stern's U01 will be released on Dec. 12<sup>th</sup>. Will you be contacting the various organizations PR people?

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Patrick SF Bellgowan PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Decoster, Tijuanna (NIH/NINDS) [E]  
**Sent:** Wednesday, December 09, 2015 10:21 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]



**Cc:** Mott, Meghan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** FW: U01 NS093334-01

The grant has been released with an issue date of 12/12/15. The issue date is when the grantee will be notified.

**From:** Conklin, Elizabeth (NIH/NINDS) [E]  
**Sent:** Wednesday, December 09, 2015 10:03 AM  
**To:** Decoster, Tijuanna (NIH/NINDS) [E]; Pree, Nia (NIH/NINDS) [E]  
**Subject:** RE: U01 NS093334-01

Hi Tia,

I just released this award.

Nia, thank you for your careful and thorough work on this one. What a bear!

Liz

**From:** Decoster, Tijuanna (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 11:04 AM  
**To:** Pree, Nia (NIH/NINDS) [E]  
**Cc:** Conklin, Elizabeth (NIH/NINDS) [E]  
**Subject:** U01 NS093334-01

Hi Nia,

Please proceed with getting this grant ready to award. Once you have completed the workup and signed off, please let me know. Liz, please let me know when you release this grant.

Thanks  
Tia

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 9 Dec 2015 15:49:29 +0000  
**To:** Emr, Marian (NIH/NINDS) [E]; McMakin, Barbara (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: U01 NS093334-01

Hi Barbara,

Tia in GMB just informed us that Dr. Stern's U01 will be released on Dec. 12<sup>th</sup>. Will you be contacting the various organizations PR people?

Thanks  
Pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Decoster, Tijuanna (NIH/NINDS) [E]  
**Sent:** Wednesday, December 09, 2015 10:21 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** FW: U01 NS093334-01

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**Sent:** Wednesday, December 09, 2015 10:03 AM  
**To:** Decoster, Tijuanna (NIH/NINDS) [E]; Pree, Nia (NIH/NINDS) [E]  
**Subject:** RE: U01 NS093334-01

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**From:** Decoster, Tijuanna (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 11:04 AM  
**To:** Pree, Nia (NIH/NINDS) [E]

**Cc:** Conklin, Elizabeth (NIH/NINDS) [E]  
**Subject:** U01 NS093334-01

Hi Nia,

Please proceed with getting this grant ready to award. Once you have completed the workup and signed off, please let me know. Liz, please let me know when you release this grant.

Thanks  
Tia

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 7 Dec 2015 18:46:29 -0500  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** Re: CTE grant

Yep. Sticky situation.  
w

**From:** Marian Emr <emrmm@ninds.nih.gov>  
**Date:** Monday, December 7, 2015 at 11:45 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzw@ninds.nih.gov>  
**Subject:** CTE grant

Hi, Walter. John B and I have had a conversation about this but let's keep in touch as things develop. Looks like FC wants to continue the discussion with his senior staff.  
Marian

Sent from my iPhone

On Dec 6, 2015, at 5:28 PM, Koroshetz, Walter (NIH/NINDS) [E] <koroshetzw@ninds.nih.gov> wrote:

OK. And did you hear that (b) (5)  
walter

Outside the Scope of the Request



**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 7 Dec 2015 16:48:38 +0000  
**To:** Burklow, John (NIH/OD) [E]  
**Subject:** Re: 60 Minutes and concussion research

Thanks for keeping me in the loop as this develops.  
Marian

Sent from my iPhone

On Dec 6, 2015, at 6:14 PM, Burklow, John (NIH/OD) [E] <BurklowJ@OD.NIH.GOV> wrote:

FYI

Sent from my iPhone

Begin forwarded message:

**From:** "Collins, Francis (NIH/OD) [E]" <collinsf@od.nih.gov>  
**Date:** December 6, 2015 at 3:56:34 PM EST  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzwa@ninds.nih.gov>  
**Cc:** "Freire, Maria (FNIH) [T]" <mfreire@fnih.org>, "Hudson, Kathy (NIH/OD) [E]" <Kathy.Hudson@nih.gov>, "Burklow, John (NIH/OD) [E]" <BurklowJ@OD.NIH.GOV>  
**Subject:** RE: 60 Minutes and concussion research

Hi again Walter,

I met with Maria and Kathy on Friday and we went over this complex situation again. I am considering modifying the guidance I gave you in my note of December 2 (copied below). But I need to discuss this again with the NIH Exec Comm, and we won't be able to meet until the week of December 14 (I'm in London until Wednesday night and then we have ACD). So let's hold tight for now.

Meanwhile, we all feel strongly that there is no need for a press release on December 11 about the Boston U award. John Burklow has already conveyed that to your communications staff.

Best, Francis

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Wednesday, December 02, 2015 6:37 AM

**To:** Collins, Francis (NIH/OD) [E]  
**Subject:** Re: 60 Minutes and concussion research

OK sounds good.  
Walter

Sent from my iPhone

On Dec 2, 2015, at 6:23 AM, Collins, Francis (NIH/OD) [E]  
<[collinsf@od.nih.gov](mailto:collinsf@od.nih.gov)> wrote:

Hi Walter,

I discussed the NFL situation with the Exec Comm yesterday – and there was unanimous sentiment for following the peer review process and having the NFL funds go to Boston U. That's what NFL signed up for – no restrictions.

John Burklow pointed out that Roger Goodell is on record speaking about NFL's desire to get the facts, including supporting Boston U. See quote at around 8 – 9 minutes into the 60 minutes piece.

My meeting with Maria on Friday may have to be moved because of a Secretarial meeting.

FC

**From:** Burklow, John (NIH/OD) [E]  
**Sent:** Tuesday, December 01, 2015 1:07 PM  
**To:** Collins, Francis (NIH/OD) [E]; NIH Director's Executive Committee  
**Subject:** 60 Minutes and concussion research

Here is the link to the 60 Minutes segment on the NFL and concussion research: <http://www.cbsnews.com/news/football-and-the-brain-nfl-60-minutes/>.

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 6 Dec 2015 17:50:46 -0500  
**To:** Chan, Leighton (NIH/CC/RMD) [E]  
**Subject:** Re: Future leadership of BRAIN initiative  
**Attachments:** FNIH Document Chan 12-2-15 chan wjk.docx

Dear Leighton

I had some comments to the protocol. Happy to discuss.

walter

NONRESPONSIVE







**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 3 Dec 2015 14:38:40 -0500  
**To:** Chan, Leighton (NIH/CC/RMD) [E]  
**Subject:** Re: SHRP research proposal

See what Maria gets back tomorrow. Francis sent me one sentence email yesterday suggesting

(b) (5)

We'll see what happens with Maria.

Walter

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 3 Dec 2015 13:46:48 +0000  
**To:** Mott, Meghan (NIH/NINDS) [E]  
**Subject:** RE: PRIORITY ACTION: Preparation for U01 award press release

OK. I'll be here!

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** Mott, Meghan (NIH/NINDS) [E]  
**Sent:** Thursday, December 03, 2015 8:31 AM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** PRIORITY ACTION: Preparation for U01 award press release

Will do. At IPRCC meeting today, will call during a break (~10:30am)

Sent from my iPhone

On Dec 3, 2015, at 7:38 AM, Emr, Marian (NIH/NINDS) [E] <[emrjm@ninds.nih.gov](mailto:emrjm@ninds.nih.gov)> wrote:

Meghan: I'm not sure that I understand what you are recommending. Please call me when you have a minute to discuss.  
Marian

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** Mott, Meghan (NIH/NINDS) [E]  
**Sent:** Wednesday, December 02, 2015 5:55 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** PRIORITY ACTION: Preparation for U01 award press release

Hi Marian,

Ok to work on the release, but can we hold off on publishing it for now? We are waiting on a few final loose ends to be tied up. Walter will let us know when it is ready to go out. Probably not until next week at the earliest.

Thanks,  
Meghan

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 2 Dec 2015 22:25:59 +0000  
**To:** Freire, Maria (FNIH) [T]  
**Subject:** RE: heads up

Or can call me in office- 310 496 3167 or cell 617 258 (b) (6)  
Thanks  
Walter

**From:** Freire, Maria (FNIH) [T]  
**Sent:** Wednesday, December 02, 2015 5:03 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: heads up

Oh boy.

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Wednesday, December 02, 2015 5:02 PM  
**To:** Freire, Maria (FNIH) [T] <[mfreire@fnih.org](mailto:mfreire@fnih.org)>  
**Subject:** RE: heads up

OK. I have a call starting at 5, can I call you directly after. FC sent email below. So doesn't sound like the plan C will work.

Walter

Hi Walter,

I discussed the NFL situation with the Exec Comm yesterday – and there was unanimous sentiment for following the peer review process and having the NFL funds go to Boston U. That's what NFL signed up for – no restrictions.

John Burklow pointed out that Roger Goodell is on record speaking about NFL's desire to get the facts, including supporting Boston U. See quote at around 8 – 9 minutes into the 60 minutes piece.

My meeting with Maria on Friday may have to be moved because of a Secretarial meeting.

FC

**From:** Freire, Maria (FNIH) [T]  
**Sent:** Wednesday, December 02, 2015 4:58 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: heads up  
**Importance:** High

Walter, I spoke to Jeff. I left you a VM. I told him I was seeing FC on Friday and that noon on the 4<sup>th</sup> was the final deadline for BU. M.

**From:** Chan, Leighton (NIH/CC/RMD) [E]  
**Sent:** 2 Dec 2015 22:16:52 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** FNIH  
**Attachments:** FNIH Document Chan 12-2-15 chan.docx

Hi Walter-

Here is the document that I would like to sent to Maria Freire. I am hoping she will share it with Francis Collins during their Friday Meeting. Please let me know if you want me to remove the footnote on page 7. I have to send it to her by 2pm tomorrow.

LC

---

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: 301-496-4733  
Fax: 301-402-0663  
Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>



**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 2 Dec 2015 19:46:43 +0000  
**To:** Decoster, Tijuanna (NIH/NINDS) [E]; Pree, Nia (NIH/NINDS) [E]  
**Subject:** RE: Preparation for U01 award press release

Thanks!

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Decoster, Tijuanna (NIH/NINDS) [E]  
**Sent:** Wednesday, December 02, 2015 2:46 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Pree, Nia (NIH/NINDS) [E]  
**Subject:** RE: Preparation for U01 award press release

Thanks Patrick - will do

We just received approval yesterday to award the grant. I will keep you informed

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Wednesday, December 02, 2015 2:05 PM  
**To:** Pree, Nia (NIH/NINDS) [E]  
**Cc:** Decoster, Tijuanna (NIH/NINDS) [E]  
**Subject:** FW: Preparation for U01 award press release

Hi Nia and Tia,

I just wanted to let you know that Walter has approved a press release to be issued regarding U01NS09334 (Stern et al) so if you can give Marian Emr and myself an estimate or a warning regarding the date of NOA for this proposal it will help them prepare.

Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 2:07 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]

**Cc:** Emr, Marian (NIH/NINDS) [E]

**Subject:** Re: Preparation for U01 award press release

Yes, I agree that press release would be important. Either NINDS or joint.  
Walter

**From:** Stern, Robert A [mailto:robstern@bu.edu]

**Sent:** Tuesday, December 01, 2015 12:01 PM

**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]

**Subject:** Preparation for U01 award press release

Hi everyone,

I hope your Thanksgivings were wonderful. Now that it is December 1, my co-PI's and I are eagerly anticipating the NoGA for the CTE U01. All four institutions (Cleveland Clinic, Banner, Brigham & Women's, and BU) are, therefore, hoping to work with NINDS if a press release will be developed and released. Or, if NINDS will not be doing a press release on the award, the four individual sites would like to do their own. Do you know if this is the type of grant for which NINDS/NIH would be issuing a press release? If so, is it appropriate timing for the Communications offices at the four institutions to be communicating with the NIH folks in anticipation of the award? Let me know when you can. Thanks much.

Regards,

Bob

Robert A. Stern, Ph.D.

Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology  
Clinical Core Director, BU Alzheimer's Disease and CTE Center  
Boston University School of Medicine

72 East Concord Street, B7800  
Boston, MA 02118

Dir. Tel: 617-638-5678 \* Nicole Gullotti (Admin. Asst.): 617-414-1195  
Fax: 617-638-5679

Email: [robstern@bu.edu](mailto:robstern@bu.edu)



**From:** Mott, Meghan (NIH/NINDS) [E]  
**Sent:** 2 Dec 2015 17:54:33 -0500  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: Preparation for U01 award press release

Hi Marian,

Ok to work on the release, but can we hold off on publishing it for now? We are waiting on a few final loose ends to be tied up. Walter will let us know when it is ready to go out. Probably not until next week at the earliest.

Thanks,  
Meghan

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 2:15 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: Preparation for U01 award press release

OCPL would be happy to work with the grantee Institutions to coordinate an NIH release timed with theirs.  
Marian

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 2:07 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** ACTION: Preparation for U01 award press release

Yes, I agree that press release would be important. Either NINDS or joint.  
Walter

**From:** Patrick Bellgowan <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Date:** Tuesday, December 1, 2015 at 1:51 PM  
**To:** Bob Stern <[bobstern@bu.edu](mailto:bobstern@bu.edu)>, "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>, Debra Babcock <[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)>  
**Cc:** Marian Emr <[emrm@ninds.nih.gov](mailto:emrm@ninds.nih.gov)>  
**Subject:** RE: Preparation for U01 award press release

Hi Bob,

It appears that there was a Press release when the 1<sup>st</sup> wave of grants were awarded. I think that with the whirlwind around CTE presently it would be great to let people know that NINDS is funding a project aimed at developing a ante mortem diagnosis but this decision is above my pay-grade.

Thanks  
pat

Patrick SF Bellgowan PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tb.htm>

**From:** Stern, Robert A [<mailto:robstern@bu.edu>]  
**Sent:** Tuesday, December 01, 2015 12:01 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]  
**Subject:** Preparation for U01 award press release

Hi everyone,  
I hope your Thanksgivings were wonderful. Now that it is December 1, my co-PI's and I are eagerly anticipating the NoGA for the CTE U01. All four institutions (Cleveland Clinic, Banner, Brigham & Women's, and BU) are, therefore, hoping to work with NINDS if a press release will be developed and released. Or, if NINDS will not be doing a press release on the award, the four individual sites would like to do their own. Do you know if this is the type of grant for which NINDS/NIH would be issuing a press release? If so, is it appropriate timing for the Communications offices at the four institutions to be communicating with the NIH folks in anticipation of the award? Let me know when you can. Thanks much.

Regards,

Bob

Robert A. Stern, Ph.D.  
Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology  
Clinical Core Director, BU Alzheimer's Disease and CTE Center  
Boston University School of Medicine

72 East Concord Street, B7800  
Boston, MA 02118

Dir. Tel: 617-638-5678 \* Nicole Gullotti (Admin. Asst.): 617-414-1195  
Fax: 617-638-5679

Email: [robstern@bu.edu](mailto:robstern@bu.edu)

**From:** Belligowan, Patrick (NIH/NINDS) [E]  
**Sent:** 2 Dec 2015 14:59:33 +0000  
**To:** Babcock, Debra (NIH/NINDS) [E]; 'Mckee, Ann C'  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: "and the TBI/CTE group"

Agreed, thank you Ann.

Pat

Patrick SF Belligowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Babcock, Debra (NIH/NINDS) [E]  
**Sent:** Wednesday, December 02, 2015 8:19 AM  
**To:** 'Mckee, Ann C'  
**Cc:** Belligowan, Patrick (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: "and the TBI/CTE group"

I think this is great Ann. Thanks for doing that! Deb

Sent with Good ([www.good.com](http://www.good.com))

-----Original Message-----

**From:** Mckee, Ann C [[amckee@bu.edu](mailto:amckee@bu.edu)]  
**Sent:** Tuesday, December 01, 2015 05:01 PM Eastern Standard Time  
**To:** Babcock, Debra (NIH/NINDS) [E]  
**Cc:** Belligowan, Patrick (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Re: "and the TBI/CTE group"

Deb,

I already asked Wayne and he got back to me. This is the list:

Elissa Flannery  
Department of Rehabilitation Medicine, Icahn School of Medicine at Mount Sinai, New York,  
NY

Patrick T. Kiernan

Alzheimer's Disease Center, Boston University School of Medicine, 72 E. Concord St., B-7800, Boston, MA

Department of Neurology, Boston University School of Medicine, 72 E. Concord Street, Boston, MA

Jesse Mez

Alzheimer's Disease Center, Boston University School of Medicine, 72 E. Concord St., B-7800, Boston, MA

Department of Neurology, Boston University School of Medicine, 72 E. Concord Street, Boston, MA

Lauren Murphy

Alzheimer's Disease Center, Boston University School of Medicine, 72 E. Concord St., B-7800, Boston, MA

Department of Neurology, Boston University School of Medicine, 72 E. Concord Street, Boston, MA

Todd M. Solomon

Alzheimer's Disease Center, Boston University School of Medicine, 72 E. Concord St., B-7800, Boston, MA

Department of Neurology, Boston University School of Medicine, 72 E. Concord Street, Boston, MA

Patrick S. F. Bellgowan

National Institute of Neurological Disorders and Stroke, National Institute of Health, North Bethesda, MD

Debra Babcock

National Institute of Neurological Disorders and Stroke, National Institute of Health, North Bethesda, MD

Walter J. Koroshetz

National Institute of Neurological Disorders and Stroke, National Institute of Health, North Bethesda, MD

Please let me know if you would like to change anything. I plan to finalize the proofs tomorrow.

Ann

On Dec 1, 2015, at 3:26 PM, Babcock, Debra (NIH/NINDS) [E]  
<[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)> wrote:

Hi Ann,

We did work on a publication agreement early on that I think we all ended up signing off on. I don't think we followed it exactly for this manuscript, and I certainly wouldn't hold the publication up for that, but it might be worth an email to Wayne to see if anyone else from his group should be included in "the TBI/CTE group". As I recall, Wayne was the one who was most concerned about setting up a publication agreement. My personal feeling is that the author list below is fine (without "the TBI/CTE group"), but in the interest of collaboration, I think it would be worth running it by Wayne to make sure he's on board.

Thanks,

Deb

Sent with Good ([www.good.com](http://www.good.com))

-----Original Message-----

**From:** McKee, Ann C [[amckee@bu.edu](mailto:amckee@bu.edu)]

**Sent:** Tuesday, December 01, 2015 08:36 AM Eastern Standard Time

**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E];  
Koroshetz, Walter (NIH/NINDS) [E]

**Subject:** "and the TBI/CTE group"

All,

In response to a query concerning the manuscript on the consensus meeting recently accepted for publication in Acta Neuropathologica, we listed the authors as:

Ann C. McKee<sup>1,2,3,4,5</sup>, Nigel J. Cairns<sup>6</sup>, Dennis W. Dickson<sup>7</sup>, Rebecca

D. Folkerth<sup>8</sup>, C. Dirk Keene<sup>9</sup>, Irene Litvan<sup>10</sup>, Daniel P. Perl<sup>11</sup>, Thor D.

Stein<sup>2,3,4,5</sup>, Jean-Paul Vonsattel<sup>12</sup>, William Stewart<sup>13</sup>, Yorghos

Tripodis<sup>3,14</sup>, John F. Crary<sup>15</sup>, Kevin F. Bieniek<sup>7</sup>, Kristen Dams-

O'Connor<sup>16</sup>, Victor E. Alvarez<sup>1,2,3,4</sup>, Wayne A. Gordon<sup>16</sup>, and the

TBI/CTE group<sup>17</sup>

I now have the page proofs from the manuscript and Acta is asking for the details of this "group" - how do I respond? Who do I include in this group - do I specify? Do I delete it? Please advise.

Ann

**Porter, Kevin (NIH/OD) [E]**

---

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Wednesday, December 02, 2015 6:37 AM  
**To:** Collins, Francis (NIH/OD) [E]  
**Subject:** Re: 60 Minutes and concussion research

**Categories:** Important

OK sounds good.  
Walter

Sent from my iPhone

On Dec 2, 2015, at 6:23 AM, Collins, Francis (NIH/OD) [E] <[collinsf@od.nih.gov](mailto:collinsf@od.nih.gov)> wrote:

Hi Walter,

I discussed the NFL situation with the Exec Comm yesterday – and there was unanimous sentiment for following the peer review process and having the NFL funds go to Boston U. That's what NFL signed up for – no restrictions.

John Burklow pointed out that Roger Goodell is on record speaking about NFL's desire to get the facts, including supporting Boston U. See quote at around 8 – 9 minutes into the 60 minutes piece.

My meeting with Maria on Friday may have to be moved because of a Secretarial meeting.

FC

---

**From:** Burklow, John (NIH/OD) [E]  
**Sent:** Tuesday, December 01, 2015 1:07 PM  
**To:** Collins, Francis (NIH/OD) [E]; NIH Director's Executive Committee  
**Subject:** 60 Minutes and concussion research

Here is the link to the 60 Minutes segment on the NFL and concussion research: <http://www.cbsnews.com/news/football-and-the-brain-nfl-60-minutes/>.

**Porter, Kevin (NIH/OD) [E]**

---

**From:** Hudson, Kathy (NIH/OD) [E]  
**Sent:** Wednesday, December 02, 2015 6:28 AM  
**To:** Collins, Francis (NIH/OD) [E]  
**Subject:** RE: 60 Minutes and concussion research  
  
**Categories:** Important

(b) (5)

A large black rectangular redaction box covers the content of the email body.

---

**From:** Collins, Francis (NIH/OD) [E]  
**Sent:** Wednesday, December 02, 2015 6:24 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Tabak, Lawrence (NIH/OD) [E]; Hudson, Kathy (NIH/OD) [E]; Burklow, John (NIH/OD) [E]  
**Subject:** FW: 60 Minutes and concussion research

Hi Walter,

I discussed the NFL situation with the Exec Comm yesterday – and there was unanimous sentiment for following the peer review process and having the NFL funds go to Boston U. That's what NFL signed up for – no restrictions.

John Burklow pointed out that Roger Goodell is on record speaking about NFL's desire to get the facts, including supporting Boston U. See quote at around 8 – 9 minutes into the 60 minutes piece.

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FC

---

**From:** Burklow, John (NIH/OD) [E]  
**Sent:** Tuesday, December 01, 2015 1:07 PM  
**To:** Collins, Francis (NIH/OD) [E]; NIH Director's Executive Committee  
**Subject:** 60 Minutes and concussion research

Here is the link to the 60 Minutes segment on the NFL and concussion research: <http://www.cbsnews.com/news/football-and-the-brain-nfl-60-minutes/>.



**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 2:09 PM  
**To:** Freire, Maria (FNIH) [T] <[mfreire@fnih.org](mailto:mfreire@fnih.org)>  
**Subject:** Re: heads up

We are working up a press release for the longitudinal study of CTE. Grant going out any day now. So last chance.

Walter

**From:** "Freire, Maria (FNIH) [T]" <[mfreire@fnih.org](mailto:mfreire@fnih.org)>  
**Date:** Tuesday, December 1, 2015 at 12:04 PM  
**To:** Leighton Chan <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)>, "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Subject:** Re: heads up

Friday morning, so please send me something by 2pm on Thursday so I have time to digest and get back to you with questions. Thanks! M.

**From:** Chan, Leighton (NIH/CC/RMD) [E]  
**Sent:** Tuesday, December 1, 2015 11:56 AM  
**To:** Freire, Maria (FNIH) [T]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: heads up

Maria-

I had a nice meeting with the extramural investigators yesterday. We are working on some options for you to present to Dr. Collins. They will be providing me with some details by Wednesday. What time is your meeting with Dr Collins on Friday? I want to make sure you have what you need.

LC

---

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: 301-496-4733  
Fax: 301-402-0663  
Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>

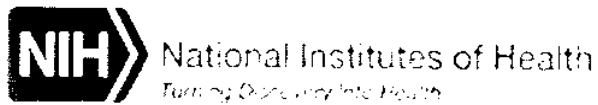
**From:** Freire, Maria (FNIH) [T]  
**Sent:** Monday, November 30, 2015 8:04 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Chan, Leighton (NIH/CC/RMD) [E]  
**Subject:** RE: heads up

OK, thanks for letting me know. It would be helpful if we spoke before my meeting on Friday. What would work for you? M.

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Monday, November 30, 2015 8:03 PM  
**To:** Freire, Maria (FNIH) [T] <[mfreire@fnih.org](mailto:mfreire@fnih.org)>  
**Cc:** Chan, Leighton (NIH/CC/RMD) [E] <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)>  
**Subject:** heads up

Dear Maria,  
Just a heads up that I gave Francis a quick update of what transpired at Council and since.  
Happy to chat. He's thinking.  
Walter

Walter Koroshetz, MD  
Director, National Institute of Neurological Disorders and Stroke



**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 1 Dec 2015 19:52:30 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: Preparation for U01 award press release

Done

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 2:17 PM  
**To:** Emr, Marian (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Re: Preparation for U01 award press release

Thanks Marian. Pat, want to hook Marian up with Bob.  
Walter

**From:** Marian Emr <[emr@ninds.nih.gov](mailto:emr@ninds.nih.gov)>  
**Date:** Tuesday, December 1, 2015 at 2:15 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetz@ninds.nih.gov](mailto:koroshetz@ninds.nih.gov)>, Patrick Bellgowan  
<[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Subject:** RE: Preparation for U01 award press release

OCPL would be happy to work with the grantee Institutions to coordinate an NIH release timed with theirs.

Marian

*Marian Emr  
Director, Office of Communications and Public Liaison-NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 2:07 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** ACTION: Preparation for U01 award press release

Yes, I agree that press release would be important. Either NINDS or joint.  
Walter

**From:** Patrick Bellgowan <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Date:** Tuesday, December 1, 2015 at 1:51 PM

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 1 Dec 2015 19:14:18 +0000  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: : Preparation for U01 award press release

that is my understanding.

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 2:13 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** RE: : Preparation for U01 award press release

Just to clarify, this research will not be funded by the Sport Health Research Program. The funds will come directly from NINDS?

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 2:12 PM  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: : Preparation for U01 award press release

Great. If the NGAs are going out soon, you'll need to contact all the PI institutions to ask them to work with us/wait for our release date. You remember the routine from last time....  
Marian

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 2:11 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** RE: : Preparation for U01 award press release

Sure. I'll start working on an announcement this week.

Best,  
Barbara

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 2:08 PM  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** FW: : Preparation for U01 award press release

Interested?

Marian

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 2:07 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** ACTION: Preparation for U01 award press release

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Walter

**From:** Patrick Bellgowan <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Date:** Tuesday, December 1, 2015 at 1:51 PM  
**To:** Bob Stern <[bobstern@bu.edu](mailto:bobstern@bu.edu)>, "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetz@ninds.nih.gov](mailto:koroshetz@ninds.nih.gov)>, Debra Babcock <[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)>  
**Cc:** Marian Emr <[emrm@ninds.nih.gov](mailto:emrm@ninds.nih.gov)>  
**Subject:** RE: Preparation for U01 award press release

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Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/ disorders/tbi/tbi.htm>

**From:** Stern, Robert A [[mailto:bobstern@bu.edu](mailto:mailto:bobstern@bu.edu)]  
**Sent:** Tuesday, December 01, 2015 12:01 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]  
**Subject:** Preparation for U01 award press release

Hi everyone,

I hope your Thanksgivings were wonderful. Now that it is December 1, my co-PI's and I are eagerly anticipating the NoGA for the CTE U01. All four institutions (Cleveland Clinic, Banner, Brigham &

Women's, and BU) are, therefore, hoping to work with NINDS if a press release will be developed and released. Or, if NINDS will not be doing a press release on the award, the four individual sites would like to do their own. Do you know if this is the type of grant for which NINDS/NIH would be issuing a press release? If so, is it appropriate timing for the Communications offices at the four institutions to be communicating with the NIH folks in anticipation of the award? Let me know when you can. Thanks much.

Regards,

Bob

Robert A. Stern, Ph.D.  
Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology  
Clinical Core Director, BU Alzheimer's Disease and CTE Center  
Boston University School of Medicine

72 East Concord Street, B7800  
Boston, MA 02118

Dir. Tel: 617-638-5678 \* Nicole Gullotti (Admin. Asst.): 617-414-1195  
Fax: 617-638-5679

Email: [bobstern@bu.edu](mailto:bobstern@bu.edu)

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 1 Dec 2015 16:15:03 +0000  
**To:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: "and the TBI/CTE group"  
**Attachments:** Publication Agreement draft v1.docx

See attached. I can't find any notes regarding the resolution of the TBI/CTE group. I'm not sure how challenging it would be to add all of the Key Personnel from the attached list to the TBI/CTE Group, if that takes approval then it might not be worth the added time.

Pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Babcock, Debra (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 10:15 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** FW: "and the TBI/CTE group"

Hi Pat,

My recollection is that we worked out a publication agreement early on. I'm at a meeting in FL now and can't access it...do you have a copy?

Deb

Sent with Good ([www.good.com](http://www.good.com))

-----Original Message-----

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Tuesday, December 01, 2015 09:34 AM Eastern Standard Time  
**To:** 'Mckee, Ann C'; Bellgowan, Patrick (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: "and the TBI/CTE group"

Could add the NINDS folks in the TBI/CTE grouping. Could add others who did work behind the scenes at BU or the other funded sites.  
If a pain could also delete.

walter

**From:** Mckee, Ann C [mailto:amckee@bu.edu]

**Sent:** Tuesday, December 01, 2015 8:36 AM

**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]

**Subject:** "and the TBI/CTE group"

All,

In response to a query concerning the manuscript on the consensus meeting recently accepted for publication in Acta Neuropathologica, we listed the authors as:

Ann C. McKee<sup>1,2,3,4,5</sup>, Nigel J. Cairns<sup>6</sup>, Dennis W. Dickson<sup>7</sup>, Rebecca D.

Folkerth<sup>8</sup>, C. Dirk Keene<sup>9</sup>, Irene Litvan<sup>10</sup>, Daniel P. Perl<sup>11</sup>, Thor D. Stein<sup>2,3,4,5</sup>,

Jean-Paul Vonsattel<sup>12</sup>, William Stewart<sup>13</sup>, Yorghos Tripodis<sup>3,14</sup>, John F. Crary<sup>15</sup>,

Kevin F. Bieniek<sup>7</sup>, Kristen Dams-O'Connor<sup>16</sup>, Victor E. Alvarez<sup>1,2,3,4</sup>, Wayne A.

Gordon<sup>16</sup>, and the TBI/CTE group<sup>17</sup>

I now have the page proofs from the manuscript and Acta is asking for the details of this "group" - how do I respond? Who do I include in this group - do I specify? Do I delete it? Please advise.

Ann





**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 1 Dec 2015 14:43:13 +0000  
**To:** 'Mckee, Ann C'  
**Subject:** Thanks for the help with Charlie Rose

Dear Ann,

Wanted to thank you again for sending me slides. Got a very short time to try to explain CTE on Charlie Rose. Unfortunately they edited out the credits so didn't get the mention you deserved. But the message is getting out. <http://www.charlierose.com/watch/60655099>

Walter

**From:** Mckee, Ann C [mailto:amckee@bu.edu]  
**Sent:** Monday, November 30, 2015 12:21 PM  
**To:** Folkerth, Rebecca Dunn,M.D.  
**Cc:** Cairns, Nigel; Dennis Dickson; Keene, Dirk (cdkeene@uw.edu); Irene Litvan; daniel Perl; Stein, Thor; Jean Paul Vonsattel; Tripodis, Yorghos; John Crary; Bieniek, Kevin F.; Dams-o'connor, Kristen; Alvarez, Victor E; Gordon, Wayne; Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]; Kiernan, Patrick; Murphy, Lauren Elizabeth  
**Subject:** Re: \*\*\* Acta Neuropathologica: Your Submission ANEU-D-15-00706R2

Thank you Rebecca!

We couldn't have done it as well without your very valuable insights.

Best,

Ann

On Nov 30, 2015, at 10:24 AM, Folkerth, Rebecca Dunn,M.D.  
<[RFOLKERTH@PARTNERS.ORG](mailto:RFOLKERTH@PARTNERS.ORG)> wrote:

Thanks again, Ann, for including a "novice" like me in this fascinating effort – I owe each of you a debt of gratitude for all I have learned from you! Rebecca

**From:** Mckee, Ann C [mailto:amckee@bu.edu]  
**Sent:** Sunday, November 29, 2015 1:39 PM  
**To:** Cairns, Nigel; Dennis Dickson; Folkerth, Rebecca Dunn,M.D.; Keene, Dirk (cdkeene@uw.edu); Irene Litvan; daniel Perl; Stein, Thor; Jean Paul Vonsattel; Tripodis, Yorghos; John Crary; Bieniek, Kevin F.; Dams-o'connor, Kristen; Alvarez, Victor E; Gordon, Wayne  
**Cc:** Babcock, Debra (NIH/NINDS) [E]; Patrick Bellgowan; Koroshetz, Walter (NIH/NINDS) [E]; Kiernan, Patrick; Murphy, Lauren Elizabeth  
**Subject:** Fwd: \*\*\* Acta Neuropathologica: Your Submission ANEU-D-15-00706R2

Authors,

The paper has been accepted.  
Thank you for all your contributions.

Ann

Begin forwarded message:

**From:** Acta Neuropathologica <[em-a.editorialmanager.com](mailto:em-a.editorialmanager.com)>  
**Subject:** \*\*\* Acta Neuropathologica: Your Submission ANEU-D-15-00706R2  
**Date:** November 29, 2015 at 1:27:51 PM EST  
**To:** "Ann C. McKee" <[amckee@bu.edu](mailto:amckee@bu.edu)>  
**Reply-To:** Acta Neuropathologica <[anp@uni-muenster.de](mailto:anp@uni-muenster.de)>

Dear Ann,

I am pleased to inform you that your manuscript, "The First NINDS/NIBIB Consensus Meeting to Define Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy", has been accepted for publication in Acta Neuropathologica and will go to print. You will receive further information (e.g. proofs) directly from the publisher.

Acta Neuropathologica has recently introduced an exciting new development: our publisher Springer has implemented a fast-track production procedure. This will markedly shorten the time from acceptance to Online First publication, our target being 10 days. Although compressed, the new publication procedure includes the usual steps of copyediting, typesetting, proofreading and incorporation of proof corrections. The 10-day schedule is however contingent upon authors returning their proof corrections within 48 hours or as close to this as possible.

Please help us by returning your proofs as quickly as possible. You should receive them within the next 5 days.

If you choose to participate in Open Choice your paper will be freely available with open access, ensuring the widest possible access to your research. Open Choice articles are also clearly indicated so users know about their enhanced access. You will receive further information on Springer's Open Choice at a later production stage.

Please remember to quote the manuscript number, ANEU-D-15-00706R2, whenever inquiring about your manuscript.

Thank you for submitting your excellent and important work to Acta Neuropathologica. We look forward to receiving further contributions from you in the future.

With kind regards,  
Werner

Werner Paulus  
Editor-in-Chief,  
Acta Neuropathologica

The information in this e-mail is intended only for the person to whom it is addressed. If you believe this e-mail was sent to you in error and the e-mail contains patient information, please contact the Partners Compliance Helpline at <http://www.partners.org/compliance>. If the e-mail was sent to you in error but does not contain patient information, please contact the sender and properly dispose of the e-mail.

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 30 Nov 2015 17:44:48 +0000  
**To:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: \*\*\* Acta Neuropathologica: Your Submission ANEU-D-15-00706R2

I don't know. They are secondary but so are a couple of others that probably didn't get recognized.

Should I set up a time to talk with Willie about Ann's comments?

pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Babcock, Debra (NIH/NINDS) [E]  
**Sent:** Monday, November 30, 2015 12:26 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: \*\*\* Acta Neuropathologica: Your Submission ANEU-D-15-00706R2

Do we know if she ever took NIBIB out of the credits?

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Monday, November 30, 2015 12:25 PM  
**To:** 'Mckee, Ann C'; Folkerth, Rebecca Dunn, M.D.  
**Cc:** Cairns, Nigel; Dennis Dickson; Keene, Dirk ([cdkeene@uw.edu](mailto:cdkeene@uw.edu)); Irene Litvan; daniel Perl; Stein, Thor; Jean Paul Vonsattel; Tripodis, Yorghos; John Crary; Bieniek, Kevin F.; Dams-o'connor, Kristen; Alvarez, Victor E; Gordon, Wayne; Babcock, Debra (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]; Kiernan, Patrick; Murphy, Lauren Elizabeth  
**Subject:** RE: \*\*\* Acta Neuropathologica: Your Submission ANEU-D-15-00706R2

Congratulations to you all. Great work!

Best wishes  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

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**Sent:** Monday, November 30, 2015 12:21 PM

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**Cc:** Cairns, Nigel; Dennis Dickson; Keene, Dirk ([cdkeene@uw.edu](mailto:cdkeene@uw.edu)); Irene Litvan; daniel Perl; Stein, Thor; Jean Paul Vonsattel; Tripodis, Yorghos; John Crary; Bieniek, Kevin F.; Dams-o'connor, Kristen; Alvarez, Victor E; Gordon, Wayne; Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]; Kiernan, Patrick; Murphy, Lauren Elizabeth

**Subject:** Re: \*\*\* Acta Neuropathologica: Your Submission ANEU-D-15-00706R2

Thank you Rebecca!

We couldn't have done it as well without your very valuable insights.

Best,

Ann

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<[RFOLKERTH@PARTNERS.ORG](mailto:RFOLKERTH@PARTNERS.ORG)> wrote:

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**Sent:** Sunday, November 29, 2015 1:39 PM

**To:** Cairns, Nigel; Dennis Dickson; Folkerth, Rebecca Dunn,M.D.; Keene, Dirk ([cdkeene@uw.edu](mailto:cdkeene@uw.edu)); irene Litvan; daniel Perl; Stein, Thor; Jean Paul Vonsattel; Tripodis, Yorghos; John Crary; Bieniek, Kevin F.; Dams-o'connor, Kristen; Alvarez, Victor E; Gordon, Wayne

**Cc:** Babcock, Debra (NIH/NINDS) [E]; Patrick Bellgowan; Koroshetz, Walter (NIH/NINDS) [E]; Kiernan, Patrick; Murphy, Lauren Elizabeth

**Subject:** Fwd: \*\*\* Acta Neuropathologica: Your Submission ANEU-D-15-00706R2

Authors,

The paper has been accepted.  
Thank you for all your contributions.

Ann

Begin forwarded message:

**From:** Acta Neuropathologica <[em@editorialmanager.com](mailto:em@editorialmanager.com)>

**Subject:** \*\*\* Acta Neuropathologica: Your Submission ANEU-D-15-00706R2

**Date:** November 29, 2015 at 1:27:51 PM EST

**To:** "Ann C. McKee" <[amckee@bu.edu](mailto:amckee@bu.edu)>

**Reply-To:** Acta Neuropathologica <[anp@uni-muenster.de](mailto:anp@uni-muenster.de)>

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Please remember to quote the manuscript number, ANEU-D-15-00706R2, whenever inquiring about your manuscript.

Thank you for submitting your excellent and important work to Acta Neuropathologica. We look forward to receiving further contributions from you in the future.

With kind regards,  
Werner

Werner Paulus  
Editor-in-Chief,  
Acta Neuropathologica

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**From:** James, Stephanie (FNIH) [T]  
**Sent:** 30 Nov 2015 14:34:23 -0500  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Wolf-Rodda, Julie (FNIH) [T]; Mott, Meghan (NIH/NINDS) [E]  
**Cc:** Wiener, Susan (FNIH) [T]  
**Subject:** RE: SHRP report

Thanks!

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Monday, November 30, 2015 2:32 PM  
**To:** James, Stephanie (FNIH) [T] <sjames@fnih.org>; Wolf-Rodda, Julie (FNIH) [T] <jwolf-rodde@fnih.org>; Mott, Meghan (NIH/NINDS) [E] <meghan.mott@nih.gov>  
**Cc:** Wiener, Susan (FNIH) [T] <swiener@fnih.org>  
**Subject:** RE: SHRP report

Hi Stephanie,

I think Mary Ellen Michel is the PO on both of those grants.  
Michel, Mary Ellen (NIH/NICHD) [E] [michelme1@mail.nih.gov](mailto:michelme1@mail.nih.gov)

Best wishes,  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.html>

**From:** James, Stephanie (FNIH) [T]  
**Sent:** Monday, November 30, 2015 12:55 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Wolf-Rodda, Julie (FNIH) [T]; Mott, Meghan (NIH/NINDS) [E]  
**Cc:** Wiener, Susan (FNIH) [T]  
**Subject:** RE: SHRP report

Patrick, can you remind me who to check with at NICHD to see if the two pilot studies that were scheduled to end on 11/30 have received an NCE?

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Tuesday, November 24, 2015 2:10 PM  
**To:** Wolf-Rodda, Julie (FNIH) [T] <[jwolf-rodde@fnih.org](mailto:jwolf-rodde@fnih.org)>; Mott, Meghan (NIH/NINDS) [E] <[meghan.mott@nih.gov](mailto:meghan.mott@nih.gov)>  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E] <[koroshetz@ninds.nih.gov](mailto:koroshetz@ninds.nih.gov)>; Francis, Tiffany (FNIH) [T] <[tfrancis@fnih.org](mailto:tfrancis@fnih.org)>; Wiener, Susan (FNIH) [T] <[swiener@fnih.org](mailto:swiener@fnih.org)>; Freire, Maria (FNIH) [T] <[mfreire@fnih.org](mailto:mfreire@fnih.org)>; James, Stephanie (FNIH) [T] <[sjames@fnih.org](mailto:sjames@fnih.org)>  
**Subject:** RE: SHRP report



Hi Julie,

There's not a lot of detail I can provide to you about their progress except the information that is publicly available.

For the two Big awards (U01's Gordon & McKee) both grants, to date, have met their Milestones for year 1 and their year 2 Milestone progress is currently under review by NINDS Program Staff. We don't expect any problems with the year 2 milestones because NINDS Program Directors are on monthly calls with both Drs. Gordon and McKee and their staff. These calls provide the opportunity to respond to any challenges or hurdles that present to the investigators in a timely fashion.

The two U01's were able to work together to harmonize their neurobehavioral protocols, develop a comprehensive TBI exposure screening form that is now being used by the NIH NeuroBioBank, and to develop a standardized neuropathological assessment form that aligns with NINDS Common Data Elements and will soon be implemented as an electronic form for use with FITBIR. (FITBIR is a joint DoD and NIH sponsored TBI repository used for data sharing). Both groups have also either completed data uploading of the neurobehavioral data or made great progress toward uploading their data into FITBIR despite the immense amount of new FITBIR form creation that was involved in uploading these data.

As you know, in year 1 they made great progress by holding the **First NINDS/NIBIB Consensus Meeting to Define Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy**. A summary of the results of that Conference were initially published on the NINDS website (<http://www.ninds.nih.gov/research/tbi/ReportFirstNIBConsensusConference.htm>). Members from both grants and neuropathologist from the Consensus working group have submitted their report for publication which has received positive reviews and is currently being revised per standard peer-review publication procedures. We expect that the paper will be officially accepted early 2016. Currently, Dr. McKee's group is working with the FITBIR operations team to develop a method by which the brain tissue slides that were used during the first consensus conference can be shared in FITBIR. The second CTE Consensus Conference will be held in the Spring and is set to build upon the results from the first consensus conference. The brain tissue slides for this second conference are due to be sent out in early January or Feb.

Using this funding Dr. McKee's brain bank has provided CTE-related tissue samples to more than 20 other scientist from all over the USA.

During the past year Dr. McKee has also published several papers related to this grant:

Stein TD, Alvarez VE, McKee AC. Chronic traumatic encephalopathy: a spectrum of neuropathological changes following repetitive brain trauma in athletes and military personnel. *Alzheimers Res Ther*. 2014;6(1):4. PubMed PMID: 24423082; PubMed Central PMCID: PMC3979082

Stein TD, Montenegro PH, Alvarez VE, Xia W, Crary JE, Tripodis Y, Daneshvar DH, Mez J, Solomon T, Meng G, Kubilus CA, Cormier KA, Meng S, Babcock K, Kiernan P, Murphy L, Nowinski CJ, Martin B, Dixon D, Stern RA, Cantu RC, Kowall NW, McKee AC. Beta-amyloid deposition in chronic traumatic encephalopathy. *Acta Neuropathol*. 2015 Jul;130(1):21-34. PubMed PMID: 25943889; PubMed Central PMCID: PMC4529056.

Stein TD, Alvarez VE, McKee AC. Concussion in Chronic Traumatic Encephalopathy. *Curr Pain Headache Rep*. 2015 Oct;19(10):47. PubMed PMID: 26260277; PubMed Central PMCID: PMC4633042.

All of the following studies are also required to upload their data into FITBIR:

- **Cortical GABA in Pediatric Sports Concussion.** *PI: Jeffrey G. Ojemann, MD, Seattle Children's Hospital*
  - This grant is now making progress and is set to end this year but will likely go into a No Cost Extension (NCE; this is where they can prolong the timeframe of the study but do NOT receive additional funds to complete the study. Very common process) due to a slow start related to the institution's replacing its MR scanner. Thus, this study is likely to end 12/31/2016
- 
- **Evaluation of Spot Light: A Concussion Injury Management App for Youth Sports.** *PIs: Lara McKenzie, PhD, Nationwide Children's Hospital, Columbus, Ohio and Dawn Comstock, PhD, University of Colorado, Denver*
  - This grant is set to end on 11/30/2015 but they may ask the NICHD for a NCE. This is listed on ClinicalTrials.gov as #NCT02249533.
- 
- **Eye Movement Dynamics: A Rapid Objective Involuntary Measure of Concussion/Mild Traumatic Brain Injury.** *PIs: Nicholas Port, PhD, and Steve Hitzeman, OD, Indiana University School of Optometry, Bloomington*
  - This is an NIDCD grant that is set to end 12/31/2015 but may also ask for a NCE.
- 
- **Imaging and Biomarkers in Adolescents Cleared for Return to Play After Concussion.** *PI: Harvey Levin, PhD, Baylor College of Medicine, Houston*
  - This NINDS grant is set to end 12/21/2015 but will go into NCE. Dr. Levin is making good progress but has been delayed by the IRB approval process.
- 
- **Somatosensory Processing — Assessing Youth Sport-Related Concussion and Recovery.** *PI: Stacy Jennifer Marcus Suskauer, MD, Kennedy Krieger Institute, Baltimore*
  - This is a NICHD grant that is set to end on 11/30/2015 but is also eligible for NCE.
- 
- **Characterization of the Brain and Serum Metabolome in Mouse Models of Concussion.** *PI: Michael J. Whalen, M.D., Massachusetts General Hospital, Boston*
  - This is an NINDS grant that is set to end 12/31/2015 but is eligible for NCE. Dr. Whalen is making excellent progress toward completing this grant.

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/grants/orders/chi/fitbir.htm>

**From:** Wolf-Rodda, Julie (FNIH) [T]  
**Sent:** Monday, November 23, 2015 5:26 PM

**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Mott, Meghan (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Francis, Tiffany (FNIH) [T]; Wiener, Susan (FNIH) [T]; Freire, Maria (FNIH) [T]; James, Stephanie (FNIH) [T]  
**Subject:** RE: SHRP report

Hi Pat,

I'm chiming in on this—and my apologies if you've already sent something that I've missed. FNIH must provide the NFL with a SHRP Report on Tuesday, December 1. The purpose is to update them on work already underway (the pilot projects and the UO1s). We have invoiced NFL for the \$2,500,000 that is their next payment for the UO1; I understand NINDS would like to receive those funds in December. I'm sure the NFL would appreciate hearing about progress. If you could send us a draft in the next few days it would be much appreciated.

Best,  
Julie

**From:** James, Stephanie (FNIH) [T]  
**Sent:** Thursday, November 12, 2015 5:55 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E] <patrick.frostbellgowan@nih.gov>; Freire, Maria (FNIH) [T] <mfreire@fni.h.org>; Mott, Meghan (NIH/NINDS) [E] <meghan.mott@nih.gov>; Wolf-Rodda, Julie (FNIH) [T] <jwolf-rod-da@fni.h.org>  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E] <koroshetz.w@ninds.nih.gov>; Francis, Tiffany (FNIH) [T] <tfrancis@fni.h.org>; Wiener, Susan (FNIH) [T] <swiener@fni.h.org>  
**Subject:** SHRP report

Hi, Pat. I wanted to check up on the status of the SHRP report you had offered to prepare for us. Can you give us an idea of when that will be ready?

Thanks, Stephanie

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Friday, October 09, 2015 2:45 PM  
**To:** James, Stephanie (FNIH) [T] <sjames@fni.h.org>; Freire, Maria (FNIH) [T] <freire.m@od.nih.gov>; Mott, Meghan (NIH/OD) [E] <mottmc@od.nih.gov>; Wolf-Rodda, Julie (FNIH) [T] <jwolf-rod-da@fni.h.org>  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E] <koroshetz.w@ninds.nih.gov>; Francis, Tiffany (FNIH) [T] <tfrancis@fni.h.org>; Gray, Felicia (FNIH) [T] <fgray.f@fni.h.org>  
**Subject:** RE: RFA teleconference

Hi Stephanie,

Sure I can put something together for you.

Thanks  
pat

Patrick SF Bellgowan, PhD

Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/divisions/tbi/tb.htm>

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**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Francis, Tiffany (FNIH) [T]; Gray, Felicia (FNIH) [T]  
**Subject:** RE: RFA teleconference

Hello, Pat. We have not yet heard anything back from NFL from our phone call last week. We will let you know as soon as we know. However, we have an annual report on the SHRP program due to NFL on December 1. This will cover the currently funded pilot projects and U01s.

We would appreciate it if you could provide a technical update on the projects, at whatever level NINDS and the other ICs feel comfortable sharing with NFL. This should also include information about when the projects are scheduled to end.

Would you be able to get this to us by Nov. 6? That will give us time to create the full report while avoiding the Thanksgiving holiday.

Thanks so much,  
Stephanie

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Friday, October 09, 2015 2:21 PM  
**To:** James, Stephanie (FNIH) [T] <[sjames@fnih.org](mailto:sjames@fnih.org)>; Freire, Maria (FNIH) [T] <[freirem@od.nih.gov](mailto:freirem@od.nih.gov)>; Mott, Meghan (NIH/OD) [E] <[mottmc@od.nih.gov](mailto:mottmc@od.nih.gov)>; Wolf-Rodda, Julie (FNIH) [T] <[jwolf-rodga@fnih.org](mailto:jwolf-rodga@fnih.org)>  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E] <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>; Francis, Tiffany (FNIH) [T] <[tfrancis@fnih.org](mailto:tfrancis@fnih.org)>; Gray, Felicia (FNIH) [T] <[fgray@fnih.org](mailto:fgray@fnih.org)>  
**Subject:** RFA teleconference

Hi All

I'm headed to Brussels next week so before the trip I wanted to check to see if there had been any further communications after the CTE RFA teleconference last week.

Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS

301-496-1447  
psfb@mail.nih.gov

<http://www.ninds.nih.gov/ disorders/tbi/tbi.htm>

**From:** James, Stephanie (FNIH) [T]  
**Sent:** Thursday, September 24, 2015 10:56 AM  
**To:** Freire, Maria (FNIH) [T]; Mott, Meghan (NIH/OD) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Wolf-Rodda, Julie (FNIH) [T]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Francis, Tiffany (FNIH) [T]; Gray, Felicia (FNIH) [T]  
**Subject:** RE: Projects

Good idea. I will ask my assistant, Tiffany Francis, to work with all of you to find a time for a pre-meeting to discuss the options for presentation to NFL. Patrick, would you like us to come over to your office for this?

Best, Stephanie

**From:** Freire, Maria (FNIH) [T]  
**Sent:** Thursday, September 24, 2015 10:41 AM  
**To:** Mott, Meghan (NIH/OD) [E] <mottmc@od.nih.gov>  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E] <koroshetz@ninds.nih.gov>; Bellgowan, Patrick (NIH/NINDS) [E] <patrick.bellgowan@nih.gov>; James, Stephanie (FNIH) [T] <siamms@fnih.org>  
**Subject:** Re: Projects

Ah, great! Yes, happy to do that. I will be traveling too but I can join by phone as well. In any event, this is terrific and we will start working with Pat ASAP. Thank you and thank you, Walter. Onward!

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** Thursday, September 24, 2015 10:34 AM  
**To:** Freire, Maria (FNIH) [T]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: Projects

Hi Maria,

Walter will be out of town at meetings in Ann Arbor and Chicago starting today until Wednesday next week. He suggested it may be best for you and Pat to go ahead and organize a meeting and he can try to call in if his schedule allows. I will also try to call in.

Thanks,  
Meghan

**From:** Freire, Maria (FNIH) [T]  
**Sent:** Tuesday, September 22, 2015 10:51 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Projects

Hi, Walter. Would it be helpful if we met with you and Patrick (or only with Patrick given your crazy schedule) to look over possible projects before the NFL folks come to see you? Best, M.

**From:** Chan, Leighton (NIH/CC/RMD) [E]  
**Sent:** 30 Nov 2015 14:46:11 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** FW: JPC  
**Attachments:** CNRM JPC CTE Prevalence Study budget (2).xls, CNRM JPC CTE Prevalence Study Proposal.docx

FYI

LC

---

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: 301-496-4733  
Fax: 301-402-0663  
Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov); <mailto:chanle@cc.nih.gov>

**From:** Perl, Daniel [mailto:[daniel.perl@usuhs.edu](mailto:daniel.perl@usuhs.edu)]  
**Sent:** Monday, November 30, 2015 2:44 PM  
**To:** Chan, Leighton (NIH/CC/RMD) [E]; Regina Armstrong  
**Subject:** Re: JPC

Leighton,

Here is a copy of the proposed study plus a proposed budget. I do think this is all do-able in 3 years, assuming the JPC can get its act together (which I think the new Director, COL Simon, can achieve) and the IRB goes along with the plan and does not drag its feet.

Let me know if you need anything further.

Dan

On Mon, Nov 30, 2015 at 11:24 AM, Chan, Leighton (NIH/CC/RMD) [E] <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)> wrote:  
Thanks Dan.

**From:** "Perl, Daniel" <[daniel.perl@usuhs.edu](mailto:daniel.perl@usuhs.edu)>  
**Date:** Monday, November 30, 2015 at 11:00 AM  
**To:** Leighton Chan <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)>  
**Cc:** Regina Armstrong <[rarmstrong@usuhs.mil](mailto:rarmstrong@usuhs.mil)>  
**Subject:** Re: JPC

Leighton,

(b) (4)

That's it for now.

Lian

On Sun, Nov 29, 2015 at 7:27 PM, Chan, Leighton (NIH/CC/RMD) [E] <[leightonchan@cc.nih.gov](mailto:leightonchan@cc.nih.gov)> wrote:  
Hi Dan: I need a ballpark figure for the project. How many cases? What will you stain for besides Tau?

How much money will it take, and over what period of time?

I send this my Monday at 4 .

LC

---

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: [301-496-4733](tel:3014964733)  
Fax: [301-402-0693](tel:3014020693)  
Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <[mailto:chanle@cc.nih.gov](mailto:mailto:chanle@cc.nih.gov)>

...  
Daniel P. Perl, MD  
Professor of Pathology (Neuropathology)  
Uniformed Services University of the Health Sciences  
F. Edward Hebert School of Medicine  
"America's Medical School"  
4301 Jones Bridge Road, Room 3-3138  
Bethesda, MD 20814

Director, Neuropathology Core  
Center for Neurosciences and Regenerative Medicine (CNRM)

tel. 301.425.5533  
e-mail: [daniel.perl@usuhhs.edu](mailto:daniel.perl@usuhhs.edu)

...



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e-mail: [daniel.perl@usuhs.edu](mailto:daniel.perl@usuhs.edu)

# NIH Year 1

## A. SENIOR/KEY PERSONNEL

Name	Project Role	Base Salary	% of Effort	Requested Salary	Fringe Benefits	Fringe Amount	Funds Requested
1 Daniel Perl	PI	0	2%	0	0	0	0
2 Sharon Shively	Research Assistant Professor	(b)(4); (b)(6)					
3 Diego Iacono	Scientist						
4				0	0	0	0
5				0	0	0	0
6				0	0	0	0
7		0		0	0	0	0
8		0		0	0	0	0
Total Senior/Key Person							(b)(4)

## B. OTHER PERSONNEL

Name	Project Role	Base Salary	% of Effort	Requested Salary	Fringe Benefits	Fringe Amount	Funds Requested
1 Patricia Lee	Histopathology Lab Manager	(b)(4); (b)(6)					
2 TBD	Histotechnician						
3 TBD	Data Analysis						
4 Natalia Epshteyn	Administrative Assistant						
5 TBD	Sample Screener						
6 TBD	Sample Screener						
7		0		0	0	0	0
8		0		0	0	0	0
Total Senior/Key Person							(b)(4)
Total Salary, Wages and Fringe Benefits (A+B)							(b)(4)

## C. EQUIPMENT

Description	Funds Requested
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
Total Equipment	0

## D. TRAVEL

1 Domestic Travel Costs (PI and Iacono)	(b)(4)
2 Foreign Travel Costs	
Total Travel Costs	

## E. PARTICIPANT/TRAINEE SUPPORT COSTS

1 Tuition/Fees/Health Insurance	
2 Stipends	
3 Travel	
4 Subsistence	
5 Other	
Number of Participants/Trainees	
Total Participant/Trainee Support Costs	0

## F. OTHER DIRECT COSTS

1 Materials and Supplies	(b)(4)
2 Publication Costs	
3 Consultant Costs	
4 ADP/Computer Services	
5 Subawards/Consortium/Contractual Costs	(b)(4)
University of Glasgow (Stewart)	\$ (b)(4)
JPC (no cost)	\$
The Brigham and Women's Hospital (Folkerth)	\$
Mayo Clinic (Dickson)	\$
6 Equipment or Facility Rental/User Fees	
7 Alterations and Renovations	
8 Service Agreements: Digitizing microscope-\$15,000. Leica lab equipment-\$15,000	(b)(4)
9	

10.

**G. DIRECT COSTS**

*Direct costs based on revised HUP indirect allocation base*

Total Other Direct Costs \_\_\_\_\_

Total Direct Costs (A-F) \_\_\_\_\_

Onsite OH Base (Total Direct less Subawards) \_\_\_\_\_

(b) (4)

**H. INDIRECT COSTS**

	Indirect Cost Type	Indirect Cost Rate %	Indirect Cost Base	Funds Requested
1.	USU offsite OH Expense	(b) (4)		(b) (4)
2.	Company wide G&A Expense			
3.	Subaward OH Expense			
4.				
Total Indirect Costs				

**I. TOTAL DIRECT AND INDIRECT COSTS**

(b) (4)
---------

**J. FEE**

--

## NIH Year 2

		1.03 Cost of living increase		32.32% Fringe Amount		
A. SENIOR/KEY PERSONNEL						
Name	Project Role	Base Salary	% of Effort	Requested Salary	Fringe Benefits	Funds Requested
1 Daniel Perl	PI		(b)(4);	0	0	0
2 Sharon Shively	Research Assistant Professor	(b)(4); (b)(6)	(b)(6)	(b)(4); (b)(6)		
3 Diego Iacono	Scientist	(6)				
4				0	0	0
5				0	0	0
6				0	0	0
7				0	0	0
8				0	0	0
				Total Senior/Key Person		
				(b) (4)		

				32.32% Fringe Amount		
B. OTHER PERSONNEL						
	Project Role	Base Salary	% of Effort	Requested Salary	Fringe Benefits	Funds Requested
1 Patricia Lee	Histopathology Lab Manager	(b)(4); (b)(6)				
2 TBD	Histotechnician					
3 TBD	Data Analysis					
4 Natalia Epshteyn	Administrative Assistant					
5 TBD	Sample Screener					
6 TBD	Sample Screener					
7				0	0	0
8				0	0	0
				Total Senior/Key Person		
				(b) (4)		
				Total Salary, Wages and Fringe Benefits (A+B)		
				(b) (4)		

C. EQUIPMENT (Exceeding \$5000)		Funds Requested
Description		
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		

Total Equipment

**D. TRAVEL**

1 Domestic Travel Costs (PI and lacono)

2 Foreign Travel Costs

Total Travel Costs

**E. PARTICIPANT/TRAINEE SUPPORT COSTS**

1 Tuition/Fees/Health Insurance

2 Stipends

3 Travel

4 Subsistence

5 Other

Number of Participants/Trainees

Total Participant/Trainee Support Costs

**F. OTHER DIRECT COSTS**

1 Materials and Supplies

2 Publication Costs

3 Consultant Costs

4 ADP/Computer Services

5 Subawards/Consortium/Contractual Costs

University of Glasgow (Stewart)

\$

JPC (no cost)

\$

the Brigham and Women's Hospital (Folkerth)

\$

Mayo Clinic (Dickson)

\$

6 Equipment or Facility Rental/User Fees

7 Alterations and Renovations

8 Service Agreements: Digitizing microscope (b) (4) Leica lab equipment (b) (4)

9

10

Total Other Direct Costs (b) (4)

**G. DIRECT COSTS**

Direct costs based on revised HJF indirect allocation base

Total Direct Costs (A-F)

Onsite OH Base (Total Direct less Subawards)

**H. INDIRECT COSTS**

	Indirect Cost Type	Indirect Cost Rate %	Indirect Cost Base
1	USU Offsite OH Expense	(b) (4)	
2	Company wide G&A Expense		
3	Subaward OH Expense		
4			

Funds Re (b) (4)

Total Indirect Costs

**I. TOTAL DIRECT AND INDIRECT COSTS**

**J. FEE**

# NIH Year 3

## A. SENIOR/KEY PERSONNEL

		1.03 Cost of living increase		32.32% Fringe Amount		
Name	Project Role	Base Salary	% of Effort	Requested Salary	Fringe Benefits	Funds Requested
1 Daniel Perl	PI	(b)(4); (b)(6)				
2 Sharon Shively	Research Assistant Professor					
3 Diego Iacono	Scientist					
4 TBD	Statistical Consultant					
5				0	0	0
6				0	0	0
7				0	0	0
8				0	0	0
Total Senior/Key Person						(b)(4)

## B. OTHER PERSONNEL

		32.32% Fringe Amount		Fringe Amount		
Name	Project Role	Base Salary	% of Effort	Requested Salary	Fringe Benefits	Funds Requested
Patricia Lee	Histopathology Lab Manager	(b)(4); (b)(6)				
TBD	Histotechnician					
TBD	Study Coordinator					
Natalia Epshteyn	Administrative Assistant					
TBD	Sample Screener					
TBD	Sample Screener					
				0	0	0
				0	0	0
Total Senior/Key Person						(b)(4)
Total Salary, Wages and Fringe Benefits (A+B)						(b)(4)

## C. EQUIPMENT (Exceeding \$5000)

Description	Funds Requested
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
Total Equipment	0

## D. TRAVEL

1 Domestic Travel Costs (PI and Iacono)	(b)(4)
2 Foreign Travel Costs	
Total Travel Costs	(b)(4)

## E. PARTICIPANT/TRAINEE SUPPORT COSTS

1 Tuition/Fees/Health Insurance	
2 Stipends	
3 Travel	
4 Subsistence	
5 Other	
Number of Participants/Trainees	
Total Participant/Trainee Support Costs	0

## F. OTHER DIRECT COSTS

1 Materials and Supplies	(b)(4)
2 Publication Costs	
3 Consultant Costs	
4 ADP/Computer Services	
5 Subawards/Consortium/Contractual Costs	
University of Glasgow (Stewart)	\$ 15,309.00
JPC (no cost)	\$
The Brigham and Women's Hospital (Folkerth)	\$ 64,851.00
Mayo Clinic (Dickson)	\$ 34,851.00
6 Equipment or Facility Rental/User Fees	
7 Alterations and Renovations	
8 Service Agreements: Digitizing microscope-\$15,000, Leica lab equipment-\$15,000,	(b)(4)
9	



10

Total Other Direct Costs

(b) (4)

**G. DIRECT COSTS**

*Direct costs based on revised HRF indirect allocation base*

Total Direct Costs (A-F)

Onsite OH Base (Total Direct less Subawards)

**H. INDIRECT COSTS**

	Indirect Cost Type	Indirect Cost Rate %	Indirect Cost Base	Funds Requested
1	USU offsite OH Expense	(b) (4)		
2	Company wide G&A Expense			
3	Subaward OH Expense			
4				0

Total Indirect Costs (b) (4)

**I. TOTAL DIRECT AND INDIRECT COSTS**

**J. FEE**

Section A SENIOR/KEY PERSONNEL		(b) (4)
Section B OTHER PERSONNEL		
Total Number Other Personnel		
TOTAL SALARY, WAGES AND FRINGE BENEFITS (A+B)		
Section C EQUIPMENT		
Section D TRAVEL		
Domestic	(b) (4)	
Foreign	0	
Section E PARTICIPANT/TRAINEE SUPPORT COSTS		0
1 Tuition/Fees/Health Insurance	0	
2 Stipends	0	
3 Travel	0	
4 Subsistence	0	
5 Other	0	
6 Number of Participants/Trainees	0	
Section F OTHER DIRECT COSTS		(b) (4)
1 Materials and Supplies	(b) (4)	
2 Publication Costs	0	
3 Consultant Costs	0	
4 ADP/Computer Services	0	
5 Subawards/Consortium/Contractual Costs	(b) (4)	
6 Equipment or Facility Rental/User Fees	0	
7 Alterations and Renovations	0	
8 Other 1	(b) (4)	
9 Other 2	0	
10 Other 3	0	
Section G DIRECT COSTS (A - F)		(b) (4)

Section H INDIRECT COSTS

Section I TOTAL DIRECT AND INDIRECT COSTS (G - H)

Section J FEE

	(b) (4)
	(b) (4)
	0



**From:** Crary, John  
**Sent:** 29 Nov 2015 19:02:10 +0000  
**To:** McKee Ann  
**Cc:** Cairns Nigel;W. Dickson Dennis M.D.;Folkerth, Rebecca  
Dunn,M.D.;Keene, Dirk (cdkeene@uw.edu);irene Litvan;daniel Perl;Stein Thor;Vonsattel Jean-  
Paul;Tripodis, Yorghos;Bieniek, Kevin F.;Dams-o'connor, Kristen;Alvarez, Victor E;Gordon,  
Wayne;Babcock, Debra (NIH/NINDS) [E];Bellgowan, Patrick (NIH/NINDS) [E];Koroshetz, Walter  
(NIH/NINDS) [E];Kiernan, Patrick;Murphy Lauren  
**Subject:** Re: \*\*\* Acta Neuropathologica: Your Submission ANEU-D-15-00706R2

Dear Ann et al.,

This is a critical milestone - these criteria will be an essential tool for everyone working with or studying patients with neurodegenerative disease. Its astounding to me how transformative this work has been - and I expect it will continue to be for many years in the future.

I am thrilled to have helped and am looking forward to being more involved moving forward!

Congratulations and all the best.

John

John F. Crary, MD-PhD  
Associate Professor  
Department of Pathology  
Fishberg Department of Neuroscience  
Friedman Brain Institute  
Ronald M. Loeb Center for Alzheimer's Disease  
Box 1194  
1 Gustave L. Levy Place  
New York, NY 10029  
Mobile: (917) 664-8165  
[john.crary@mountsinai.org](mailto:john.crary@mountsinai.org) <<mailto:john.crary@mountsinai.org>>  
[www.crarylab.org](http://www.crarylab.org) <http://www.crarylab.org>

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---

On Nov 29, 2015, at 1:39 PM, McKee, Ann C <[ameckee@bu.edu](mailto:ameckee@bu.edu)> <<mailto:ameckee@bu.edu>>> wrote:

Authors,

**From:** Litvan, Irene  
**Sent:** 29 Nov 2015 18:44:49 +0000  
**To:** Ann McKee  
**Cc:** Cairns, Nigel;Dennis Dickson;Folkerth, Rebecca Dunn,M.D.;Keene, Dirk (cdkeene@uw.edu);daniel Perl;Stein, Thor;Vonsattel;Tripodis, Yorghos;John Crary;Bieniek, Kevin F.;Dams-o'connor, Kristen;Alvarez, Victor E;Gordon, Wayne;Babcock, Debra (NIH/NINDS) [E];Bellgowan, Patrick (NIH/NINDS) [E];Koroshetz, Walter (NIH/NINDS) [E];Kiernan, Patrick;Murphy, Lauren Elizabeth  
**Subject:** Re: \*\*\* Acta Neuropathologica: Your Submission ANEU-D-15-00706R2

Congratulations Ann for all your efforts in moving the field forward. This is truly an important step forward. Irene

Irene Litvan, M.D., FAAN, FANA  
Tasch Endowed Professor in Parkinson Disease Research  
Director of the Movement Disorders Center  
UC San Diego Department of Neurosciences  
8950 Villa La Jolla Drive, Suite C112  
La Jolla, CA 92037

Phone: (858) 822-5872  
FAX: (858) 822-5743

Assistant: Priscilla Mendoza  
[pemendoza@ucsd.edu](mailto:pemendoza@ucsd.edu)  
(858) 822-5871

On Nov 29, 2015, at 12:39 PM, McKee, Ann C' <[ameckee@bu.edu](mailto:ameckee@bu.edu)> wrote:

**Porter, Kevin (NIH/OD) [E]**

---

**From:** Tabak, Lawrence (NIH/OD) [E]  
**Sent:** Sunday, November 29, 2015 2:35 PM  
**To:** Collins, Francis (NIH/OD) [E]; Hudson, Kathy (NIH/OD) [E]; Wood, Gretchen (NIH/OD) [E]  
**Subject:** RE: NFL and NIH  
  
**Follow Up Flag:** Follow up  
**Flag Status:** Completed

Ok – thanks. Glad to hear you are continuing to mend.

---

**From:** Collins, Francis (NIH/OD) [E]  
**Sent:** Sunday, November 29, 2015 2:34 PM  
**To:** Tabak, Lawrence (NIH/OD) [E]; Hudson, Kathy (NIH/OD) [E]; Wood, Gretchen (NIH/OD) [E]  
**Subject:** RE: NFL and NIH

I think this NFL topic can wait until Wednesday (b) (6)  
(b) (6)

FC

---

**From:** Tabak, Lawrence (NIH/OD) [E]  
**Sent:** Sunday, November 29, 2015 2:18 PM  
**To:** Collins, Francis (NIH/OD) [E]; Hudson, Kathy (NIH/OD) [E]; Wood, Gretchen (NIH/OD) [E]  
**Subject:** RE: NFL and NIH

Francis,  
Is it time sensitive? Catchup will not be until Wed (I will be in a scif during our normal Tuesday time).  
How are you feeling?  
Larry

---

**From:** Collins, Francis (NIH/OD) [E]  
**Sent:** Sunday, November 29, 2015 2:09 PM  
**To:** Tabak, Lawrence (NIH/OD) [E]; Hudson, Kathy (NIH/OD) [E]; Wood, Gretchen (NIH/OD) [E]  
**Subject:** NFL and NIH

I just spoke with Walter K. For this week's catch up, need to add an item on the NFL, NIH, FNIH, and Concussion research.

FC



**From:** Mckee, Ann C  
**Sent:** 29 Nov 2015 02:13:10 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Kiernan, Patrick; Murphy, Lauren Elizabeth  
**Subject:** Fwd: Acta resubmission

Begin forwarded message:

**From:** "Mckee, Ann C" <[amckee@bu.edu](mailto:amckee@bu.edu)>  
**Subject:** Acta resubmission  
**Date:** November 28, 2015 at 9:12:22 PM EST  
**To:** "Cairns, Nigel" <[cairnsn@neuro.wustl.edu](mailto:cairnsn@neuro.wustl.edu)>, Dennis Dickson <[dickson.dennis@mayo.edu](mailto:dickson.dennis@mayo.edu)>, "Folkerth, Rebecca Dunn,M.D." <[RFOLKERTH@PARTNERS.ORG](mailto:RFOLKERTH@PARTNERS.ORG)>, "Keene, Dirk (edkeene@uw.edu)" <[edkeene@uw.edu](mailto:edkeene@uw.edu)>, Irene Litvan <[ilitvan@uesd.edu](mailto:ilitvan@uesd.edu)>, daniel Perl <[daniel.perl@usuhs.edu](mailto:daniel.perl@usuhs.edu)>, Thor Stein <[tdstein@bu.edu](mailto:tdstein@bu.edu)>, Jean Paul Vonsattel <[jgv2001@columbia.edu](mailto:jgv2001@columbia.edu)>, william Stewart <[William.Stewart@glasgow.ac.uk](mailto:William.Stewart@glasgow.ac.uk)>, yorghos Tripodis <[yorghos@bu.edu](mailto:yorghos@bu.edu)>, John Crary <[john.crary@mountsinai.org](mailto:john.crary@mountsinai.org)>, "Bieniek, Kevin F." <[Bieniek.Kevin@mayo.edu](mailto:Bieniek.Kevin@mayo.edu)>, "Dams-o'connor, Kristen" <[kristen.dams-o'connor@mountsinai.org](mailto:kristen.dams-o'connor@mountsinai.org)>, "Gordon, Wayne" <[wayne.gordon@mountsinai.org](mailto:wayne.gordon@mountsinai.org)>

All,

Thank you for your last comments, I resubmitted the manuscript to Acta today as I was on deadline from the editor. In the final submission, I tried to accommodate as many of your final suggestions as possible, recognizing that in matters of mixed opinion, the majority opinion had precedent:

I eliminated the comments on Guam PDC.

The editor of Acta suggested that the tables showing the raw data be included as supplementary tables, and since this information would be readily available to any reader of the manuscript, I followed his suggestion and included the raw data tables as supplementary tables (also, to clarify, supplementary Table 2 very clearly indicates that one of the cases of GPDC had a history of TBI).

I kept the Geddes reference to the rugby player as it is one of the few, early reports of CTE in young individuals.

In reference to the recent paper of Ling et al., I included that their brain bank cohort consists of neurodegenerative disease as well as controls.

In matters regarding “staging” of the cases, I followed the suggestions of the reviewers and clarified the stages of the submitted cases as CTE III and CTE IV and cited the paper in Brain where the staging system was described. At our next consensus conference we will revisit the staging of cases following methods we previously agreed on.

Best wishes,

Ann

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 27 Nov 2015 22:28:40 +0000  
**To:** 'Mckee, Ann C'  
**Subject:** RE: Manuscript: First NINDS/NIBIB Consensus Meeting to Define Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy

Thanks. Any other brain banks out there that should be screened?  
Walter

**From:** Mckee, Ann C [mailto:amckee@bu.edu]  
**Sent:** Wednesday, November 25, 2015 7:05 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Re: Manuscript: First NINDS/NIBIB Consensus Meeting to Define Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy

Hi Walter,

I think they probably included some "iffy" cases as the 1 figure they included didn't show diagnostic features of CTE. Nevertheless, I know some of their cases are bonafide so the percentage is most likely lower, but still important.

Ann

On Nov 24, 2015, at 6:01 PM, Koroshetz, Walter (NIH/NINDS) [E]  
<[koroshetzwa@ninds.nih.gov](mailto:koroshetzwa@ninds.nih.gov)> wrote:

thanks Ann. what's your take on the Queens Square paper?  
Walter

Sent from my iPhone

On Nov 24, 2015, at 5:08 PM, Mckee, Ann C <[amckee@bu.edu](mailto:amckee@bu.edu)> wrote:

Actually please use this version of the manuscript for review

On Nov 24, 2015, at 4:59 PM, Mckee, Ann C  
<[amckee@bu.edu](mailto:amckee@bu.edu)> wrote:

Dear Co-authors,

The Acta submission "The First NINDS/NIBIB Consensus Meeting to Define Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy" has changed status to "Accepted with revisions". The specific formatting requests from Acta and reviews are listed below this email. I prepared a response to the reviews (enclosed) as well as a revised manuscript (enclosed). The editor has

requested that I resubmit the manuscript very soon, so I would like to resubmit the manuscript this Friday, November 26, 2015. If I do not hear from you by Friday 12 noon EST, I will assume you approve of the final submission.

Thanks very much for all your hard work!

Best regards,  
Ann

From Acta:

Please carefully consider the following technical requirements:

- (1) Type of paper will be "Consensus Paper". Therefore, please use "Other" rather than "Original Paper" as type of paper.
- (2) Figure parts should be identified with lower case roman letters on figures and throughout text including legends (a, b, c etc, not A, B, C etc).
- (3) pdf is not an acceptable file format.
- (4) Headings of tables (title, authors) should be deleted.
- (5) Please consider whether (b) (4)

(b) (4)

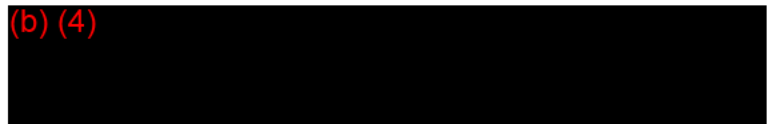
Comments for Authors:

(b) (4)



Further very minor issue:

(b) (4)



<McKee et al. CTE CONSENSUS  
revised11.24.15.docx><ACTA Response to Reviewers  
CTE NINDS11.24.15.docx><aSupplementary Table 1.  
McKee et al. Reviewer's evaluation of CTE cases.docx>

<McKee et al. CTE CONSENSUS2 revised11.24.15.docx>

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 27 Nov 2015 18:31:54 +0000  
**To:** Chan, Leighton (NIH/CC/RMD) [E]; James, Stephanie (FNIH) [T]; Freire, Maria (FNIH) [T]  
**Cc:** Wolf-Rodda, Julie (FNIH) [T]  
**Subject:** RE: SHRP research proposal

Yes, recall that the first study design was for ~100 million to follow athletes for 20 years. At that time it was out of what was possible financially. Maybe things have changed.

Our compromise was to break it down to a piece that could potentially be completed in 7 years. The strategy was to focus on those with symptoms along with an appropriate control group. The deliverable was to define the clinical syndrome(s).

- 1) The most likely accomplishment would be a detailed description of progressive cognitive impairment/dementia along with imaging correlation—want CSF, MR and tau PET and maybe FDG PET.
- 2) The second goal would be to study and follow those with primarily behavioral/mood disorder and over 7 years nail down whether there is conversion to cognitive impairment. If not then will be difficult to ascribe to CTE unless there is something specific about the pattern of neuropsych abnormalities.. Could also be that there is no causal relationship. MR, PET, CSF may also be important.

Numbers of patients for #1 could be as low as 40-60 as long as not enrolling folks over 70 when Alzheimers going to be prevalent. Not sure need control group as looking for things that are outside the range of normal.

Numbers of patients for #2 is entirely unknown so want as many as you can get—at least 60. Want a matched control group – asymptomatic players or people with mood disorder.

We did not propose to do a prospective study of asymptomatic NFL players because we thought the follow-up period would be too long to say whether they have trouble or not, too costly. I also thought that it was best to define the syndrome first. Then know what you are looking for and could start screening for subtle changes core to the condition.

Best,

Walter

**From:** Chan, Leighton (NIH/CC/RMD) [E]  
**Sent:** Friday, November 27, 2015 8:54 AM  
**To:** James, Stephanie (FNIH) [T]; Freire, Maria (FNIH) [T]  
**Cc:** Wolf-Rodda, Julie (FNIH) [T]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Re: SHRP research proposal

Maria and Stephanie- Thanks for the guidance. This is very helpful. I will get an estimated cost per subject from the extramural team and start with that. My sense is that it will be about \$3-4 million/year for all 4 sites depending on the costs for imaging. I hope that the extramural sites will agree to reduced indirects. This could have a profound impact on the availability of funds.

It is important to note that we know very little about CTE in terms of its time course. We suspect that the time between exposure and symptoms is years if not decades. We also have no current proven way to diagnosis it in vivo. So, unless we get lucky and the PET ligands can differentiate between CTE and other neurodegenerative diseases, it is unlikely \$15 million will bring us a definitive study. Frankly, most of the other TBI natural history studies (DoD and NCAA) are 15 years in length. I suspect that it may take us this long to get fundamental answers even if we are able to combine forces with the NINDS funded BU group. So, I would shoot for a 15 year study funded in 5 year increments, total cost about \$60 million over that time frame.

Let me talk to the other teams and get their input. I will get you a more detailed proposal in time for your meeting with Francis.

LC

---

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: 301-496-4733  
Fax: 301-402-0663  
Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>

**From:** "James, Stephanie (FNIH) [T]" <[sjames@fnih.org](mailto:sjames@fnih.org)>  
**Date:** Thursday, November 26, 2015 at 10:01 AM  
**To:** "Freire, Maria (FNIH) [T]" <[mfreire@fnih.org](mailto:mfreire@fnih.org)>, Leighton Chan <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)>  
**Cc:** "Wolf-Rodda, Julie (FNIH) [T]" <[jwolf-rodde@fnih.org](mailto:jwolf-rodde@fnih.org)>, Walter Koroshetz <[koroshetz@ninds.nih.gov](mailto:koroshetz@ninds.nih.gov)>  
**Subject:** RE: SHRP research proposal

I might suggest that once you resolve the indirect cost issue with the other institutions, one way to overcome the impasse with the NFL about available funding is to provide a concept document that indicates what can be achieved at different funding levels, starting with what we know is still available within the original donation and working your way up in increments (perhaps \$2-5M each) to what you think a thorough longitudinal study that would really answer the questions would require. This would give the NFL folks a better idea of what they would be paying for, and perhaps could serve to get the conversation off zero.

The Research Plan can wait until we have some clarity on available funding and thus what the project will actually look like.

Happy Thanksgiving,  
Stephanie

**From:** Freire, Maria (FNIH) [T]  
**Sent:** Thursday, November 26, 2015 7:43 AM  
**To:** Chan, Leighton (NIH/CC/RMD) [E]



**Cc:** James, Stephanie (FNIH) [T]; Wolf-Rodda, Julie (FNIH) [T]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: SHRP research proposal

Thank you, Leighton. For my discussion with Francis on the 4<sup>th</sup>, I will need to have the names, affiliations and overall information of the different parties that would make up the final group. We can piece some of this information together from what you have provided but we need to flesh-out the bones a bit more. Specifically, I need to be able to paint a clear picture of what will be the final proposal to NFL, the goals and who will do what. I don't need a detailed research program, obviously.

I am hopeful that NFL will give us a better idea of the budget by then- I keep asking Jeff for this, as you know. Frankly, this is the chicken and egg problem: they want to know how much a study will cost and we need to know how much funding is available so you can plan the scope of work. I have been trying to break the cycle but then another cook comes into the kitchen and we go back to square one. Let's see if we can stop that and get the train on the tracks and moving.

Have a great Thanksgiving, M.

**From:** Chan, Leighton (NIH/CC/RMD) [E]  
**Sent:** Tuesday, November 24, 2015 4:40 PM  
**To:** Freire, Maria (FNIH) [T] <[mfreire@fnih.org](mailto:mfreire@fnih.org)>  
**Cc:** James, Stephanie (FNIH) [T] <[sjames@fnih.org](mailto:sjames@fnih.org)>; Wolf-Rodda, Julie (FNIH) [T] <[jwolf-rod@fnih.org](mailto:jwolf-rod@fnih.org)>  
**Subject:** Re: SHRP research proposal

Maria-

I just sent this note off to the potential collaborators at UNC and Wisconsin. It outlines the general parameters with which I am comfortable. Please let me know what you might need for your meeting with Francis on the 4th.

LC

---

Leighton Chan, MD, MPH  
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Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: 301-496-4733  
Fax: 301-402-0663  
Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 25 Nov 2015 22:41:19 +0000  
**To:** Taylor, Anna (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Re: Frank Gifford

Thanks, I hadn't seen this one. This should probably get some serious NBC coverage.

Thanks  
Pat

Patrick SF Bellgowan, PhD  
Program Director  
NINDS / NIH  
301-496-1447  
Pat.bellgowan@nih.gov

> On Nov 25, 2015, at 5:35 PM, "Taylor, Anna (NIH/NINDS) [E]" <tayloranna@ninds.nih.gov> wrote:  
>  
> [http://mobile.nytimes.com/2015/11/26/sports/football/frank-gifford-had-etc-family-says.html?\\_r=0&referrer=https://news.google.com](http://mobile.nytimes.com/2015/11/26/sports/football/frank-gifford-had-etc-family-says.html?_r=0&referrer=https://news.google.com)  
>  
> In case you aren't aware of this story...  
>  
>  
>  
> Sent with Good

**From:** Perl, Daniel  
**Sent:** 25 Nov 2015 15:39:35 -0500  
**To:** William Stewart  
**Cc:** Mckee, Ann C; Cairns, Nigel; Dennis Dickson; Folkerth, Rebecca Dunn, M.D.; Keene, Dirk (cdkeene@uw.edu); Irene Litvan; Stein, Thor; Jean Paul Vonsattel; Tripodis, Yorghos; Bieniek, Kevin F.; Crary, John; Dams-o'connor, Kristen; Alvarez, Victor E; Gordon, Wayne; Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]; Murphy, Lauren Elizabeth; Kiernan, Patrick  
**Subject:** Re: Manuscript: First NINDS/NIBIB Consensus Meeting to Define Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy

Dear all,

I have just read the manuscript, reviews and on-line comments. All-in-all, a very nice job. Ann in putting this together. The only point I would make is to agree with (b) (4)

(b) (4)

Otherwise, I am fine with the manuscript.

Have a happy Thanksgiving all.

Dan

On Wed, Nov 25, 2015 at 7:35 AM, William Stewart <[William.Stewart@glasgow.ac.uk](mailto:William.Stewart@glasgow.ac.uk)> wrote:

Thanks Ann

And good news on sympathetic reviews

Comments on manuscript and responses:

(b) (4)



WS

**Dr Willie Stewart**

Consultant Neuropathologist

Honorary Clinical Associate Professor

Dept of Neuropathology

Laboratory Medicine Building

Queen Elizabeth University Hospital

Glasgow G51 4TF

+44(0)141 354 3535

<http://www.gla.ac.uk/researchinstitutes/neurosciencepsychology/staff/williamstewart/#tabs=0>

**From:** Mckee, Ann C [mailto:[amckee@bu.edu](mailto:amckee@bu.edu)]

**Sent:** 24 November 2015 22:08

**To:** Cairns, Nigel; Dennis Dickson; Folkerth, Rebecca Dunn, M.D.; Keene, Dirk ([cdkeene@uw.edu](mailto:cdkeene@uw.edu)); Irene Litvan; daniel Perl; Stein, Thor; Jean Paul Vonsattel; William Stewart; Tripodis, Yorghos; Bieniek, Kevin F.; Crary, John; Dams-o'connor, Kristen; Alvarez, Victor E; Gordon, Wayne; Babcock, Debra (NIH/NINDS) [E]; [patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov); Koroshetz, Walter (NIH/NINDS) [E]

**Cc:** Murphy, Lauren Elizabeth; Kiernan, Patrick

**Subject:** Re: Manuscript: First NINDS/NIBIB Consensus Meeting to Define Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy

Actually please use this version of the manuscript for review

On Nov 24, 2015, at 4:59 PM, Mckee, Ann C <[amckee@bu.edu](mailto:amckee@bu.edu)> wrote:

Dear Co-authors,

The Acta submission "The First NINDS/NIBIB Consensus Meeting to Define Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy" has changed status to "Accepted with revisions". The specific formatting requests from Acta and reviews are listed below this email. I prepared a response to the reviews (enclosed) as well as a revised manuscript (enclosed). The editor has requested that I resubmit the manuscript very soon, so I would like to resubmit the manuscript this Friday, November 26, 2015. If I do not hear from you by Friday 12 noon EST, I will assume you approve of the final submission.

Thanks very much for all your hard work!

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 25 Nov 2015 00:43:58 +0000  
**To:** Chan, Leighton (NIH/CC/RMD) [E]  
**Subject:** Re: SHRP research proposal

Great. so use your mobile?

301 222 (b) (6)

W

Sent from my iPhone

On Nov 24, 2015, at 7:21 PM, Chan, Leighton (NIH/CC/RMD) [E] <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)> wrote:

Sure. After 4 is fine. I will be in MA.

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: 301-496-4733  
Fax: 301-402-0463  
Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)

On Nov 24, 2015, at 7:16 PM, Koroshetz, Walter (NIH/NINDS) [E]  
<[koroshetzwa@ninds.nih.gov](mailto:koroshetzwa@ninds.nih.gov)> wrote:

dear Leighton  
was visiting U of Kentucky today so just saw this. tomorrow should be  
free by 4pm. Would it work for call after 4?

Walter

Sent from my iPhone

On Nov 23, 2015, at 3:31 PM, Chan, Leighton (NIH/CC/RMD) [E]  
<[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)> wrote:

It was fine. Maria was not on, just Julia Wolf-Rodda and  
Stephanie James. I asked them if the NFL had made any  
decisions related to funding NINDS (BU). They have not  
heard from them. I am hoping that the NFL makes a move  
in this direction before Maria's meeting with Francis on the  
4<sup>th</sup> of December.

My major questions for FNIH were around FNIH

(b) (5)

(b) (5)

Do you have time to chat about this later today or tomorrow?

LC

---

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical  
Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604  
Bethesda, MD 20892-1604

Phone: 301-496-4733

Fax: 301-402-0663

Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>

**From:** Koroshetz, Walter (NIH/NINDS) [E]

**Sent:** Monday, November 23, 2015 3:12 PM

**To:** Chan, Leighton (NIH/CC/RMD) [E]

**Subject:** Re: Automatic reply: SHRP research proposal

Sorry, wasn't free to join. How did it go?

Walter

Sent from my iPhone

On Nov 23, 2015, at 8:31 AM, Chan, Leighton (NIH/CC/RMD) [E]  
<[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)> wrote:

Julie- This is for our call today.

Walter- you are welcome to join us at 10:30-11

today. Dia-ID: 877-662 (b) (6)

Passcode (b) (6)

LC

---

Leighton Chan, MD, MPH

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Building 10, Room 1-1469 10 Center Drive, MSC  
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Email:

[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>

**From:** "Wolf-Rodda, Julie (FNIH) [T]" <[jwolf-rodde@fni-h.org](mailto:jwolf-rodde@fni-h.org)>

**Date:** Thursday, November 19, 2015 at 8:43 AM

**To:** Leighton Chan <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)>

**Subject:** Automatic reply: SHRP research proposal

Thank you for your message. I will be traveling for business on November 19-20 and will have limited access to email. If your message is urgent, please contact Anisa Sanghrajka at [a.sanghrajka@fni-h.org](mailto:a.sanghrajka@fni-h.org). Otherwise, I will respond to your message upon my return.

Thanks,

Julie Wolf-Rodda  
Director of Development  
Foundation for the National Institutes of Health  
(FNIH)  
301-402-6027 direct  
[jwolf-rodde@fni-h.org](mailto:jwolf-rodde@fni-h.org)  
<FNIH project Infrastructure.docx>



**From:** Litvan, Irene  
**Sent:** 24 Nov 2015 22:44:11 +0000  
**To:** Ann McKee  
**Cc:** Cairns, Nigel;Dennis Dickson;Folkerth, Rebecca Dunn,M.D.;Keene, Dirk (cdkeene@uw.edu);daniel Perl;Stein, Thor;Vonsattel;William Stewart;Tripodis, Yorghos;Bieniek, Kevin F.;Crary, John;Dams-o'connor, Kristen;Alvarez, Victor E;Gordon, Wayne;Babcock, Debra (NIH/NINDS) [E];Bellgowan, Patrick (NIH/NINDS) [E];Koroshetz, Walter (NIH/NINDS) [E];Murphy, Lauren Elizabeth;Kiernan, Patrick  
**Subject:** Re: Manuscript: First NINDS/NIBIB Consensus Meeting to Define Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy

Great job Ann! An important contribution to advance science. Irene

Irene Litvan, M.D., FAAN, FANA  
Tasch Endowed Professor in Parkinson Disease Research  
Director of the Movement Disorders Center  
UC San Diego Department of Neurosciences  
8950 Villa La Jolla Drive, Suite C112  
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Phone: (858) 822-5872  
FAX: (858) 822-5743

Assistant: Priscilla Mendoza  
[pcmendoza@ucsd.edu](mailto:pcmendoza@ucsd.edu)  
(858) 822-5871

**From:** James, Stephanie (FNIH) [T]  
**Sent:** 24 Nov 2015 17:31:55 -0500  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Re: SHRP report

Okay, thanks

Sent from my BlackBerry 10 smartphone.

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Tuesday, November 24, 2015 2:48 PM  
**To:** James, Stephanie (FNIH) [T]  
**Subject:** RE: SHRP report

Hi Stephanie,

The Milestones are not public information.

Best wishes,  
Pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** James, Stephanie (FNIH) [T]  
**Sent:** Tuesday, November 24, 2015 2:37 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Wolf-Rodda, Julie (FNIH) [T]; Mott, Meghan (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Francis, Tiffany (FNIH) [T]; Wiener, Susan (FNIH) [T]; Freire, Maria (FNIH) [T]  
**Subject:** Re: SHRP report

Thanks very much, Patrick. Are the U01 milestones public information? If so, could you let us know what those are?

Happy Thanksgiving,  
Stephanie

Sent from my BlackBerry 10 smartphone.

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Tuesday, November 24, 2015 2:09 PM  
**To:** Wolf-Rodda, Julie (FNIH) [T]; Mott, Meghan (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Francis, Tiffany (FNIH) [T]; Wiener, Susan (FNIH) [T]; Freire, Maria (FNIH) [T]; James, Stephanie (FNIH) [T]  
**Subject:** RE: SHRP report

Hi Julie,

There's not a lot of detail I can provide to you about their progress except the information that is publicly available.

For the two Big awards (U01's Gordon & McKee) both grants, to date, have met their Milestones for year 1 and their year 2 Milestone progress is currently under review by NINDS Program Staff. We don't expect any problems with the year 2 milestones because NINDS Program Directors are on monthly calls with both Drs. Gordon and McKee and their staff. These calls provide the opportunity to respond to any challenges or hurdles that present to the investigators in a timely fashion.

The two U01's were able to work together to harmonize their neurobehavioral protocols, develop a comprehensive TBI exposure screening form that is now being used by the NIH NeuroBioBank, and to develop a standardized neuropathological assessment form that aligns with NINDS Common Data Elements and will soon be implemented as an electronic form for use with FITBIR. (FITBIR is a joint DoD and NIH sponsored TBI repository used for data sharing). Both groups have also either completed data uploading of the neurobehavioral data or made great progress toward uploading their data into FITBIR despite the immense amount of new FITBIR form creation that was involved in uploading these data.

As you know, in year 1 they made great progress by holding the First NINDS/NIBIB Consensus Meeting to Define Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy. A summary of the results of that Conference were initially published on the NINDS website

(<http://www.ninds.nih.gov/research/tbi/ReportFirstNIHConsensusConference.htm>). Members from both grants and neuropathologist from the Consensus working group have submitted their report for publication which has received positive reviews and is currently being revised per standard peer-review publication procedures. We expect that the paper will be officially accepted early 2016. Currently, Dr. McKee's group is working with the FITBIR operations team to develop a method by which the brain tissue slides that were used during the first consensus conference can be shared in FITBIR. The second CTE Consensus Conference will be held in the Spring and is set to build upon the results from the first consensus conference. The brain tissue slides for this second conference are due to be sent out in early January or Feb.

Using this funding Dr. McKee's brain bank has provided CTE-related tissue samples to more than 20 other scientist from all over the USA.

During the past year Dr. McKee has also published several papers related to this grant:

Stein TD, Alvarez VE, McKee AC. Chronic traumatic encephalopathy: a spectrum of neuropathological changes following repetitive brain trauma in athletes and military personnel. *Alzheimers Res Ther.* 2014;6(1):4. PubMed PMID: 24423082; PubMed Central PMCID: PMC3979082

Stein TD, Montenegro PH, Alvarez VE, Xia W, Crary JF, Tripodis Y, Daneshvar DH, Mez J, Solomon T, Meng G, Kubilus CA, Cormier KA, Meng S, Babcock K, Kiernan P, Murphy L, Nowinski CJ, Martin B, Dixon D, Stern RA, Cantu RC, Kowall NW, McKee AC. Beta-amyloid deposition in chronic traumatic encephalopathy. *Acta Neuropathol.* 2015 Jul;130(1):21-34. PubMed PMID: 25943889, PubMed Central PMCID: PMC4529056.

Stein TD, Alvarez VE, McKee AC. Concussion in Chronic Traumatic Encephalopathy.

All of the following studies are also required to upload their data into FITBIR:

- **Cortical GABA in Pediatric Sports Concussion.** *PI: Jeffrey G. Ojemann, MD, Seattle Children's Hospital*
  - This grant is now making progress and is set to end this year but will likely go into a No Cost Extension (NCE; this is where they can prolong the timeframe of the study but do NOT receive additional funds to complete the study. Very common process) due to a slow start related to the institution's replacing its MR scanner. Thus, this study is likely to end 12/31/2016
- 
- **Evaluation of Spot Light: A Concussion Injury Management App for Youth Sports.** *PIs: Lara McKenzie, PhD, Nationwide Children's Hospital, Columbus, Ohio and Dawn Comstock, PhD, University of Colorado, Denver*
  - This grant is set to end on 11/30/2015 but they may ask the NICHD for a NCE. This is listed on ClinicalTrials.gov as #NCT02249533.
- 
- **Eye Movement Dynamics: A Rapid Objective Involuntary Measure of Concussion/Mild Traumatic Brain Injury.** *PIs: Nicholas Port, PhD, and Steve Hitzeman, OD, Indiana University School of Optometry, Bloomington*
  - This is an NIDCD grant that is set to end 12/31/2015 but may also ask for a NCE.
- 
- **Imaging and Biomarkers in Adolescents Cleared for Return to Play After Concussion.** *PI: Harvey Levin, PhD, Baylor College of Medicine, Houston*
  - This NINDS grant is set to end 12/21/2015 but will go into NCE. Dr. Levin is making good progress but had been delayed by the IRB approval process.
- 
- **Somatosensory Processing — Assessing Youth Sport-Related Concussion and Recovery.** *PI: Stacy Jennifer Marcus Suskauer, MD, Kennedy Krieger Institute, Baltimore*
  - This is a NICHD grant that is set to end on 11/30/2015 but is also eligible for NCE.
- 
- **Characterization of the Brain and Serum Metabolome in Mouse Models of Concussion.** *PI: Michael J. Whalen, M.D., Massachusetts General Hospital, Boston*
  - This is an NINDS grant that is set to end 12/31/2015 but is eligible for NCE. Dr. Whalen is making excellent progress toward completing this grant.

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/divisions/ot/tbi/tbi.htm>

**From:** Wolf-Rodda, Julie (FNIH) [T]  
**Sent:** Monday, November 23, 2015 5:26 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Mott, Meghan (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Francis, Tiffany (FNIH) [T]; Wiener, Susan (FNIH) [T]; Freire, Maria (FNIH) [T]; James, Stephanie (FNIH) [T]  
**Subject:** RE: SHRP report

Hi Pat,

I'm chiming in on this—and my apologies if you've already sent something that I've missed. FNIH must provide the NFL with a SHRP Report on Tuesday, December 1. The purpose is to update them on work already underway (the pilot projects and the UO1s). We have invoiced NFL for the \$2,500,000 that is their next payment for the UO1; I understand NINDS would like to receive those funds in December. I'm sure the NFL would appreciate hearing about progress. If you could send us a draft in the next few days it would be much appreciated.

Best,  
Julie

**From:** James, Stephanie (FNIH) [T]  
**Sent:** Thursday, November 12, 2015 5:55 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E] <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>; Freire, Maria (FNIH) [T] <[mfreire@fni.h.org](mailto:mfreire@fni.h.org)>; Mott, Meghan (NIH/NINDS) [E] <[meghan.mott@nih.gov](mailto:meghan.mott@nih.gov)>; Wolf-Rodda, Julie (FNIH) [T] <[jwolf-rodna@fni.h.org](mailto:jwolf-rodna@fni.h.org)>  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E] <[koroshetz.w@ninds.nih.gov](mailto:koroshetz.w@ninds.nih.gov)>; Francis, Tiffany (FNIH) [T] <[tfrancis@fni.h.org](mailto:tfrancis@fni.h.org)>; Wiener, Susan (FNIH) [T] <[swiener@fni.h.org](mailto:swiener@fni.h.org)>  
**Subject:** SHRP report

Hi, Pat. I wanted to check up on the status of the SHRP report you had offered to prepare for us. Can you give us an idea of when that will be ready?

Thanks, Stephanie

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Friday, October 09, 2015 2:45 PM  
**To:** James, Stephanie (FNIH) [T] <[sjames@fni.h.org](mailto:sjames@fni.h.org)>; Freire, Maria (FNIH) [T] <[mfreire@od.nih.gov](mailto:mfreire@od.nih.gov)>; Mott, Meghan (NIH/OD) [E] <[mottmc@od.nih.gov](mailto:mottmc@od.nih.gov)>; Wolf-Rodda, Julie (FNIH) [T] <[jwolf-rodna@fni.h.org](mailto:jwolf-rodna@fni.h.org)>  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E] <[koroshetz.w@ninds.nih.gov](mailto:koroshetz.w@ninds.nih.gov)>; Francis, Tiffany (FNIH) [T] <[tfrancis@fni.h.org](mailto:tfrancis@fni.h.org)>; Gray, Felicia (FNIH) [T] <[fgray@fni.h.org](mailto:fgray@fni.h.org)>  
**Subject:** RE: RFA teleconference

Hi Stephanie,

Sure - can put something together for you.

Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-495-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tb/tb.html>

**From:** James, Stephanie (FNIH) [T]  
**Sent:** Friday, October 09, 2015 2:26 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Freire, Maria (FNIH) [T]; Mott, Meghan (NIH/OD) [E]; Wolf-Rodda, Julie (FNIH) [T]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Francis, Tiffany (FNIH) [T]; Gray, Felicia (FNIH) [T]  
**Subject:** RE: RFA teleconference

Hello, Pat. We have not yet heard anything back from NFL from our phone call last week. We will let you know as soon as we know. However, we have an annual report on the SHRP program due to NFL on December 1. This will cover the currently funded pilot projects and U01s.

We would appreciate it if you could provide a technical update on the projects, at whatever level NINDS and the other ICs feel comfortable sharing with NFL. This should also include information about when the projects are scheduled to end.

Would you be able to get this to us by Nov. 6? That will give us time to create the full report while avoiding the Thanksgiving holiday.

Thanks so much,  
Stephanie

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Friday, October 09, 2015 2:21 PM  
**To:** James, Stephanie (FNIH) [T] <[sjames@fnih.org](mailto:sjames@fnih.org)>; Freire, Maria (FNIH) [T] <[freiremc@od.nih.gov](mailto:freiremc@od.nih.gov)>; Mott, Meghan (NIH/OD) [E] <[mottmc@od.nih.gov](mailto:mottmc@od.nih.gov)>; Wolf-Rodda, Julie (FNIH) [T] <[jwolf-rodde@fnih.org](mailto:jwolf-rodde@fnih.org)>  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E] <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>; Francis, Tiffany (FNIH) [T] <[tfrancis@fnih.org](mailto:tfrancis@fnih.org)>; Gray, Felicia (FNIH) [T] <[fgray@fnih.org](mailto:fgray@fnih.org)>  
**Subject:** RFA teleconference

Hi All

I'm headed to Brussels next week so before the trip I wanted to check to see if there had been any further communications after the CTE RFA teleconference last week.

Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/dorders/cbi/tbi.htm>

**From:** James, Stephanie (FNIH) [T]  
**Sent:** Thursday, September 24, 2015 10:56 AM  
**To:** Freire, Maria (FNIH) [T]; Mott, Meghan (NIH/OD) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Wolf-Rodda, Julie (FNIH) [T]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Francis, Tiffany (FNIH) [T]; Gray, Felicia (FNIH) [T]  
**Subject:** RE: Projects

Good idea. I will ask my assistant, Tiffany Francis, to work with all of you to find a time for a pre-meeting to discuss the options for presentation to NFL. Patrick, would you like us to come over to your office for this?

Best, Stephanie

**From:** Freire, Maria (FNIH) [T]  
**Sent:** Thursday, September 24, 2015 10:41 AM  
**To:** Mott, Meghan (NIH/OD) [E] <[mottmc@od.nih.gov](mailto:mottmc@od.nih.gov)>  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E] <[koroshetz@ninds.nih.gov](mailto:koroshetz@ninds.nih.gov)>; Bellgowan, Patrick (NIH/NINDS) [E] <[patrick.fosterbellgowan@nih.gov](mailto:patrick.fosterbellgowan@nih.gov)>; James, Stephanie (FNIH) [T] <[sjames@fnih.org](mailto:sjames@fnih.org)>  
**Subject:** Re: Projects

Ah, great! Yes, happy to do that. I will be traveling too but I can join by phone as well. In any event, this is terrific and we will start working with Pat ASAP. Thank you and thank you, Walter. Onward!

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** Thursday, September 24, 2015 10:34 AM  
**To:** Freire, Maria (FNIH) [T]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: Projects

Hi Maria,

Walter will be out of town at meetings in Ann Arbor and Chicago starting today until Wednesday next week. He suggested it may be best for you and Pat to go ahead and organize a meeting and he can try to call in if his schedule allows. I will also try to call in.

Thanks,

Meghan

**From:** Freire, Maria (FNIH) [T]  
**Sent:** Tuesday, September 22, 2015 10:51 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Projects

Hi, Walter. Would it be helpful if we met with you and Patrick (or only with Patrick given your crazy schedule) to look over possible projects before the NFL folks come to see you? Best, M.



**From:** Armstrong, Regina  
**Sent:** 24 Nov 2015 17:11:26 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Chan, Leighton (NIH/CC/RMD) [E]; Regina Armstrong  
**Subject:** Re: <no subject>

Walter,

I recommended to Dan to work with Dr. Rice right away to bring the right DoD leadership into the discussion when Leighton is ready. We have been working on plans for the analysis of the JPC cases. Dan would need to let others push the implementation. I don't expect the JPC lead (COL Simon) would have a problem with the funding being from NFL.

For the CNRM, it is important to have the process and research plans be supported by you, Dean Kellermann, and Dr. Rice. Then we can involve others with their help for HJF and DoD as needed.

I don't know if you knew (b) (6) (from Thailand) is at MGH this month for a stroke elective. I went up to Boston last week to catch up with (b) (6) e seems to be doing great and thoroughly enjoying her clinical experience. Your connections have been a long term advantage among their network!

I hope you have a great holiday.  
Take care,  
Regina

On Tue, Nov 24, 2015 at 4:57 PM, Koroshetz, Walter (NIH/NINDS) [E]  
<[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)> wrote:  
Thanks Leighton. My thoughts.

(b) (5)



Walter

**From:** Leighton Chan <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)>  
**Date:** Tuesday, November 24, 2015 at 4:36 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetz@ninds.nih.gov](mailto:koroshetz@ninds.nih.gov)>  
**Cc:** Regina Armstrong <[rarmstrong@usuhs.mil](mailto:rarmstrong@usuhs.mil)>  
**Subject:** <no subject>

I just sent this off to (b) (4). It does not commit us to anything, but let's them know the general parameters I am comfortable with. If they balk, we can pull out.

LC

---

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: [301-496-4733](tel:301-496-4733)  
Fax: [301-402-0663](tel:301-402-0663)  
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Regina C. Armstrong, Ph.D.  
Director, Center for Neuroscience and Regenerative Medicine  
Professor, Department of Anatomy, Physiology and Genetics  
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(b) (4)  
Hi

I am very excited about the possibility of working together. Thanks for sending the attachments. I have read through all the materials you sent, including the critiques and your response. It is clear that you put a lot of time and energy into the proposal and have assembled a great team. I love that you have experience with (b) (4)

(b) (4)

(b) (4)

Needless to say, I am treating your documents as confidential, and have not distributed them.

Unfortunately, there are a few more moving parts to this project than when we last talked. Dr. John Gallin (the head of the NIH CC and my boss), as well as Dr. Michael Gottesman (the Director of Intramural Research) are now aware of this proposal and wanted to make sure Francis Collins is briefed. Maria Freire from the FNIH will do this on Dec 4th. I do not feel comfortable going forward until he approves the general outline. So, from an administrative standpoint, we are on hold until then. I am very optimistic about this collaboration, but we still have some pretty tricky waters to navigate.

We also need to wait and see how much money will be available for the (b) (4) study. While the funds available are likely to be substantial, it is hard to plan until we have a solid number. How much is available will, in part, be determined by your institution's willingness to be flexible on indirect costs. The NFL is in a position to require that only a certain level of indirect costs be charged to their donation. For example, the NFL could say that maximum indirect costs they will pay is 15%. If your institution chooses to participate in this collaboration, they would have to agree to this. Do you think that you could get their buy in? I hope so. It would mean access to millions more dollars to perform the science.

As I mentioned in our last meeting, this proposal will need to be substantially different than the original ROI you proposed. As such, we are likely to assign a small portion of the funds (several hundred thousand \$) be used by (b) (4)

(b) (4)

(b) (4)

If all goes well, two to three years into the project, we will have the prevalence of CTE in this very large, longstanding, "population based" cohort. A quick and necessary win for us given that most of our other outcomes will take a very long time to develop.

I am glad that you had a chance to talk to (b) (4). I do think that there is great synergy in adding (b) (4) data to yours. We have been up and running for several years. So, in general, if we stick with the outcome measures selected by Lou and I, and use similar MRI sequences, we already have a jump on TBI controls. We are just now starting to enroll healthy controls and could easily alter the collection of these data to fit into our collaboration. Luckily, Ramon previously laid the groundwork for (b) (4) at NIH. I think that we may even have a (b) (4) and a methodology for moving the tracer from Delaware to NIH in a couple of hours. The only other thing I need to figure out is how to get CSF. This is not something we do currently.

I think that the main issues for us to decide is what cohorts to follow, how frequently they should be seen, and for how long. In large part, this will be dictated by the science but also by the funds available. It should also be informed by what BU is being funded to do. However, even if we were to have access to \$16 million, after you take out indirect costs and divide it among the sites, I am not sure that it will last long enough to give us the answers we would like. CTE may take decades to develop and we may just need to find a way to follow people for that length of time. So we need to grapple with this, but I would like to do so with the hope that there may be more resources out there to support this beyond the initial investment.

I also want to address the issue of (b) (4). This issue is not directly addressed in this proposal; however, I think that we all know that the limitations of the (b) (4) (b) (4) and my epidemiology group does as well. This could be another fruitful area of collaboration.

We also need to think about leadership. This is a unique situation and very high profile. I suspect that, since the funds are coming through FNIH and the NIH Intramural Research Program, the NIH leadership may want either Walter or I to have overall control of the finances and science related to this gift. If the leadership does work out this way, you will find that Walter and I have a very "light touch." We are both more interested in getting results than in getting credit and neither of us have the time or the inclination to micromanage. We also have no interest in "commandeering" a project into which you and your team have put so much time and energy. So, from my standpoint, your team should do the day-to-day management of (b) (4), properly resourced. I am sure you will have questions about this important issue and we can negotiate the details of the reporting lines once we get a firm go ahead.

We will also need a group to serve as the review and oversight body for this work. My suggestion would be the (b) (4) (b) (4)

group already provides review and oversight for all the CNRM TBI research projects. I have been in touch with Art and I think that they would be willing to provide formal review of the work before it begins and then follow-up annually.

We suggest that we attempt to get a unified IRB. This may not be possible, but we should push for it. There is a lot of desire to move in this direction, and HHS has just proposed overhauling the common rule. So the time is right. Could make our lives a lot easier!

So that's my brain dump for now. Have a Happy Thanksgiving and lets try and get on the phone next week.

**From:** Chan, Leighton (NIH/CC/RMD) [E]  
**Sent:** 24 Nov 2015 08:55:50 -0500  
**To:** Koretsky, Alan (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Re: CNRM and PET

Alan- Perhaps-

(b) (5)



LC

**From:** Alan Koretsky <KoretskyA@ninds.nih.gov>  
**Date:** Tuesday, November 24, 2015 at 8:43 AM  
**To:** Leighton Chan <chanl@cc.nih.gov>, "Willard, Alan (NIH/NINDS) [E]" <Alan.W@ninds.nih.gov>  
**Subject:** CNRM and PET

Hello Leighton and Alan,

Wondering if there is any money in CNRM for equipment upgrades.

Peter Herscovitz needs to upgrade two cyclotrons. TBI projects associated with CNRM use the PET. TBI share would be about \$30,000 to the upgrade.

Not sure if there is even a mechanism to do this.

Thanks  
Alan

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 23 Nov 2015 17:05:33 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Fwd: NIH IRP - NFL  
**Attachments:** Infrastructure and logistical planning.docx, ATT00001.htm

Sent from my iPhone

Begin forwarded message:

**From:** "Chan, Leighton (NIH/CC/RMD) [E]" <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)>  
**Date:** November 19, 2015 at 6:03:57 PM EST  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetz/w@ninds.nih.gov](mailto:koroshetz/w@ninds.nih.gov)>  
**Subject:** NIH IRP - NFL

Hi Walter-

(b) (5)



LC

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Leighton Chan, MD, MPH

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Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: 301-496-4733

Fax: 301-402-0663

Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>

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**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 21 Nov 2015 22:46:24 -0500  
**To:** Freire, Maria (FNIH) [T]  
**Subject:** Re: SHRP research proposal

Thanks Maria. Is Dec 4th still good timing to fill in FC.  
walter

**From:** "Freire, Maria (FNIH) [T]" <mfreire@fnih.org>  
**Date:** Wednesday, November 18, 2015 at 7:09 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetz@ninds.nih.gov>  
**Subject:** Fw: SHRP research proposal

Walter, FYI. M.

**From:** Wolf-Rodda, Julie (FNIH) [T] <jwolf-rod@fnih.org>  
**Sent:** Wednesday, November 18, 2015 7:02 PM  
**To:** Chan, Leighton (NIH/CC/RMD) [E]  
**Cc:** Freire, Maria (FNIH) [T]; James, Stephanie (FNIH) [T]  
**Subject:** SHRP research proposal

Dear Leighton,

Thanks for your call earlier today. I appreciated the opportunity to hear your thoughts on the research you're proposing for funding via the Sports and Health Research Program (SHRP) and discuss next steps with the research plan.

I was pleased to hear that you endorse the idea that the NFL should fund a portion of the NINDS award for the CTE longitudinal study, and that Russ Lonser may also be on board with the idea. As Dr. Freire mentioned when we spoke earlier, that is the FNIH's preference as well, and we understand from Jeff Miller that it is still under consideration by the NFL.

Walter Koroshetz did OK my sending you an existing Research Plan as an example of what yours might look like when complete. The attached Research Plan 2 outlines plans for the CTE Neuropathology Study. That award was made in 2013. Additional info and a link to the RFA are available here: <http://www.fnih.org/what-we-do/current-research-programs/shrp-cte-neuropathology>

As we discussed, knowing that the cost of your proposal may exceed available funds from the NFL, I would suggest proposing a concept that can be achieved within the bounds of the roughly \$16.6M available from the NFL gift, less any amount that may go to the recipient of the NINDS award. By using a scalable budget, you could speak to the additional benefit that would come from additional funding. Please remember that you are presenting a scientific proposal for how a portion of a gift already made to the FNIH might be used; you would not be engaging in fundraising. And, as FNIH would be part of the discussion with NFL, we would ensure that no lines are crossed.

Your suggestion that this proposal, which would be a CNRM protocol, be approved through usual CNRM processes makes good sense. When he gave me the OK to send you Research Plan 2, Walter very much endorsed that idea. When your Research Plan has the necessary approvals on your end, please send it to FNIH. We will then review it and add in the anticipated FNIH direct/indirect costs (you'll see that these also appear in Research Plan 2), share it with NFL, and arrange a meeting to discuss it—either in person or via telephone—including yourself and any others you'd like to include, NFL (Jeff Miller any others he'd like to include), and FNIH (Dr. Freire, Dr. James and me).

If you have further questions as you review this or prepare your own plan, please don't hesitate to contact me. I look forward to talking again soon.

Best,  
Julie

**Julie Wolf-Rodda**  
Director of Development  
Foundation for the National Institutes of Health  
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Direct (301) 402-6027 | [jwolf-rodde@fnih.org](mailto:jwolf-rodde@fnih.org)

**REDISCOVER THE FNIH AT [fnih.org](http://fnih.org)**



**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 21 Nov 2015 21:41:42 -0500  
**To:** Chan, Leighton (NIH/CC/RMD) [E]  
**Subject:** Re: NFL

I think (b) (4) already funded to do some of this on the (b) (4) hat  
funded from NIH-NFL.

walter

**From:** Leighton Chan <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)>  
**Date:** Friday, November 20, 2015 at 2:51 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Subject:** NFL

I think we would like to add a (b) (4) ect into the proposal. This would be using the DOD brain  
bank to get a sense of the background incidence of CTE. It would be a quick win for the project and a  
nice addition to the recent data coming from the Mayo Clinic. I will start to flesh this one out.

LC

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 21 Nov 2015 21:25:42 -0500  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Rieff, Heather (NIH/NINDS) [E]  
**Cc:** Scott, Paul (NIH/NINDS) [E]; Zalutsky, Robert (NIH/NINDS) [E]; Mott, Meghan (NIH/NINDS) [E]  
**Subject:** Re: House Energy & Commerce Committee Concussion Roundtable

Thanks Pat. Would add neuropathologists to speak to CTE— Ann McKee, Dennis Dickson, Dan Perl.

Walter

**From:** Patrick Bellgowan <patrick.frostbellgowan@nih.gov>  
**Date:** Friday, November 20, 2015 at 6:27 PM  
**To:** "Rieff, Heather (NIH/NINDS) [E]" <rieffh@ninds.nih.gov>, "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzwa@ninds.nih.gov>  
**Cc:** Paul Scott <ScottP@ninds.nih.gov>, "Zalutsky, Robert (NIH/NINDS) [E]" <zalutskb@ninds.nih.gov>, Meghan Mott <meghan.mott@nih.gov>  
**Subject:** RE: House Energy & Commerce Committee Concussion Roundtable

This is probably way too many names but now you have a choice....

NIH (Walter; other ICs (do you want to include NICHD?))

NICHD – Valerie Maholmes

NIMH- Farris Tuma [fruma@mail.nih.gov](mailto:fruma@mail.nih.gov) (?)

DoD – Col Todd Rasmussen [todd.e.rasmussen.mil@gmail.com](mailto:todd.e.rasmussen.mil@gmail.com);

Col Sidney Hinds [sidney.hinds.mil@gmail.com](mailto:sidney.hinds.mil@gmail.com) (DVBIC)

Rauch, Terry M CIV OSD HA (US) [terry.m.rauch.osd@hqa.mil](mailto:terry.m.rauch.osd@hqa.mil)

Gerard Riedy - NICOE

VA— Tim O'Leary <[timothy.oleary@va.gov](mailto:timothy.oleary@va.gov)>

Stewart Hoffman [Stuart.Hoffman@va.gov](mailto:Stuart.Hoffman@va.gov)

ACL/HHS

Miller, Cate (ACL/NIDILRR) [Cate.Miller@acl.hhs.gov](mailto:Cate.Miller@acl.hhs.gov)

CDC

Bell, Jeneita (CDC/ONDIEH/NCIPC) [hqp8@cdc.gov](mailto:hqp8@cdc.gov)

Breiding, Matthew J. (CDC/ONDIEH/NCIPC) <[dmv8@CDC.GOV](mailto:dmv8@CDC.GOV)>

Academia/Medical Research Centers -- He mentioned

General TBI/concussion

Geoff Manly (UCSF)

David Hovda (UCLA)

John Povlishock (VCU)

Doug Smith (UPenn)

#### Rehab

Wayne Gordon (Mount Sinai)

Joseph Giacino (Spalding Rehab Hospital)

#### Sports Concussion

Robert C. Cantu (Boston University)

Dawn Comstock (U of Denver)

Mike McCrea (Medical College of Wisconsin)

Christopher Giza (UCLA)

Ross Zafonte (Harvard)

Steve Broglio (U of Michigan)

Kevin Guskiewicz (UNC – Chapel Hill)

Thomas McAllister (Indiana University)

Harvey Levin (Baylor College of Medicine)

Margot Putukian (Princeton)

#### Pediatric

Gerard Gioia (Children's National)

Ann-Christine Duhaime (MGH)

#### Veterans/Active Duty

David Cifu (VCU)

Murray Stein (UCSD)

David Brody (Washington University; St. Louis)

#### Blood based biomarkers:

Elaine Peskind (VA Puget Sound)

Kevin Wang (U of Florida)

Ramon Diaz Arrastia (USUHS)

#### OneMind for Research (non-profit)

Ramona Hicks

General Pete Chiarelli

#### Brain Injury Association (non-profit)

Susan Connors [sconnors@biausa.org](mailto:sconnors@biausa.org)

#### Contractor

COL Dallas Hack (ret.) [dallishack@gmail.com](mailto:dallishack@gmail.com)

#### NHL

Ruben Echemendia: [rechemendia@comcast.net](mailto:rechemendia@comcast.net)

#### Boxing

Barry D. Jordan

#### NCAA

Brian Hainline

Former Players

Cindy Parlow (USA Soccer)

NFL

US Soccer? US Olympics? NFL Players Association?

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tb/tb.htm>

**From:** Rieff, Heather (NIH/NINDS) [E]

**Sent:** Friday, November 20, 2015 5:00 PM

**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]

**Cc:** Scott, Paul (NIH/NINDS) [E]; Zalutsky, Robert (NIH/NINDS) [E]; Mott, Meghan (NIH/NINDS) [E]

**Subject:** House Energy & Commerce Committee Concussion Roundtable

Walter and Pat-

I spoke with John Ohly, House Energy and Commerce Committee staffer, about his plans to put together a Roundtable for Committee members on Concussion—what we know, where the science is, what's needed to achieve success in this area. He realizes there are lots of different issues and lots of ways to come at the issue. But he'd like to have as broad a group as possible to represent and raise as many of these perspectives as possible. At this point he's still trying to aim for December 10<sup>th</sup> (but realizes that is not totally realistic, and so early January might be a possibility).

He asked if we could suggest potential participants from these agencies/groups:

NIH (Walter; other ICs (do you want to include NICHD?))

DoD – he has been put in touch with Dallas Hack, who I said we have interacted with a lot

VA— ???

Other agencies at HHS -- ???

Academia/Medical Research Centers – He mentioned Geoff Manly (UCSF) and Mike McCrea (Medical College of Wisconsin) but would like other suggestions from us as well.

NCAA and NFL will also be invited

Please let me know your suggestions. I told him I'd get back to him in the next few days. He's hoping to have a more concrete plan in the next week or so. Let me know if you have any questions.

Thanks,  
Heather

Heather Rieff, Ph.D.

Office of Science Policy and Planning  
National Institute of Neurological Disorders and Stroke  
NIH, HHS  
301-496-9271  
[riefta@ninds.nih.gov](mailto:riefta@ninds.nih.gov)

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 20 Nov 2015 00:08:27 +0000  
**To:** Gallin, John (NIH/CC/OD) [E]; Chan, Leighton (NIH/CC/RMD) [E]  
**Cc:** Gottesman, Michael (NIH/OD) [E]  
**Subject:** RE: NFL

Maria meets with Francis on Dec 4<sup>th</sup> and was going to lay out the plan. So will prepare with Leighton and Maria for this timeline.

Walter

**From:** Gallin, John (NIH/CC/OD) [E]  
**Sent:** Thursday, November 19, 2015 7:01 PM  
**To:** Chan, Leighton (NIH/CC/RMD) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Gottesman, Michael (NIH/OD) [E]  
**Subject:** NFL

Leighton

I spoke with Walter and Michael this evening. We all agree Francis needs to be briefed. Walter will prepare a written briefing and run it by all of us. Thanks for briefing me this afternoon.

John

**John I. Gallin, M.D.**  
**Director, Clinical Center**  
**National Institutes of Health**  
**10 Center Drive, RM 6-2551, MSC 1504**  
**Bethesda, MD 20892-1504**  
**Phone: (301) 496-4114**  
**Fax: (301) 402-0244**  
**Email: jig@nih.gov**



**From:** Rieff, Heather (NIH/NINDS) [E]  
**Sent:** 18 Nov 2015 15:11:11 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: Potential Concussion Roundtable for Members

Ok thanks. Agree. Would you want to include NICHD or other ICs?  
I'm going to reach out to the staffer and will make the suggestion re: VA.  
Heather

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Wednesday, November 18, 2015 3:09 PM  
**To:** Rieff, Heather (NIH/NINDS) [E]  
**Subject:** Re: Potential Concussion Roundtable for Members

Think we want to be at the table. Will be lots of agendas and interests on display, especially given the movie coming out~ Dec 10th/

They should include VA.  
walter

**From:** "Rieff, Heather (NIH/NINDS) [E]" <rieffh@ninds.nih.gov>  
**Date:** Wednesday, November 18, 2015 at 3:05 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetz@ninds.nih.gov>, Paul Scott <ScottP@ninds.nih.gov>, Paula Walker <walkerp@ninds.nih.gov>  
**Cc:** Meghan Mott <meghan.mott@nih.gov>  
**Subject:** Potential Concussion Roundtable for Members

Walter- We received the email below from John Ohly, House Energy and Commerce Committee staff, on the idea of putting together a "roundtable or forum with a range of stakeholders from government (DOD, NIH, HHS), athletics (NFL, NCAA, etc), academia and medical research community, and potentially some advocacy groups" to discuss concussion research/prevention/treatment. The discussion(s) would be open to Members but closed to the public.

It sounds like this is still in the planning stages, although John asked if we could look at Dec 10<sup>th</sup> or dates around it as possibilities.

Let me know your thoughts when you have a chance. I've cc-ed Paula who can comment on your availability around that time.

Thanks,  
Heather

---

**From:** Ohly, John [mailto:john.ohly@mail.house.gov]  
**Sent:** Wednesday, November 18, 2015 2:27 PM  
**To:** Torborg, Christine (NIH/NINDS) [E]  
**Subject:** Concussions

Good Afternoon Christine,

It has been some time since we touched-base on the issue of concussions. Recently, however, I received the green light to move forward with a proposal that I hope will help advance the dialogue on the issue. The concept, at a high level, is to bring key stakeholders to the table for a discussion (or discussions) about where we are today and where we need to go to improve our understanding, diagnosis and treatment of concussions. Areas I would like to address include, but are not limited to:

- the state of the science (what we know, do not know, etc);
- what are the critical knowledge gaps and why do they exist;
- what are the most critical short and long term objectives if we hope to achieve meaningful progress minimizing the risks of concussions (whether in fundamental understanding of TBI/mTBI, diagnosis, treatment, prevention, education/public awareness, etc)
- who is doing what in the research field and how do those efforts contribute to the short-and-long term objectives; and,
- what, if any, coordination exists or is needed to ensure that disparate research projects contribute to short-and-long term objectives (without stifling innovation).

A key part of this endeavor is to advance the conversation and relevancy of this issue beyond traditional boundaries. One example is the overwhelming association of concussions with sports. Athletes are certainly at risk and thus key constituency but, at its core, this is a public health issue – not just a sports issue. In addition, all too often public debate centers on the “risk” or “danger” of concussions. This is an opportunity to take the narrative a step further and highlight the challenges associated in addressing the risks of concussions, especially in light of gaps in the scientific and medical understanding of the head injuries.

The vision, at least at present, is to begin with a roundtable or forum with a range of stakeholders from government (DOD, NIH, HHS), athletics (NFL, NCAA, etc), academia and medical research community, and potentially some advocacy groups. Obviously, that could become a rather large group so I will need to do some homework to keep it manageable without artificially limiting the scope or range of opinions. I believe the initial event would be open to Members but closed to the public with the hope of encouraging a candid dialogue.

I am just beginning my outreach but given the importance of Dr. Koroshetz (or a similarly qualified representative from NIH) to the discussion, I wanted to put it on your radar as soon as possible. Ideally, we would like to schedule something before the Members depart in December but I also realize that is a fairly short timeline to bring all the relevant parties to the table. Tentatively, I am targeting December 10 but that may shift. I will keep you posted as the details take shape but if you can look into the feasibility of that date, or dates around that time, I would greatly appreciate your assistance.

In addition, I may reach out for NIH's thoughts/assistance with regard to other participants. It is my hope that working with you all and other key stakeholders, we can pull together a group of the best minds and a diversity of perspectives to advance our understanding and ability to address this challenge.

As always, happy to discuss if you have thoughts or questions.

Thanks,  
John Ohly  
House Committee on Energy and Commerce

**From:** Wolf-Rodda, Julie (FNIH) [T]  
**Sent:** 18 Nov 2015 14:33:16 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/NINDS) [E]; James, Stephanie (FNIH) [T]  
**Subject:** SHRP -- info for Leighton Chan  
**Attachments:** SHRP Research Plan 2 Collaborative Research on CTE (U01) fully executed March 2013.pdf

Hi Walter,

I just spoke with Leighton Chan, who wanted guidance on how to fill out the Research Plan template for the project he's proposing for SHRP funds. We spoke about a number of things, including the level of internal NIH review he should have (I gather this would definitely include you and several others), how he might present the budget, and how the plan might ultimately be presented to NFL. He asked to see an example of an earlier research plan. I thought perhaps the one for the CTE Neuropathology Study (attached) might be good to show him—but I wanted your OK before sharing it with him. What do you think?

Thanks for your guidance.

Best,  
Julie

Julie Wolf-Rodda  
Director of Development  
Foundation for the National Institutes of Health  
9650 Rockville Pike | Bethesda, MD 20814 | [fnih.org](http://fnih.org)  
Direct (301) 402-6027 | [jwolf-rodga@fnih.org](mailto:jwolf-rodga@fnih.org)

REDISCOVER THE FNIH AT [fnih.org](http://fnih.org)



**Collaborative Research on Chronic Traumatic Encephalopathy and Delayed  
Effects of Traumatic Brain Injury: Neuropathology and Neuroimaging  
Correlation**

**RESEARCH PLAN – SCHEDULE NO. 2**

This **RESEARCH PLAN – SCHEDULE NO. 2** (hereinafter referred to as the "Research Plan"), dated as of March 12 2013, describes research that will be initiated and carried out by the National Institutes of Health ("NIH") and made possible by the Foundation for the National Institutes of Health, Inc., ("FNIH") through a gift from the National Football League ("NFL").

**WHEREAS**, the NFL and FNIH have entered into that certain Master Letter of Agreement, dated as of September 1, 2012 (as amended, supplemented or otherwise modified from time to time, the "Agreement"; capitalized terms used and not otherwise defined herein shall have the meaning set forth in the Agreement); and

**WHEREAS**, the Agreement contemplates that the parties will agree to certain Research Plans as part of the Program, which Research Plans shall set forth certain details and specifications necessary to accomplish research in the scientific areas provided.

**NOW, THEREFORE**, the NFL, FNIH and NIH hereby agree as follows:

1. **AREA OF RESEARCH:** This initiative will provide a competitive opportunity for a multicenter team to: 1) more fully characterize the neuropathology associated with chronic traumatic encephalopathy (CTE) and delayed effects of traumatic brain injury (TBI) through systematic, rigorous, and collaborative studies of post-mortem biospecimens; 2) validate the neuropathological criteria for a post-mortem diagnosis of CTE and delayed post-traumatic neurodegenerative diseases through independent and blinded analyses; 3) provide a better understanding of the incidence and prevalence of CTE, and 4) identify neuroimaging signatures of the neuropathology as a foundation for the development of diagnostic tools in the future. Specific research areas of interest include:
  - a. Similarities and differences between the neuropathology of CTE and the delayed effects of TBI.
  - b. Validation studies for the post-mortem diagnosis of CTE and the delayed effects of TBI.
  - c. Identification of a neuroimaging signature on post-mortem brain specimens that correlates with the histological data.
  - d. Development of a brain donor program that leverages the resources available through the NIH Neurobiobank to enable studies aimed at a better understanding of the incidence and prevalence of CTE; correlating clinical signs, symptoms, and risk factors for CTE with neuropathology.
  - e. Hypothesis-driven projects to elucidate the biologic basis of CTE and the delayed effects of TBI.
2. **DESCRIPTION OF WORK EXPECTED TO BE ACCOMPLISHED:** This research plan entails funding one of the grant applications received by NIH in response to a Request for Applications (RFA) for research on chronic traumatic encephalopathy and delayed effects of traumatic brain injury emphasizing the correlation between neuropathology and neuroimaging. The U01 Cooperative Agreement is the recommended funding mechanism for this effort because it allows for

significant NIH Program staff involvement, which will be required to monitor the progress, benchmarks and timelines established for this multicenter initiative. This initiative will support a multicenter, systematic and comprehensive investigation of the neuropathology of CTE and the delayed effects of TBI using post-mortem biospecimens, and histological and neuroimaging tools as a foundation for future studies to develop *in vivo* diagnostics. The principal criteria for success of the initiative will be the following:

- a. Collaborative research on post-mortem brain tissue to clarify and expand our understanding of the neuropathology associated with CTE and the delayed effects of TBI.
  - b. Establishment of a brain-donor program to link high quality behavioral information with neuropathology.
  - c. Coordinated neuroimaging and neuropathology research on post-mortem brain tissue as a foundation for developing diagnostic tools on live subjects.
3. **TIMELINE:** It is expected that an RFA will be issued in March 2013 with a grant application due date of June 1, 2013 and review in late summer of 2013 for a NINDS Council funding decision in October 2013. Research support will be for 4 years.
  4. **REPORTING SCHEDULE:** The FNIH will provide annual financial and scientific progress report to the NFL on this initiative.
  5. **USE OF FUNDS:** The anticipated cost of this initiative is as follows.

Oct-13	2,500,000	for research grant(s)
Oct-14	2,500,000	for research grant(s)
Oct-15	2,500,000	for research grant(s)
Oct-16	2,500,000	for research grant(s)

FNIH direct costs:	106,452	(includes travel 4 FNIH staff to NYC 1/year, 1 SB meeting in DC & events staff costs/year, travel for 2 Principal Investigators to 1 SB meeting in DC/year, FNIH staff time)
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Subtotal:	10,106,452
FNIH admin @1%	101,065
<b>TOTAL</b>	<b><u>10,207,517</u></b>

6. **PAYMENT TERMS:**

Payment 0 - \$2,551,880 from funds already transferred to FNIH  
 Payment 1 - \$2,551,879 due to FNIH by June 1, 2014 (for year 2)  
 Payment 2 - \$2,551,879 due to FNIH by June 1, 2015 (for year 3)  
 Payment 3 - \$2,551,879 due to FNIH by June 1, 2016 (for year 4)

7. **KEY FNIH AND NIH PERSONNEL:**

- a. **FNIH** – Andrea Baruchin, Director NIH Relations; Julie Wolf-Rodda, Director of Partnership Development; Stephanie James, Director of Science
- b. **NIH/NINDS** – Walter Koroshetz, Deputy Director; Ramona Hicks, Program Manager; Rebecca Frederick, AAAS Science Policy Fellow

IN WITNESS WHEREOF, the parties have executed this Research Plan, effective as of the date first written above.

THE NATIONAL FOOTBALL LEAGUE

By: [Signature]  
Name: Robert Pelham  
Title: CEO  
Date: 2/19/2013

FOUNDATION FOR THE NATIONAL INSTITUTES OF HEALTH, INC.

By: [Signature]  
Name: Charles A. Sanders, MD  
Title: Chairman  
Date: 3-12-2013  
Tax ID No: 52-1886675

THE NATIONAL INSTITUTES OF HEALTH (NINDS)

By: [Signature]  
Name: [Signature]  
Title: Director NINDS  
Date: 2/22/2013

**From:** Chan, Leighton (NIH/CC/RMD) [E]  
**Sent:** 18 Nov 2015 14:05:22 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** NFL

Great-

(b) (5)



(b) (5)



LC

---

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: 301-496-4733  
Fax: 301-402-0663  
Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Wednesday, November 18, 2015 1:49 PM  
**To:** Chan, Leighton (NIH/CC/RMD) [E]  
**Subject:** Re: Robert Stern

(b) (5)



Walter

**From:** Leighton Chan <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)>  
**Date:** Tuesday, November 17, 2015 at 5:09 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Subject:** Robert Stern

(b) (5)





LC

---

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: 301-496-4733

Fax: 301-402-0663

Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>

**From:** Chan, Leighton (NIH/CC/RMD) [E]  
**Sent:** 17 Nov 2015 12:37:36 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** FW: SHRP update

Hi Walter- See below

Just got off the phone with Russ. Got time for another call?

LC

---

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: 301-496-4733  
Fax: 301-402-0663  
Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>

**From:** Freire, Maria (FNIH) [T]  
**Sent:** Tuesday, November 17, 2015 11:37 AM  
**To:** Chan, Leighton (NIH/CC/RMD) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; James, Stephanie (FNIH) [T]; Wolf-Rodda, Julie (FNIH) [T]  
**Subject:** SHRP update

Leighton,

We just had a call with Russ and Jeff Miller in which we assured them that FNIH could accommodate support for a longitudinal study through you, if that is what NIH ultimately decides is the best path forward. We noted that we have sent you the research plan template and that you were working on a proposal, for which Jeff was grateful. We did not discuss budget, although we did make the point that we are still asking NFL to consider partial support for the NINDS RFA. It is our understanding that Russ will call you today to discuss the proposal. Jeff also mentioned that you had called him last week but that you had not connected yet. Once you have completed the research plan, please send it to us so we can formally send it to NFL for their consideration, according to our agreement with them. I will update Francis know where we are at my next meeting, December 4<sup>th</sup>, or earlier if needed. Best, Maria

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 17 Nov 2015 11:37:29 -0500  
**To:** Freire, Maria (FNIH) [T]  
**Subject:** Re: SHRP update

Thanks Maria.  
walter

**From:** "Freire, Maria (FNIH) [T]" <mfreire@fnih.org>  
**Date:** Tuesday, November 17, 2015 at 11:36 AM  
**To:** Leighton Chan <chanle@cc.nih.gov>  
**Cc:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzw@ninds.nih.gov>, "James, Stephanie (FNIH) [T]" <sjames@fnih.org>, Julia Wolf-Rodda <jwolf-rodde@fnih.org>  
**Subject:** SHRP update

Leighton,

We just had a call with Russ and Jeff Miller in which we assured them that FNIH could accommodate support for a longitudinal study through you, if that is what NIH ultimately decides is the best path forward. We noted that we have sent you the research plan template and that you were working on a proposal, for which Jeff was grateful. We did not discuss budget, although we did make the point that we are still asking NFL to consider partial support for the NINDS RFA. It is our understanding that Russ will call you today to discuss the proposal. Jeff also mentioned that you had called him last week but that you had not connected yet. Once you have completed the research plan, please send it to us so we can formally send it to NFL for their consideration, according to our agreement with them. I will update Francis know where we are at my next meeting, December 4<sup>th</sup>, or earlier if needed. Best, Maria

**From:** Freire, Maria (FNIH) [T]  
**Sent:** 16 Nov 2015 21:05:26 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Re: Conference Call

I have a meeting Dec 4th but I can get to him earlier, if needed.

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Monday, November 16, 2015 9:03 PM  
**To:** Freire, Maria (FNIH) [T]  
**Subject:** Re: Conference Call

yep. I have been speaking with Leighton. Question is when to pass plan by FC?  
Walter

Sent from my iPhone

On Nov 16, 2015, at 3:03 PM, Freire, Maria (FNIH) [T] <[mfreire@fnih.org](mailto:mfreire@fnih.org)> wrote:

Walter, FYI. M.

**From:** Lonser, Russell (NIH/NINDS) [V]  
**Sent:** Monday, November 16, 2015 2:49 PM  
**To:** Freire, Maria (FNIH) [T] <[mfreire@fnih.org](mailto:mfreire@fnih.org)>; 'Miller, Jeff' <[Jeff.Miller@NFL.com](mailto:Jeff.Miller@NFL.com)>  
**Cc:** James, Stephanie (FNIH) [T] <[sjames@fnih.org](mailto:sjames@fnih.org)>; Wolf-Rodda, Julie (FNIH) [T] <[jwolf-rodde@fnih.org](mailto:jwolf-rodde@fnih.org)>; Gray, Felicia (FNIH) [T] <[fgray@fnih.org](mailto:fgray@fnih.org)>  
**Subject:** Re: Conference Call

Great. Thanks.

**From:** "Freire, Maria (FNIH) [T]" <[mfreire@fnih.org](mailto:mfreire@fnih.org)>  
**Date:** Monday, November 16, 2015 2:40 PM  
**To:** Jeffrey Miller <[Jeff.Miller@NFL.com](mailto:Jeff.Miller@NFL.com)>, Russell Lonser <[lonserR@ninds.nih.gov](mailto:lonserR@ninds.nih.gov)>  
**Cc:** "James, Stephanie (FNIH) [T]" <[sjames@fnih.org](mailto:sjames@fnih.org)>, "Wolf-Rodda, Julie (FNIH) [T]" <[jwolf-rodde@fnih.org](mailto:jwolf-rodde@fnih.org)>, "Gray, Felicia (FNIH) [T]" <[fgray@fnih.org](mailto:fgray@fnih.org)>  
**Subject:** RE: Conference Call

OK, great. Let's confirm tomorrow at 11am. Please use this dial-in information:

Phone Number: 877-662-(b) (6)  
Passcode: (b) (6)

**From:** Miller, Jeff [<mailto:Jeff.Miller@NFL.com>]  
**Sent:** Monday, November 16, 2015 1:37 PM  
**To:** Lonser, Russell (NIH/NINDS) [V] <[LonserR@ninds.nih.gov](mailto:LonserR@ninds.nih.gov)>; Freire, Maria

(FNIH) [T] <mfreire@fnih.org>

**Cc:** James, Stephanie (FNIH) [T] <s.james@fnih.org>; Wolf-Rodda, Julie (FNIH) [T] <jwolf\_rodde@fnih.org>

**Subject:** RE: Conference Call

Sounds good.

**From:** Lonser, Russell (NIH/NINDS) [V] [mailto:LonserR@ninds.nih.gov]

**Sent:** Monday, November 16, 2015 1:20 PM

**To:** Freire, Maria (FNIH) [T]; Miller, Jeff

**Cc:** James, Stephanie (FNIH) [T]; Wolf-Rodda, Julie (FNIH) [T]

**Subject:** Re: Conference Call

How about 11 AM tomorrow? Jeff, does that work for you?

**From:** "Freire, Maria (FNIH) [T]" <mfreire@fnih.org>

**Date:** Monday, November 16, 2015 1:11 PM

**To:** Russell Lonser <lonserR@ninds.nih.gov>, Jeffrey Miller <Jeff.Miller@NFL.com>

**Cc:** "James, Stephanie (FNIH) [T]" <s.james@fnih.org>, "Wolf-Rodda, Julie (FNIH) [T]" <jwolf\_rodde@fnih.org>

**Subject:** RE: Conference Call

Hi, Russ, thanks for your note. We are available tomorrow from 11 – 2pm and Friday after 2pm. Unfortunately, I am chairing the FDA Science Board on Wednesday and in NC on Thursday. Do any of these windows work? I will be traveling overseas the week of Thanksgiving, so this week is better or after the 30<sup>th</sup>. Best, Maria

**From:** Lonser, Russell (NIH/NINDS) [V]

**Sent:** Monday, November 16, 2015 12:55 PM

**To:** Freire, Maria (FNIH) [T] <mfreire@fnih.org>; Jeffrey Miller <Jeff.Miller@NFL.com>

**Subject:** Conference Call

Hi Maria,

Jeff Miller and I were wanting to see if we could set up a conference call this week. We have been talking with Leighton Chan (he said he has had conversations with you, as well) and others about potential funding opportunities in NIH/CNRM.

Do you have time to talk this week?

Best,

Russ

Russell R. Lonser, M.D.  
Professor and Chair

Department of Neurological Surgery  
Ohio State University Wexner Medical Center  
410 West 10th Avenue  
Columbus, Ohio 43221  
Phone: 614-685-6985

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 13 Nov 2015 01:15:34 +0000  
**To:** 'Lonser, Russell'; 'Richard Ellenbogen'; 'Hunt Batjer'  
**Subject:** RE: brain bank stuides coming out with high frequency of finding CTE

Wow. That's amazing. Hypothesizing that Phospho Tau starting out in 20 year olds in LC.  
walter

**From:** Lonser, Russell [mailto:Russell.Lonser@osumc.edu]  
**Sent:** Thursday, November 12, 2015 1:35 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; 'Richard Ellenbogen'; 'Hunt Batjer'  
**Subject:** Re: brain bank stuides coming out with high frequency of finding CTE

Here are a couple of articles (one is the Braak). A good study would be to define the distribution of abnormal tau (see if it is diagnostic of what would be considered CTE) in normal patients.

**From:** Walter Koroshetz <koroshetzw@ninds.nih.gov>  
**Date:** Wednesday, November 11, 2015 8:45 PM  
**To:** Russell Lonser <Russell.Lonser@osumc.edu>, 'Richard Ellenbogen' <rge@neurosurgery.washington.edu>, Hunt Batjer <hunt.Batjer@UTSouthwestern.edu>  
**Subject:** Re: brain bank stuides coming out with high frequency of finding CTE

Have never seen that from Braak. Do you have a reference?  
Walter

**From:** Russell Lonser <Russell.Lonser@osumc.edu>  
**Date:** Tuesday, November 10, 2015 at 10:22 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzw@ninds.nih.gov>, Richard Ellenbogen <rge@neurosurgery.washington.edu>, Hunt Batjer <Hunt.Batjer@UTSouthwestern.edu>  
**Subject:** RE: brain bank stuides coming out with high frequency of finding CTE

A large problem is that none of the studies have examined clinically normal individuals. Prior pathology studies (Braak) have shown that nearly every person (autopsy brain) older then 10 years of age (in age related amounts) has abnormal tau in brain but no clinical effect.

Sent with Good ([www.good.com](http://www.good.com))

-----Original Message-----

**From:** Koroshetz, Walter (NIH/NINDS) [E] [mailto:koroshetzw@ninds.nih.gov]  
**Sent:** Tuesday, November 10, 2015 10:16 AM Eastern Standard Time  
**To:** Lonser, Russell; Richard Ellenbogen; Hunt Batjer  
**Subject:** Re: brain bank stuides coming out with high frequency of finding CTE

yes. it's really an unknown. From public health standpoint it really Increases importance of careful longitudinal study to see what constellation of findings predicts progression to cognitive impairment, and when one can make that prediction accurately.

of note the early descriptions by Corsellis did include a behavioral syndrome before the cognitive decline.

if there is a behavioral syndrome that does not progress to cognitive impairment that would be tough to ID.  
would have to have unique features.

Would have to study high risk "normal" group prospectively with matched controls

walter

Walter

Sent from my iPhone

On Nov 10, 2015, at 5:20 AM, Lonser, Russell <[Russell.Lonser@osumc.edu](mailto:Russell.Lonser@osumc.edu)> wrote:

Thanks Walter. Does question the clinical significance of the pathologic findings.

**From:** Walter Koroshetz <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>

**Date:** Monday, November 9, 2015 at 10:49 AM

**To:** Jeffrey Miller <[Jeff.Miller@NFL.com](mailto:Jeff.Miller@NFL.com)>, "Ellenbogen, Richard (rge@neurosurgery.washington.edu)" <[rge@neurosurgery.washington.edu](mailto:rge@neurosurgery.washington.edu)>, Russell Lonser <[russel.lonser@osumc.edu](mailto:russel.lonser@osumc.edu)>, Hunt Batjer <[hunt.Batjer@UTSouthwestern.edu](mailto:hunt.Batjer@UTSouthwestern.edu)>, "Freire, Maria (FNIH) [T]" <[mfreire@fnih.org](mailto:mfreire@fnih.org)>

**Subject:** brain bank studies coming out with high frequency of finding CTE

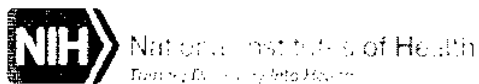
FYI- The CTE consensus guidelines from the grantees allowed others to start looking in their brain banks. Attached two studies of reports of finding CTE in Brain Banks. These are not biased for professional athletes but are biased for people who die with neurological disorders.

But raises possibility that CTE may be relatively common in persons with history of various types of TBI. If so, then the clinical significance of the pathologic finding becomes the BIG question for the public health.

Walter

Walter Koroshetz, MD

Director, National Institute of Neurological Disorders and Stroke



<image001.png>



**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 12 Nov 2015 20:47:23 +0000  
**To:** Mott, Meghan (NIH/NINDS) [E]  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Re: Meeting Request to discuss CTE/Brain Injury

I'll head over. I was thinking that this meeting was unnecessary but her persistence won out

Patrick SF Bellgowan, PhD  
Program Director  
NINDS / NIH  
301-496-1447  
[Pat.bellgowan@nih.gov](mailto:Pat.bellgowan@nih.gov)

On Nov 12, 2015, at 3:35 PM, "Mott, Meghan (NIH/NINDS) [E]" <[meghan.mott@nih.gov](mailto:meghan.mott@nih.gov)> wrote:

Hi Pat,

You are welcome to join the meeting if you want to! We are headed back to 31 now from NSC.

Thanks,  
Meghan

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Thursday, November 12, 2015 10:04 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Re: Meeting Request to discuss CTE/Brain Injury

So I spoke with the TRACK and TED investigators/ surgeons and pathologist who agree that brains are needed but they need to be characterized by, at least, a retrospective interview. I'm at the BD2K meeting in intramural campus today if u want me to join your meeting.

It seems that Paul Allen foundation has a strong interest in jumping into the TBI field. I discussed some of the gaps and opportunities and am organizing another call if you have any more "impactful" or high risk projects that they could either sponsor or contribute to I would be happy to forward to them

Thanks  
Pat

Patrick SF Bellgowan, PhD  
Program Director  
NINDS / NIH

301-496-1447

[Pat.bellgowan@nih.gov](mailto:Pat.bellgowan@nih.gov)

On Nov 8, 2015, at 8:20 PM, "Koroshetz, Walter (NIH/NINDS) [E]"  
<[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)> wrote:

I see. So this would be the severe cases which usually go onto brain death.  
MVA's and bad falls.

Might ask someone like Povlishock if this is a need for the field.

Walter

Sent from my iPhone

On Nov 5, 2015, at 9:58 PM, Bellgowan, Patrick (NIH/NINDS) [E]  
<[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)> wrote:

Hi Walter,

Here is a better description of where this stands: (I sent this message to Anna Taylor to help answer some of the questions)  
At a recent TBI conference I met with Dr Rosseau who is a Member at Large, Board of Directors, Association of Neurological Surgeons (AANS) and (according to Wikipedia) one of President Obama's candidates to be Surgeon General. Dr. Rosseau was taken aback by the lack of TBI brain donations and is ready to present a plan to the Directors of the Association for Neurological Surgeons that would make it a standard of professional practice to have Neurosurgeons present at the death of TBI patient ask the family about brain donation. This could be a huge bonus for the TBI field. I need to provide her with an overview of how this might work using the NeuroBiobank. It seems pretty straightforward to me with the following exceptions:

- 1) Do the banks have a standard Informed Consent that the neurosurgeons could use?
- 2) Are there established inclusion/exclusion criteria for donation of TBI brains?
- 3) would there be in costs to the Hospital and/or doctor if this were implemented?

Here is her Wikipedia page, it seems she has pretty strong political connections:

[https://en.wikipedia.org/wiki/Gail\\_Rosseau](https://en.wikipedia.org/wiki/Gail_Rosseau)

Patrick SF Bellgowan, PhD

Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Thursday, November 05, 2015 5:21 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Re: Meeting Request to discuss CTE/Brain Injury

Got it. Thanks Pat  
W

Sent from my iPhone

On Nov 5, 2015, at 3:50 PM, Bellgowan, Patrick (NIH/NINDS) [E]  
<[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)> wrote:

She is a neurosurgeon who is a current board member on the neurosurgeon association. She would like to propose that the neurosurgeon associate consider asking for brain donation in cases where the surgeon is required to be attending. I presented that the neurobiobank would be a great resource if she could get Drs to do that as part of professional service. I mentioned your name but am not sure she needs to speak with you. She's a pure clinician and thus it was challenging to explain how the neurobiobank works e.g. She had never heard of NINDS. But she is sincere about bringing this forward.

Pat

Patrick SF Bellgowan, PhD  
Program Director  
NINDS / NIH  
301-496-1447  
[Pat.bellgowan@nih.gov](mailto:Pat.bellgowan@nih.gov)

On Nov 5, 2015, at 2:28 PM, "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)> wrote:

Dear Pat,  
Any idea what the Innova person wants to discuss?

Walter

**From:** Paula Walker  
<[walkerp@ninds.nih.gov](mailto:walkerp@ninds.nih.gov)>  
**Date:** Thursday, November 5, 2015  
at 1:10 PM  
**To:** "Koroshetz, Walter (NIH/NINDS)  
[E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Subject:** Meeting Request to discuss  
CTE/Brain Injury

Hi Walter:

Meghan took a call requesting a meeting with you and Dr. Rosseau, Vice Chairman of Neurosciences at Inova Fairfax Hospital. She would like to meet with you to discuss CTE/Brain Injury. She spoke with Pat Berigwan yesterday.

Meghan offered her next Thursday, November 12<sup>th</sup> in the afternoon.

Do you want to meet with her and if so, who else would you like to invite?

Thanks.

Paula Walker

**From:** Mancini, Barbara  
[mailto:[Barbara.Mancini@inova.org](mailto:Barbara.Mancini@inova.org)]  
**Sent:** Thursday, November 05, 2015  
12:28 PM  
**To:** Walker, Paula (NIH/NINDS) [E]  
**Subject:** please schedule meeting  
with Dr.Koroshetz and Dr. Rosseau

Paula,

I just spoke with Meghan Mott about scheduling a meeting to discuss CTE/Brain Injury next Thursday at 230 with Dr Rosseau, who is our Vice

Chairman of Neurosciences at Inova Fairfax Hospital and Dr. Koroshetz. She is currently attending the DOD Blast Injury Research Program in Mclean VA and yesterday spoke to Patrick Bellgowan about some important recommendations that she would like to discuss with Dr. Koroshetz.

Megan thought next Thursday, November 12 at 230 would be the best time for them to meet next week. Please confirm this appointment so I can add it to her calendar.

Thank you

Barbara Mancini

## **Barbara Mancini,**

RN, MBA, CNRN,FAHA  
Director of Growth And Operations  
Neurosciences  
Inova Fairfax Medical Campus  
Office 703-776-3693  
Cell 571-237-**(b) (6)**  
Fax 703-776-4018

**From:** Freire, Maria (FNIH) [T]  
**Sent:** 12 Nov 2015 17:20:33 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** FW: "Concussion" Article

Walter, FYI. M.

**From:** Klock, Kevin (FNIH) [T]  
**Sent:** Thursday, November 12, 2015 4:46 PM  
**To:** Freire, Maria (FNIH) [T] <mfreire@fnih.org>; James, Stephanie (FNIH) [T] <sjames@fnih.org>  
**Subject:** "Concussion" Article

Article by a major NFL beat writer (Mike Freeman). Says "perhaps the movie's greatest accomplishment is the mainstreaming of the neurological science."

[http://bleacherreport.com/articles/2588458-for-nfl-fans-concussion-movie-will-be-heartbreaking-enlightening-disturbing?utm\\_source=cn.com&utm\\_medium=referral&utm\\_campaign=editorial](http://bleacherreport.com/articles/2588458-for-nfl-fans-concussion-movie-will-be-heartbreaking-enlightening-disturbing?utm_source=cn.com&utm_medium=referral&utm_campaign=editorial)

**Kevin A. Klock, JD**  
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ORIGINAL ARTICLE

## Stages of the Pathologic Process in Alzheimer Disease: Age Categories From 1 to 100 Years

Heiko Braak, MD, Dietmar R. Thal, MD, Estifanos Ghebremedhin, MD, and Kelly Del Tredici, MD, PhD

### Abstract

Two thousand three hundred and thirty-two nonselected brains from 1- to 100-year-old individuals were examined using immunocytochemistry (AT8) and Gallyas silver staining for abnormal tau; immunocytochemistry (4G8) and Campbell-Switzer staining were used for the detection of  $\beta$ -amyloid. A total of 342 cases was negative in the Gallyas stain but when restaged for AT8 only 10 were immunonegative. Fifty-eight cases had subcortical tau predominantly in the locus coeruleus, but there was no abnormal cortical tau (ie, theoretical Stages a-c). Cortical involvement (ie, initial tau in neurites) was identified first in the transentorhinal region (Stage Ia, 38 cases). Transentorhinal pyramidal cells displayed pretangle material (Stage Ib, 236 cases). Pretangles gradually became argyrophilic neurofibrillary tangles (NFTs) that progressed in parallel with NFT Stages I to VI. Pretangles restricted to subcortical sites were seen chiefly at younger ages. Of the total cases, 1,031 (44.2%) had  $\beta$ -amyloid plaques. The first plaques occurred in the neocortex after the onset of tauopathy in the brainstem. Plaques generally developed in the 40s in 4% of all cases, culminating in their tenth decade (75%).  $\beta$ -amyloid plaques and NFTs were significantly correlated ( $p < 0.0001$ ). These data suggest that tauopathy associated with sporadic Alzheimer disease may begin earlier than previously thought and possibly in the lower brainstem rather than in the transentorhinal region.

**Key Words:** Alzheimer disease;  $\beta$ -amyloid; Brainstem; Hyperphosphorylated tau protein; Locus coeruleus; Pretangles neurofibrillary tangles; Neuronal threads.

### INTRODUCTION

From beginning to end, the pathologic processes underlying sporadic (versus familial) Alzheimer disease (AD) are

confined to the human CNS and chiefly include intraneuronal formation of abnormal tau protein and extracellular deposition of  $\beta$ -amyloid protein (1). Alzheimer disease-related lesions develop at given predilection sites within the brain and progress according to a predictable sequence from there to hitherto uninvolved areas (2-7).

Once initiated, the process progresses for decades without remission until it crosses a threshold to clinically recognizable dysfunction (6). Recently, we found that intraneuronal lesions associated with AD occur before puberty or in early young adulthood and most often affect noradrenergic projection neurons of the locus coeruleus, one of several subcortical nuclei that generate diffuse projections to the cerebral cortex (8). Abnormal tau can be visualized by immunohistochemistry with the antibody AT8, which recognizes a phosphate-dependent epitope at serine 202 and threonine 205 (9). Alzheimer disease may begin with misfolded and abnormally phosphorylated tau protein in the proximal axon of caeruleus projection neurons (8). Thereafter, similar material fills the somatodendritic compartment of involved cells. This soluble and nonargyrophilic "pretangle" material gradually aggregates into insoluble fibrillary and argyrophilic neuropil threads (NTs) in dendritic processes and into neurofibrillary tangles (NFTs) in neuronal somata. These inert neurofibrillary changes of the Alzheimer type are resistant to autophagy and other endogenous cellular removal mechanisms (10-15).

To obtain greater insight into the AD-related pathologic processes in a large cohort, tau lesions were reexamined in 2,332 nonselected autopsy cases ranging in age from 1 to 100 years. Particular attention was paid to a subpopulation consisting of 342 cases, which, when they were studied with only the Gallyas silver technique, lacked argyrophilic intraneuronal lesions (NFTs/NTs) at the typical cortical predilection sites. Subsequently, all 342 cases were assessed by immunohistochemistry for abnormally phosphorylated tau protein (AT8). Sections of 100  $\mu$ m thickness were made through medial portions of the temporal lobe and through the midbrain and pontine tegmentum to assess brainstem nuclei. The new findings presented here supplement data from an earlier report regarding the frequency of AD-associated argyrophilic lesions in the cerebral cortex in individuals ranging from 26 to 95 years (3).

### MATERIALS AND METHODS

#### Study Cohort

This retrospective autopsy study was performed in compliance with university ethics committee guidelines as well as

From Clinical Neuroanatomy, Department of Neurology (HB, KDT) and Laboratory for Neuropathology, Institute of Pathology (DL, FG), Center for Clinical Research, University of Ulm, Ulm, Germany, and Department of Anatomy and Developmental Biology (FG), School of Biomedical Sciences, University of Queensland, Brisbane, Australia.

Send correspondence and reprint requests to Heiko Braak, MD, Clinical Neuroanatomy, Department of Neurology, Center for Clinical Research, University of Ulm, Helmholtzstrasse 51, 89081 Ulm, Germany. E-mail: heiko.braak@uni-ulm.de

This study was supported by the German Research Council (Deutsche Forschungsgemeinschaft, Grant No. TR1069/1-1 and TR1064/4-1) and the Alzheimer Research Initiative (Alzheimer Forschung Initiative, Grant No. 10810).

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site ([www.neurology.org](http://www.neurology.org)).

German federal and state law governing human tissue usage. Consent for autopsy was obtained for all cases. Brains had been obtained at autopsy and included nonselected cases from affiliated university hospitals. One individual (17-year-old adolescent male) had Down syndrome. The only exclusionary criterion was the presence of tanopathy other than AD or argyrophilic grain disease (AGD), such as Niemann-Pick disease type C, subacute sclerosing panencephalitis, progressive supranuclear palsy, Pick disease, or corticobasal degeneration (16). Neuropathologic diagnoses for all cases were made for AD and AGD, as described (2, 4, 17–19). The 2,332 cases were grouped into 10 age categories by decade (Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>). The ratio of females to males in each age category is shown in Table 1.

### Tissue Fixation, Embedding, and Sectioning

Brainstems and at least a single hemisphere from all individuals were fixed by immersion in 4% buffered aqueous formaldehyde. A set of 2 tissue blocks was excised, embedded in polyethylene glycol (PEG 1000, Merck, Darmstadt, Germany), and sectioned at 100  $\mu$ m, as previously described (4, 8, 20). This section thickness allows for the superimposition of multiple structures, including nerve cells with their entire dendritic tree. The first block was cut at midline level through medial portions of the temporal lobe and encompassed anterior (i.e., uncus) portions of the hippocampal formation and the parahippocampal gyrus (entorhinal region), including the adjoining transentorhinal region as well as portions of the occipitotemporal gyrus and additional gyri of the basal temporal neocortex. The second block was cut through the occipital lobe perpendicular to the calcarine fissure and included high-order visual association areas (peristriate region), a first-order visual association area (parastriate area), and the primary visual field (striate area) (4).

From 342 cases that were negative in the Gallyas stain (i.e., they displayed no argyrophilic NFTs/NTs in the cerebral cortex, particularly in the transentorhinal region), a set of additional blocks was cut perpendicular to the brainstem axis of Meynert. One block was cut through posterior portions of the medulla oblongata at the level of the dorsal motor nucleus of the vagal nerve. A second block showed the pontine tegmentum and contained portions of the locus coeruleus and the

dorsal raphe nucleus. The third block was excised at the level of the inferior colliculus and contained posterior portions of the substantia nigra and supratrochlear portions of the dorsal raphe nucleus (8, 21).

### Staining and Immunocytochemistry

Collections of free-floating sections from all blocks for each case were processed with the following techniques: Pigment-Nissl staining served to show the presence and extent of lipofuscin deposits (aldehyde fuchsin) and basophilic material (Darrow red) (20) and silver staining with the Campbell-Switzer and Gallyas methods to exploit the physical development of nucleation sites. These advanced silver techniques are reliable and are used to visualize  $\beta$ -amyloid deposition (Campbell-Switzer) and argyrophilic neurofibrillary lesions (Gallyas) (4, 17, 19, 20, 22).

Immunohistochemistry included the use of the following antibodies: monoclonal antibody PHF-Tau (1:2000; Clone AT8; Pierce Biotechnology, Rockford, IL) detected hyperphosphorylated tau protein in pretangle material and Alzheimer-type neurofibrillary changes; monoclonal anti  $\beta$ -amyloid antibody (1:5000; Clone 4G8; Covance, Dedham, MA) was used for the detection of  $\beta$ -amyloid deposition.  $\beta$ -amyloid plaque phases were assessed as previously published (5). All immunohistochemistry procedures could be performed on the material that had been stored for long periods in formaldehyde (23).

Tissue sections for immunoreactions were treated for 30 minutes in a mixture of 10% methanol plus 10% concentrated (30% w H<sub>2</sub>O) and 80% Tris. After pretreatment with 100% formic acid for 3 minutes to facilitate the  $\beta$ -amyloid immunoreactions, blocking with bovine serum albumin was performed to prevent nonspecific binding. Subsequently, each of the various sets of free-floating sections was incubated for 18 hours at 20°C using the primary antibodies. After incubation with secondary biotinylated antibody (anti-mouse IgG, 1:200; Vector Laboratories, Burlingame, CA) for 1.5 hours, immunoreactions were visualized with the avidin-biotin complex (ABC, Vectastain; Vector Laboratories) for 2 hours and the chromogen 3,3'-diaminobenzidine tetrahydrochloride (DAB D5637; Sigma, Taufkirchen, Germany). Omission of the primary antibody resulted in nonstaining. Positive and negative control sections were routinely included. The tissue sections were cleared and mounted in a synthetic resin (Permount; Fisher, Fair Lawn, NJ). All sections were viewed, and AD staging was performed with a Vanox AHB53 Olympus microscope (Olympus Optical Co., Tokyo, Japan). Digital micrographs were obtained using the Soft Imaging System (Münster, Germany).

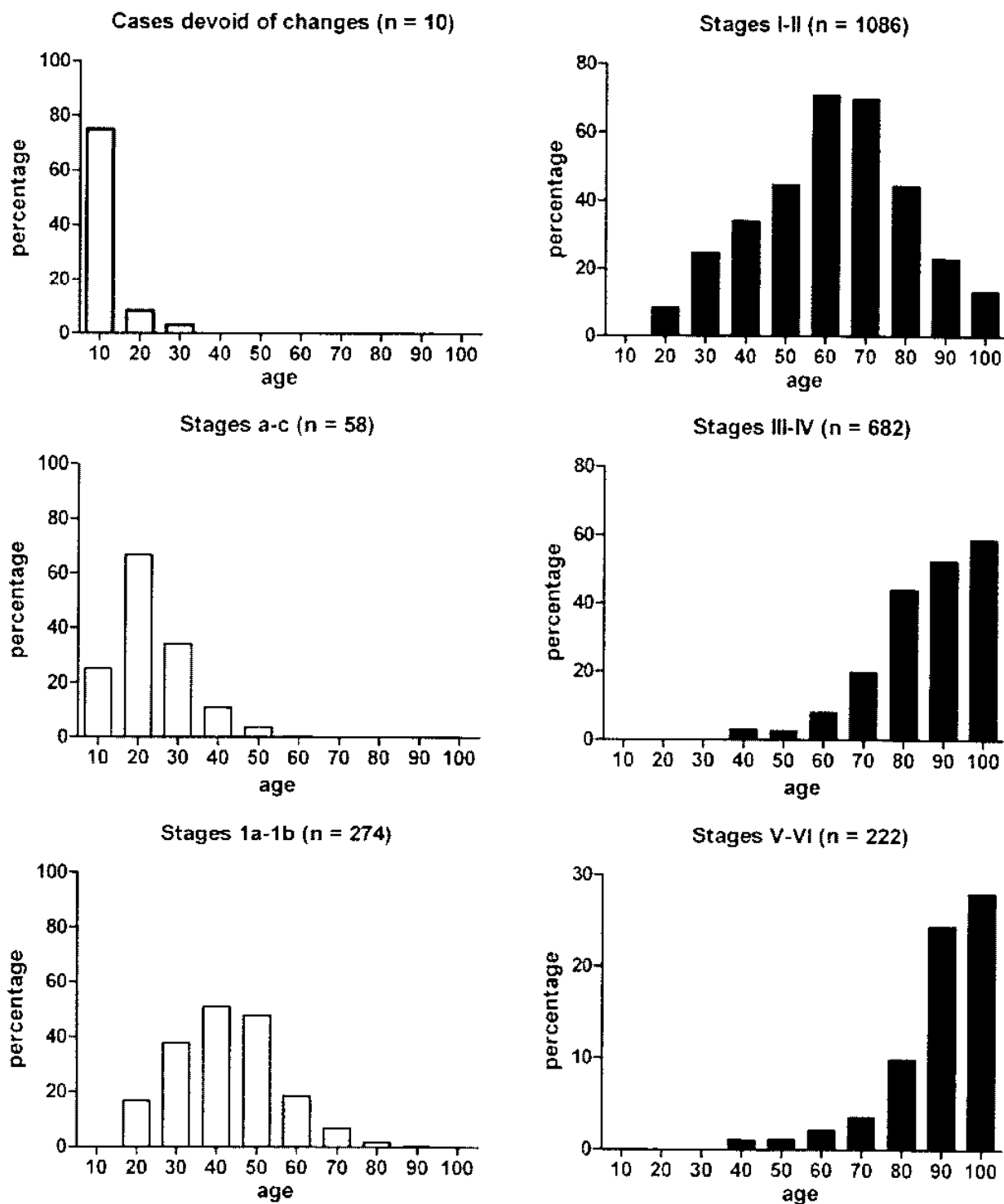
### Statistics

Statistical analysis was performed using the Student *t*-test for independent samples to compare normally distributed continuous variables between 2 groups. The Mann-Whitney *U*-test was used to analyze between group comparisons of ordered variables, and the Spearman  $\rho$  statistics was used for measuring rank correlations. Calculations for males and females were performed separately. Partial correlation analysis was performed to examine the relationship among different pathologic variables after adjusting for the effects of age. Computations were performed with the aid of IBM SPSS, release 19, 2010

**TABLE 1.** Distribution of All Cases by Sex and Age Groups

Age Category, y	Females (n = 1,049)		Males (n = 1,283)		Total (n = 2,332)
	N	%	N	%	
1–10	3	37.5	5	62.5	8
11–20	5	20.8	19	79.2	24
21–30	28	45.9	32	54.1	60
31–40	47	47.0	53	53.0	100
41–50	90	47.9	98	52.1	188
51–60	112	44.9	128	55.1	240
61–70	182	37.6	216	62.4	398
71–80	276	48.4	294	51.6	570
81–90	259	53.5	225	46.5	484
91–100	47	62.7	28	37.3	75



**Development of AT8-ir pathology (n = 2332)**

(SPSS, Inc, Chicago, IL) and GraphPad prism V5.0 (GraphPad Software, San Diego, CA).

## RESULTS

### Absence of Intraneuronal Lesions

Complete absence of intraneuronal inclusions of AD-related abnormally phosphorylated tau protein within the brain was found in 10 of 2,332 cases; these are designated as “cases devoid of changes” in Figure 1 and “no changes” in Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>. These “AD-free” cases were encountered in young age categories: 6 persons were younger than 10 years; 2 were younger than 20 years, and the eldest were 22 and 23 years (Fig 1, Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>). These cases did not exhibit  $\beta$ -amyloid plaques.

### Intraneuronal AT8-Immunoreactive Abnormal tau Protein (Pretangle Material)

#### Pretangle Stage a

The first AD-related intraneuronal brain changes were seen in brainstem nuclei with diffuse projections to the cerebral cortex (24–29), most frequently in the locus coeruleus (8, 30–38). Alterations visible by light microscopy developed first in nerve cell processes, possibly the proximal portions of the axon close to the soma but outside the initial segment, where abnormally phosphorylated tau appeared abruptly without precursor or intermediate forms in those areas. The present cohort contained only cases in which immunoreactive neurites were limited to the pontine tegmentum in or close to the locus coeruleus; these are designated “a” in Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>. Forty of 2,332 cases were classified as pretangle Stage a cases and occurred mainly in young age groups.

#### Pretangle Stage b

Twelve cases (designated Stage b) showed involvement confined to the locus coeruleus; however, in these cases, involvement included somatodendritic compartments of locus coeruleus noradrenergic projection cells (Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>). Normal projection neurons in the locus coeruleus have smoothly contoured cell bodies. By contrast, they often displayed spiked protrusions along their outer somatic rim in the Stage b cases. In addition, the AT8-immunoreactive (ir) pretangle material extended further into the axon and was also observed in more remote portions of the central tegmental tract (i.e., in the superior cerebellar peduncle and in the midbrain tegmentum lateral to the medial longitudinal fascicle). On the other hand, AT8-ir axons at the level of the dorsal motor nucleus of the vagal nerve within fiber bundles descending to the spinal cord were infrequently seen (8, 39).

All pretangle Stage a and Stage b cases exhibited AT8-ir material in the locus coeruleus in the absence of lesions in the anteromedial temporal cortex. Notably, none of these cases had isolated tau-ir neurons in any other subcortical nuclei with diffuse projections to the cerebral cortex (Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>).

#### Pretangle Stage c

Six of 2,332 cases displayed more widely distributed subcortical lesions in the absence of cortical tau pathology. In this group, AT8-ir nerve cells were found not only in the locus coeruleus but also in other nonthalamic nuclei with cortical projections, such as nuclei of the upper raphe system or magnocellular nuclei of the basal forebrain. These cases are designated “c” (Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>).

In summary, 58 of 2,332 cases (i.e., pretangle Stages a–c) did not show any cortical AT8-ir projection neurons (or portions thereof) in AD predilection sites of the temporal lobe, including the transentorhinal region (Figs. 1 and 2A, Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>) (8). Cases characterized by these 3 lesion distribution patterns usually occurred in young age groups. As anticipated, tissue sections from these pretangle stage cases stained for lipofuscin pigment and basophilic material did not reveal any obvious pathologic alterations, such as loss of basophilic material or displacement of cell nuclei to the periphery.

#### Pretangle Stages 1a and 1b

In addition to subcortical pathologic findings, 38 of 2,332 cases displayed mild cortical lesions consisting only of AT8-ir pretangle material in nerve cell processes; such lesions originally had escaped recognition in Gallyas silver stained sections. These subtle lesions occurred in medial portions of the temporal lobe (particularly in the transentorhinal region) in structures that were most probably axons. Such cases are designated pretangle Stage 1a (Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>). Remarkably, no cases in this group displayed even slight cortical pathologic findings in the absence of subcortical AT8-ir lesions.

Finally, in addition to the pretangle lesions described previously, 236 of 2,332 cases showed the presence of AT8-ir nonargyrophilic pyramidal cells in the cerebral cortex. Some cases displayed only a single affected pyramidal cell, whereas others exhibited greater numbers of involved neurons. The pretangle material filled the entire somatodendritic domain of the pyramidal cells; no intermediary abnormal forms of the pathologic changes were detectable. Affected neurons occurred preferentially in the transentorhinal region, in which abnormal tau material was confined to cortical projection cells and was not present in local circuit neurons or nonneuronal cells. Such cases are designated in Table 2 as pretangle Stage 1b. All 1a and 1b cases ( $n = 274$ ) had subcortical lesions similar to those

**FIGURE 1.** Development of abnormal intraneuronal tau deposits in 2,332 nonselected autopsy cases. White columns represent the relative frequency of cases devoid of any tau deposits. Pale blue columns show the development of subtle subcortical lesions in cases with Stages a to c pathology. Columns in medium blue show an extension of these nonargyrophilic lesions into portions of the cerebral cortex (Stages 1a and 1b). Development of the pretangle material into argyrophilic neurofibrillary lesions characterizes Stages I to VI as follows: deep blue for Stage I and II cases, dark blue for Stage III and IV cases, and black for Stage V and VI cases.

seen in Stages a to c. Nonargyrophilic lesions in the cerebral cortex did not occur in the absence of AT8-ir subcortical pathologic finding. Their prevalence increased during the second and third decades and was maximal in the fourth decade (Fig. 1). From the fourth decade onward, all individuals in the cohort had some degree of AD-associated lesions (Fig. 2A).

### Intraneuronal Gallyas-Positive Abnormal tau Protein: Neurofibrillary Stages I to VI

Cases displaying AT8-ir and Gallyas-positive material are indicated by roman numerals in Figure 2A (see also Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>). The somatodendritic pretangle material had become insoluble and argyrophilic, forming neurofibrillary lesions, i.e. dendritic NTs and somatic NFTs. The first lesions were usually seen in the transentorhinal region (2). Argyrophilic lesions at subcortical sites were observed only in cases with advanced NFT stages. In NFT Stages I to VI, nerve cells filled with pretangle material were also present. Gallyas-positive neurons alone (i.e. absence of cells with pretangle material) were not observed in this cohort. It is known that nerve cells with NTs/NTs survive for years (40, 41). However, they die prematurely, and extraneuronal remnants of the argyrophilic material remain as "ghost" tangles in the neuropil thereafter (42). Here, ghost tangles were only present in combination with recently formed intraneuronal NFTs and never in isolation. Moreover, ghost tangles were observed only in cases with advanced NFT stages.

The 589 NFT Stage I cases were characterized by low numbers of Gallyas-positive pyramidal cells that were predominantly in the transentorhinal region. The 497 NFT Stage II cases had additional lesions in both the entorhinal region proper and hippocampal formation. Early (i.e. pretangle Stages a to c and Stages Ia and Ib, NFT Stages I and II) AD-related intraneuronal lesions were observed chiefly in young age categories (Fig. 2A, Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>). The intraneuronal pathologic findings during these early stages were not accompanied by insoluble extracellular amyloid deposits with the exception of a 17-year-old adolescent male with Down syndrome (8).

There were 491 NFT Stage III cases that displayed a progression of the intraneuronal lesions into the basal neocortical areas of the temporal lobe; in 191 NFT Stage IV cases, they reached insular and basal frontal areas. The 138 NFT Stage V

cases displayed involvement of nearly the entire prefrontal cortex as well as the high-order sensory association neocortex, whereas in the 84 NFT Stage VI cases, the premotor and primary motor areas as well as sensory first-order association areas and primary fields were affected. The prevalence of late NFT Stages (V and VI) increased with age (Fig. 1A; Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>). NFT Stages V and VI (222 cases) were frequently combined with late stages of  $\beta$ -amyloid deposition (Table 2 and Fig. 2B) (3).

### Extracellular $\beta$ -Amyloid Protein Aggregation

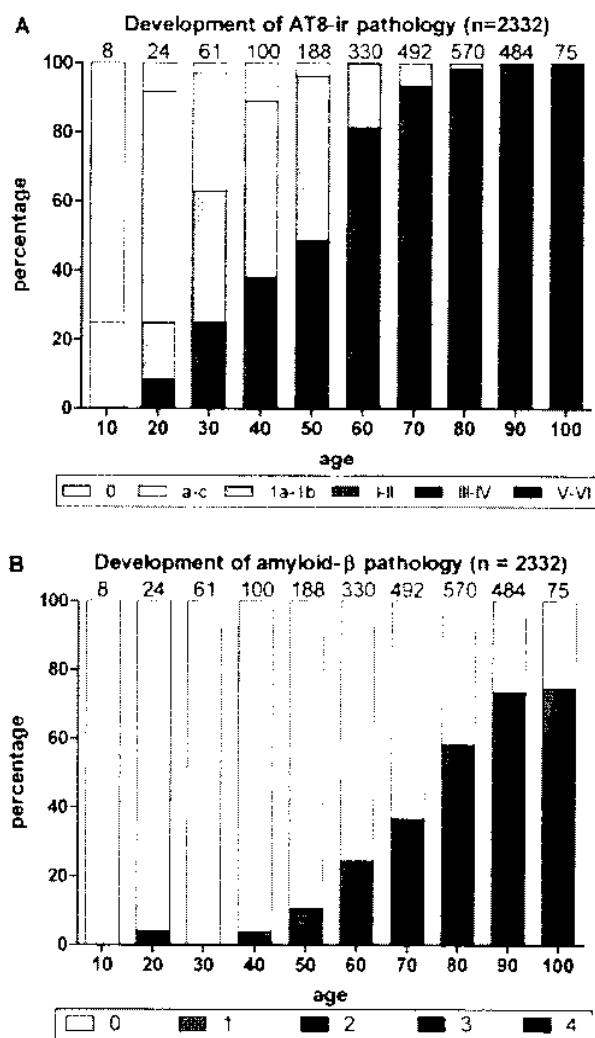
All 1,031 cases that displayed the presence of  $\beta$ -amyloid plaques also showed abnormal tau protein in specific nerve cell populations. Notably, in this cohort of 2,332 individuals, no  $\beta$ -amyloid deposits were observed in the 10 cases with no AD-related intraneuronal tau protein changes. With the exception of the 17-year-old adolescent male with Down syndrome with advanced  $\beta$ -amyloid pathologic lesions and stage a pretangle lesions,  $\beta$ -amyloid plaque deposition began to appear between ages 30 and 40 years, a point when such cases already exhibited pretangle Stage Ia or Ib (Fig. 2B and Table 2). The prevalence of  $\beta$ -amyloid plaques assessed according to Thal et al (5) increased in higher age groups (Fig. 2B and Table 2; Table, Supplemental Digital Content 2, <http://links.lww.com/NEN/A274>) (2, 5, 6).

### Statistical Analyses

Males were overrepresented across all age decades ranging from 1 to 80 years (58% males), whereas females were only predominant at ages older than 80 years (54.7% females) (Fig. 2B and Table 1). The cohort contained a greater number of older females than older males (Student *t*-test,  $p < 0.0001$ ), and there were more younger males than younger females. The severity of AD-related pathologic findings (AT8 pathologic findings, NFTs, and  $\beta$ -amyloid) was significantly higher in females than in males (all  $p < 0.0001$ , Mann-Whitney *U* tests), possibly attributable to the predominance of females at higher ages. There was a significant correlation between  $\beta$ -amyloid deposits and NFT pathologic findings in both females and males (females,  $r = 0.69$ ,  $p < 0.0001$ ; males,  $r = 0.5$ ,  $p < 0.0001$ ), between  $\beta$ -amyloid deposition and AT8 pathology (females,  $r = 0.64$ ,  $p < 0.0001$ ; males,  $r = 0.52$ ,  $p < 0.0001$ ), and between AT8 and AGD pathologic findings (females,  $r = 0.51$ ,  $p < 0.0001$ ; males,  $r = 0.56$ ,  $p < 0.0001$ ), even after controlling

**TABLE 2.** Distribution of Amyloid- $\beta$  (A $\beta$ ) Pathology by AT8-Immunoreactivity Pathology

AT8-Immunoreactivity Pathology	A $\beta$ Pathology					Total
	Phase 0 (n = 1,301, 55.8%)	Phase 1 (n = 350, 15.0%)	Phase 2 (n = 418, 17.9%)	Phase 3 (n = 177, 7.6%)	Phase 4 (n = 86, 3.7%)	
0	10 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	10 (100)
a-c	77 (98.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	58 (100)
1a, 1b	252 (92.0)	14 (5.1)	8 (2.9)	0 (0.0)	0 (0.0)	274 (100)
I	448 (76.1)	29 (8.1)	35 (8.1)	4 (0.7)	0 (0.0)	589 (100)
II	278 (55.3)	112 (22.5)	98 (19.7)	10 (2.0)	2 (0.4)	497 (100)
III	263 (41.3)	96 (19.6)	156 (31.8)	25 (5.1)	11 (2.2)	491 (100)
IV	49 (25.7)	28 (14.7)	69 (36.1)	33 (17.3)	12 (6.3)	191 (100)
V	7 (5.1)	9 (6.5)	50 (21.7)	64 (28.4)	28 (20.3)	138 (100)
VI	0 (0.0)	2 (2.4)	9 (10.7)	41 (48.8)	32 (38.3)	84 (100)



**FIGURE 2.** Development of AT8-immunoreactivity (ir) versus  $\beta$ -amyloid pathologic findings. **(A)** White columns indicate the relative frequency of 2,332 nonselected autopsies, cases devoid of any abnormal intraneuronal tau deposits. Columns in shades of blue indicate the relative frequency of cases with all types of intraneuronal lesions. **(B)** Development of extracellular  $\beta$ -amyloid deposits. Purple areas within the columns indicate subgroups of cases showing plaque-like  $\beta$ -amyloid deposits in temporal neocortex (Phase 1, light purple), all cortex and neocortical association areas (Phases 2 and 3, middle purple and dark purple), or in virtually all cerebral cortical regions (Phase 4, black). Note the relatively late appearance of  $\beta$ -amyloid plaques.

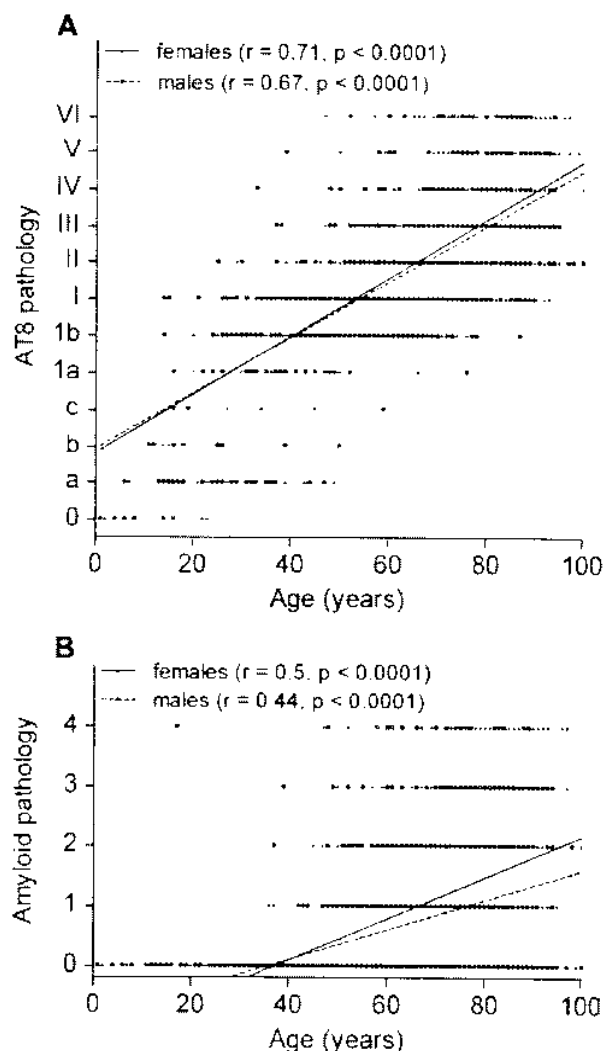
for the effects of age (data not shown). In contrast, the correlation between argyrophilic NFT and AGD pathologic findings was diminished after controlling for age ( $r = 0.07$ ,  $p = 0.11$ ).

There was a significant increase of both AT8 and  $\beta$ -amyloid pathologic findings with age (Fig. 3). The slopes of the regression lines between age and AT8 pathologic findings were similar for both sexes ( $p = 0.23$ ; Fig. 3). However, the

slope of the regression line between age and  $\beta$ -amyloid deposition was greater ( $p < 0.001$ ) in females than in males, indicating that the age-associated increase in  $\beta$ -amyloid burden is greater in females (Fig. 3; Table, Supplemental Digital Content 2, <http://links.lww.com/NEU/A2741>).

## DISCUSSION

Clinically recognizable AD has long been viewed as a disorder closely associated with old age. In fact, many consider it to be caused by the aging process itself or, at the very least,



**FIGURE 3.** Scatter plots of AD-related pathologic findings (AT8 and  $\beta$ -amyloid) by age with separate regression lines for males and females. **(A)** There is a significant correlation between AT8 pathology and age, but there is no significant difference between the slopes of the regression lines of males and females ( $p = 0.23$ ). **(B)** There is a significant correlation between  $\beta$ -amyloid pathology and age in males and females; the slope of regression line between age and  $\beta$ -amyloid deposition was greater ( $p < 0.001$ ) in females than in males.

It also has been pointed out that the disease process in AD requires an inordinately long prodromal period that lasts for 5 or more decades (51-54). Our current findings indicate that the AD-associated process may manifest itself in young individuals of both sexes as well as in the absence of



any harmful influences clearly attributable to "old age" (Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>). In addition, pretangle and NFT-bearing nerve cells are capable of surviving into the ninth decade (40, 41). Thus, advanced age per se is not a precondition for the formation of the AD-associated tau lesions; rather, there is now strong evidence that the pathologic process underlying AD is not "age-dependent" but an uncommonly slowly progressive one that frequently extends into old age (55).

We observed 52 cases in younger age groups with abnormal tau only in noradrenergic projection neurons of the locus coeruleus and, initially, only in portions of neuronal processes, probably proximal axons (pretangle Stage "a"; Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>). In these cases, the first pretangle material was identified without immunohistochemically detectable precursor or intermediary forms. During formation, neither the axonal initial segment nor the somatodendritic compartment of affected nerve cells showed any traces of pretangle material. In other words, there is no patent evidence for a transfer of pretangle material from the soma of involved cells into the affected neuronal process. As such, our findings are in accord with the assumption that the pretangle material that purportedly occurs in axons originates from normal tau proteins bound to axonal microtubules. Nevertheless, inasmuch as the shape and diameter of the involved nerve cell processes remained unchanged, the present results do not support the tau microtubule hypothesis, which claims that hyperphosphorylated tau becomes detached from microtubules and induces failed microtubule transport owing to the accumulation of improperly transported material (56–59).

Moreover, the soluble pretangle material did not seem to be incompatible with or toxic to cell functions because nerve cell nuclei or somatodendritic compartments of affected neurons did not display signs of acute reactive responses that would have indicated a life-threatening event (i.e., neuronal cell death) (60). Neurons do not undergo cell death during pretangle Phases a to c and 1a and 1b when they are producing large amounts of AT8-ir pretangle material (42, 61). The pretangles underwent modification during the lifetimes of the individuals examined until nonbiodegradable Gallyas-reactive NFTs/NTs became evident and, in the long run, the argyrophilic NFTs/NTs result in dysfunction and death of at least some neuronal types, for example, neurons of nuclei with ex-

tensive projections to the cortex and neurons in layer II of the entorhinal cortex and the first sector of the Ammon's horn (2).

The pretangle stages proposed here rest, in part, on the assumption that the AT8-immunoreactive lesions are the earliest (up to now immunohistochemically detectable) ones along a disease continuum. If one views sporadic AD as a dynamic process, it follows that pretangle pathology in individuals without clinically manifest or pathologically confirmed AD may represent neuropathologic markers of a condition that ultimately leads to the manifestations of clinical disease. A further assumption for staging of the pretangle lesions is that the pathologic process associated with NFT Stages I to VI increases in extent with disease duration. A potential methodological drawback to this approach is that the development of the pathology can only be reconstructed with the help of cross-sectional data obtained at autopsy. As such, the inferences drawn from these data permit only (but, arguably, admissible and reasonable) assumptions. Validated biologic markers that can be measured longitudinally could help to confirm, correct, or refute the existence and significance of the proposed pretangle phase (Fig. 4).

In conclusion, the results presented here corroborate those of a very recent study performed on a much smaller cohort, namely, the pathologic process associated with sporadic AD commences with intraneuritic formation of pretangle material in the lower brainstem rather than in the transentorhinal region (Fig. 4; Table, Supplemental Digital Content 1, <http://links.lww.com/NEN/A273>) (8). That abnormal tau protein occurred in pretangle stages or early NFT stages without the presence of insoluble  $\beta$ -amyloid plaques (1,291/2,332 cases) means that not only a rethinking of currently existing neuropathologic staging NFT categories for AD is necessary but also a rethinking of the hypothesis that  $\beta$ -amyloid drives AD pathogenesis and secondarily induces the formation of abnormal tau protein (46, 62–68). Sporadic AD may be the result of two separate assaults: first, a tauopathy, possibly beginning in childhood; and second, negative influences of  $\beta$ -amyloid after a given threshold is crossed.  $\beta$ -amyloid might be capable of exacerbating the underlying tauopathy so that it develops into clinical AD (69–71). If the pretangle material is not regressive or transient (72), our findings may indicate that the pathologic process leading to abnormal tau pathology and ultimately capable of inducing NFT formation does not begin

**FIGURE 4.** Summary of stages in the development of Alzheimer disease (AD)-associated tau pathology. **(A)** Postulated phases in the development of early AD-associated tau pathology. Cellular processes of brainstem nerve cells (e.g., caeruleus neurons) are the earliest structures that display AT8-immunoreactive pretangle material (Stage a). The material fills the soma and dendritic processes of a few neuromelanin-containing caeruleus neurons (Stage b). In Stage c, pretangle material occurs in nerve cells of other nonthalamic brainstem nuclei with diffuse cortical projections (upper raphe nuclei, magnocellular nuclei of the basal forebrain, hypothalamic tuberomammillary nucleus). **(B)** The regions involved in Stages a to c are illustrated schematically and accompanied by a block diagram of key regions and their interconnectivity. Involvement of the locus coeruleus is indicated by black framing. **(C)** In Stage 1a, portions of neuronal processes containing pretangle material appear in the transentorhinal region. These processes may represent pathologically altered terminals of caeruleus axons. In Stage 1b, isolated pyramidal cell somata of the transentorhinal region together with their cellular processes become filled with pretangle material and, thereafter, increase in number. **(D–F)** Schemata as in **B** but without the brainstem illustrating the medial temporal regions. The 4 brain schemata are accompanied by color-coded boxes showing subcortical pretangle Stages a, b, and c (black), cortical pretangle Stages 1a and 1b (dark red), NFT/NT Stages I and II (dark red), NFT/NT Stages III and IV (medium red), and NFT/NT Stages V and VI (light red). The close interconnections by axonal projections between the locus coeruleus and transentorhinal region permits speculation as to whether disease progression of tau lesions in AD could be attributable to anterograde induction of tau pathology from one nerve cell to the next in the neuronal chain.

in the transentorhinal region but in select subcortical nuclei, it may commence before puberty or in early young adulthood. Currently, too little is known about the pace at which the pathologic process develops. Some individuals were still at NFT Stages I and II at 90 years and older (Fig. 2A). Thus, although all individuals in this study who were 40 years and older exhibited pretangles (owing to a considerable variability in the rate of progression), only a proportion of them would have gone on to develop AD had they lived longer.

If other groups replicate our present findings and confirm that the AD-related tanopathy begins in noradrenergic projection neurons of the locus coeruleus, it might be possible to intervene with therapeutic means earlier than at present, that is, during the first decades of life, by protecting catecholamine projection cells and/or preventing them from developing the pretangle material (73–75).

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## Neurodegeneration and Sport

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The recent interest in concussion in sport has resulted in significant media focus about chronic traumatic encephalopathy (CTE), although a direct causative link(s) between concussion and CTE is not established. Typically, sport-related CTE occurs in a retired athlete with or without a history of concussion(s) who presents with a constellation of cognitive, mood, and/or behavioral symptoms and who has postmortem findings of tau deposition within the brain. There are many confounding variables, however, that can account for brain tau deposition, including genetic mutations, drugs, normal aging, environmental factors, postmortem brain processing, and toxins. To understand the roles of such factors in neurodegenerative diseases that may occur in athletes, this article reviews some neurodegenerative diseases that may present with similar findings in nonathletes. The article also reviews pathological changes identified with normal aging, and reviews the pathological findings of CTE in light of all these factors. While many of these athletes have a history of exposure to head impacts as a part of contact sport, there is insufficient evidence to establish causation between sports concussion and CTE. It is likely that many of the cases with neuropathological findings represent the normal aging process, the effects of opiate abuse, or a variant of frontotemporal lobar degeneration. Whether particular genetic causes may place athletes at greater risk of neurodegenerative disease is yet to be determined.

**KEY WORDS:** Chronic traumatic encephalopathy; Concussion; Sport; Tauopathy; Traumatic brain injury

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There has been significant interest in the prevalence of neurodegenerative diseases in athletes during the past decade, especially those involved in contact sports who may have been exposed to concussive and subconcussive impacts during their sporting careers. The publication of a number of anecdotal case reports and case series<sup>1–3</sup> has resulted in the general media affording this issue prominence in their coverage and has subsequently resulted in legal actions against sporting organizations.<sup>4</sup> The availability cascade involves the neglect of empirical data in favor of highly publicized and emotional case findings, with perpetuation of biased perception,<sup>5,6</sup> and aptly describes the media and public preoccupation associated with sports concussion.

The methodological limitations of case series analysis do not allow the determination of causal relationships between putative risks (eg, concussion or subconcussive injury) and the clinicopathological entity of modern chronic traumatic encephalopathy (CTE).<sup>7</sup> In addition, selection and/or ascertainment bias, the lack of suitable controls,<sup>8</sup> confounders,<sup>9</sup> and retrospectively

collected historical data limit the conclusions that can be drawn from the publications to date.

Significant emphasis in the published cases is placed on the protein tau deposition in specific regions of the brain with CTE being described as a unique tauopathy.<sup>8</sup> To understand the limitations of the published cases, and to appreciate the nature of neurodegenerative disease in this population, it is critical to examine the role of tau protein both in normal aging and disease states.

### CHRONIC TRAUMATIC ENCEPHALOPATHY

Historically,<sup>10</sup> CTE or dementia pugilistica (classic CTE<sup>11</sup>) were terms used to refer to a small group of professional boxers who experienced repeated head trauma for lengthy periods of time and developed a neurodegenerative condition with macroscopic brain injury at postmortem (such as cavum septum pellucidum with septal fenestration) and with characteristic neuropathological change including neurofibrillary tangles (NFT) and amyloid beta deposition

throughout the brain.<sup>11–14</sup> More recently, US research groups, including McKee et al<sup>5</sup> and Omalu et al<sup>1</sup> (see below) have defined an entity (Modern CTE<sup>15</sup>) that encompasses a heterogeneous group of postmortem findings in athletes who have a history of having played contact sport. The details of all published cases as well as the differences between classical CTE and modern CTE have been systematically reviewed by Gardner et al.<sup>11</sup>

## MODERN CTE—INDEX CASES

Omalu et al<sup>1</sup> reported the first case of modern CTE in 2005, in a 50-year-old National Football League (NFL) player who died of a heart attack 12 years after retirement. Concussion history and neurocognitive details were not provided other than he was described as having a “deficit in memory and judgement” and based on subsequent family interviews, the patient was said to have had the features of a dysthymic disorder based on *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* criteria. At autopsy, the brain was macroscopically normal, with no evidence of atrophy (weight 1565 g), no changes to the cortex, white matter or deep grey structures (aside from pigmentation of the substantia nigra, which was attenuated for age), and no ventricular enlargement.

The conventional histological examination demonstrated normal cerebral cortex, white matter, and brainstem, with mild to moderate neuronal dropout of the nigral pars compacta and pars reticulata, without Lewy bodies. Mild neuronal dropout was also noted in the cerebellar cortex, while cerebellar white matter was normal. Using immunohistochemistry, they identified a small number of diffuse amyloid plaques, sparse tau-positive neurofibrillary threads and sparse NFT in the cerebral cortex, but not in the hippocampus, subcortical nuclei, or brainstem. In summary, this case, which was reported as representing CTE, was actually one of a brain of normal size and weight, no atrophy, and a pattern of tau and amyloid plaque found in normal aging<sup>16</sup> in someone of his age.

Subsequently, Omalu et al<sup>1</sup> added 4 more cases to the above-mentioned case, and published the case series. In all 5 cases, retired sports athletes (4 NFL, 1 wrestler) committed suicide or parasuicide, and at postmortem examination, similar findings were identified. In each case, the brain was normal to unaided gross visual inspection, with no evidence of atrophy. In each case there was evidence of sparse to moderate (or sparse-to-frequent) tau immunopositive, neocortical and subcortical, NFT and neuritic threads. The distribution of tau within the cerebral cortex, including the frontotemporal region, was not described. The authors suggested that the psychiatric illness leading to suicide was caused by CTE. The issue of suicide in former athletes has been systematically reviewed by Iverson<sup>17</sup> who found that there was insufficient scientific evidence to conclude that a causal relationship between CTE and suicide in former athletes exists.

## MODERN CTE—CASE SERIES

Researchers from Boston University published a series of 3 cases of CTE, in 2009,<sup>1</sup> and in 2013 published a larger series on

modern CTE predominantly arising in retired American football players.<sup>5</sup> In that article, they reviewed the autopsy findings from 85 subjects with a history of mild traumatic brain injury, including American football players, boxers, an autistic patient, ice-hockey players, and military veterans. The neuropathological definition of CTE used in their study were:

- Perivascular foci of tau astrocytic tangles and NFT;
- Irregular cortical distribution of tau NFT and astrocytic tangles with a predilection for the depth of cerebral sulci;
- Clusters of subpial and periventricular astrocytic tangles in the cerebral cortex, diencephalon, basal ganglia and brainstem; and
- NFT in the cerebral cortex located preferentially in the superficial layers.

Gardner et al<sup>11</sup> performed a systematic review of all published cases of CTE, and of the 85 cases described by McKee et al,<sup>5</sup> it was demonstrated that after exclusion of nonathletes and those with other conditions, only 15 cases of pure CTE (ie, with no other pathology) were demonstrated. The majority of the cases in McKee et al<sup>5</sup> demonstrated significant other histopathology and immunohistochemistry findings, including  $\alpha$ 3-kd transactive response-DNA-binding protein (TDP-43) and motor neuron disease (MND), amyloid beta plaques, alpha-synuclein, Lewy body disease, frontotemporal lobar degeneration (FTLD-tau), and FTLD-TDP. It is also important to note that 23% of their published CTE cases had clinical symptoms but no abnormal neuropathological findings.

Another group looking at the neuropathological entity of modern CTE has also published a small case series. Hazrati et al<sup>18</sup> performed a consecutive case series brain autopsy study of 6 former Canadian Football League players with a history of neurocognitive decline, and 3 (50%) demonstrated neuropathological changes consistent with modern CTE; however, all 3 cases demonstrated comorbid pathology such as vascular disease, Alzheimer disease (AD), and cancer. The other 3 cases were diagnosed with AD, amyotrophic lateral sclerosis (ALS), and Parkinson disease.

## CTE—PROPOSED CLASSIFICATIONS

McKee et al<sup>5</sup> have proposed a series of neuropathological stages of this condition, which presupposes that modern CTE is a progressive neurodegenerative condition (Table 1). It is important to note that no scientific evidence has been presented based on prospective cohort studies to support this contention that CTE is a progressive entity.

In the 15 pure CTE cases in their published series,<sup>5</sup> 3 were stage I, 4 were stage II, 6 were stage III, and 2 were stage IV. TDP-43 was found in approximately half of the stage I cases, three-quarters of stage II, and most cases of stages III and IV.

In contrast, Omalu et al<sup>1</sup> published a review of a heterogeneous group of postmortem examinations in athletes, some of which included whole brain examination, whereas in more than half the cases, the whole brain was not available, and the authors were restricted to selected sections of cortex and hippocampus. In this

**TABLE 1. Neuropathological Classification of Modern CTE<sup>a</sup>**

McKee et al. <sup>1</sup>	Omalu et al. <sup>12</sup>
Stage I: Normal brain weight, with p-tau pathology restricted to discrete foci in the cerebral cortex (most commonly in the superior dorsolateral, or lateral frontal cortices) and typically around small vessels at the depths of sulci.	Phenotype 1: a combination of sparse to frequent NFTs and NTs in the cerebral cortex and brainstem with or without NFTs and NTs in the subcortical nuclei/basal ganglia; no NFTs and NTs in the cerebellum and no diffuse amyloid plaques in the cerebral cortex.
Stage II: Normal brain weight, with multiple epicenters at the depths of the cerebral sulci and localized spread of neurofibrillary pathology from these epicenters to the superficial layers of adjacent cortex. The medial temporal lobe is spared neurofibrillary tau pathology.	Phenotype 2: a combination of sparse to frequent NFTs and NTs in the cerebral cortex and brainstem with or without NFTs and NTs in the subcortical nuclei/basal ganglia; no NFTs and NTs in the cerebellum and sparse to frequent diffuse and nodular plaques in the cerebral cortex.
Stage III: Mild reduction in brain weight, with p-tau pathology is widespread, the frontal, insular, temporal and parietal cortices show new oligodendrocyte degeneration with greatest severity in the frontal and temporal lobes, concentrated at the depths of the sulci. Also in stage III CTE, the amygdala, hippocampus and entorhinal cortex show neurofibrillary pathology.	Phenotype 3: a combination of moderate to frequent NFTs and NTs in brainstem nuclei, brainstem predominantly; none to sparse NFTs and NTs in the cerebral cortex and subcortical nuclei/basal ganglia; no NFTs and NTs in the cerebellum and no diffuse amyloid plaques in the cerebral cortex.
Stage IV: Marked reduction in brain weight with cortical atrophy and severe tau pathology affecting most regions of the cerebral cortex and medial temporal lobe, sparing calcare cortex in all but the most severe cases.	Phenotype 4: a combination of none to sparse to some NFTs and NTs in the cerebral cortex, brainstem, and subcortical nuclei/basal ganglia; overpresent, no NFTs and NTs in the cerebellum and no diffuse amyloid plaques in the cerebral cortex.

NT, neurofibrillary tangles; NFT, neurofibrillary tangles.

study, the authors developed a classification system for CTE<sup>11</sup> (Table 1). The authors describe these phenotypes as emerging, but do not expand further on the utility of this proposed classification system.

It should be noted that in addition to the different classification systems, there are also differences between the 2 groups with proposed definitions of causation. Omalu et al.<sup>12</sup> state that CTE is "caused by single, episodic, or repetitive" trauma, whereas McKee et al.<sup>1</sup> state that CTE "occurs after repetitive mild traumatic brain injury." Thus, the Omalu group suggests that a single concussion may result in CTE, while the McKee group suggests that multiple concussions are required to cause CTE.

## CTE—CLINICAL PRESENTATION

Clinically, subjects with modern CTE are described as falling into 2 broad groups: a younger population that presents with mood and behavioral disturbances, and an older population who present with cognitive impairment and were more likely to progress to dementia.<sup>18</sup> Unfortunately, with such small samples and the methodological limitations with case series selection bias and retrospective recall data, further research is needed to clarify whether such symptoms represent a specific disease process or reflect coexistent mood (eg, depression) or cognitive disease (eg, frontotemporal dementia) in an aging population.<sup>19</sup> McKee et al.<sup>1</sup> suggest that the symptomatic onset of CTE occurs 8 to 10 years after repetitive head injury, and Omalu et al. suggest that there is a "long latent period between initial play and manifestation of symptoms,"<sup>11</sup> but do not define "long latent period."

In a recent review article, Jordan<sup>20</sup> proposed clinical criteria for the diagnosis of CTE, which classified clinical features into 4 categories in line with other neurological diseases: definite, probable, possible, and improbable CTE. He recommended that, in light of the lack of currently available biomarkers to observe the natural history of CTE, characterization of preclinical and prodromal CTE (similar to the preclinical phases that have been documented in AD) is premature.

Montenigro et al.<sup>6</sup> propose alternative clinical criteria, and suggest that the clinical syndrome should be referred to as traumatic encephalopathy syndrome (TES), and to reserve the term CTE for the pathological condition. However, they further suggest that based upon the symptoms and signs of TES, that CTE can be diagnosed as probable, possible, and unlikely.

## LIMITATIONS OF THE MODERN CTE STUDIES

The initial series published by Omalu et al.<sup>4</sup> included brains that demonstrated normal weight and gross macroscopic appearance, with no evidence of focal or diffuse atrophy. The brains each demonstrated some cortical and subcortical tau deposition, but as described below, this is a normal finding with aging. It is highly likely that these cases were not those of CTE, but rather suicidal tendencies in people who happened to have once played sport. The acquisition bias in the selected cases, and the absence of a control group, with the absence of sufficient clinical data, limits further application of this series.

The published CTE series from the Boston group<sup>1</sup> is an autopsy series with significant ascertainment bias, and none of these data were reported: prospective data collection; ante-mortem clinical,

psychological and neurocognitive assessment; prospective ascertainment of concussion data; prospective collection of drug and alcohol abuse data, and familial and genetic assessment.

The McKee et al<sup>1</sup> study did include 18 control brains of people with no history of cognitive impairment or brain trauma, and were selected from the Framingham Heart Study. However, a control group needs to be reflective of the population being studied, and should only differ from the cases in the variable being studied. That is to say, in testing the hypothesis that a history of concussion exposes athletes to a greater risk of CTE than athletes without a history of concussion, the control group should include athletes with a similar sporting history to the cases, with the exception of no history of concussion. The control group should have a similar demographic profile to cases, similar history of drug exposure, and similar genetic profile. If these variables are not adequately controlled for, then it is reasonable to suggest that the control group is inadequate.

That a number of retired athletes had psychological disorders is to be expected in any retired elite professional athlete group. The suggestion that suicide risk is increased in retired athletes with CTE has been made by Onuma and others.<sup>9</sup> Iverson<sup>43</sup> reviewed the incidence of depression, anxiety, suicide, drug abuse, alcohol abuse, and chronic pain in retired NFL players, and demonstrated the multifactorial nature of suicide risk, and concluded that "the association between the neuropathology of CTE and suicide has not satisfied basic criteria relating to the consistency, strength, temporality, specificity or coherence of the correlation." The reported suicide rate in retired NFL players was lower than that of the general population.<sup>44</sup>

Iverson noted that half of all retired players admitted to opioid use during their football careers, and that two-thirds of these reported abusing opioids. The correlation between opioid abuse and hyperphosphorylated tau deposition is well described,<sup>22</sup> and should be factored as a key variable in any assessment of causation.

Reviewing the Boston group's<sup>1</sup> stages suggests that they can be interpreted differently, and that they may not represent a spectrum, or timeline, of CTE development, but rather may represent 2 distinct pathological entities. Stages I and II may represent tau deposition seen in normal aging brains, while stages III and IV may represent forms of FTLD. Given the findings from Braak et al<sup>11</sup> that 100% of those over 30 years of age demonstrate tau pathology in the brain at autopsy, as do ~90% of those aged over 10 years of age, it is expected that all autopsied brains in the Boston series would contain tau pathology simply reflecting the age demographic of the population being studied.

With regard to stages III and IV, the prominent distribution of tau deposition in frontal and temporal lobes is typical of FTLD-tau. McKee et al<sup>1</sup> argue that the superficial cortical layering of tau is unique to CTE, yet it is well recognized that similar tau distribution is present in the same cortical layers in other tauopathies such as amyotrophic lateral sclerosis and parkinsonism-dementia complex (ALS-PDC), a condition seen in the Western Pacific Islands, including Guam.<sup>45,46</sup> In a subsequent

publication from the Boston group,<sup>29</sup> they acknowledge the correlation between CTE and FTLD and state that "because CTE is accompanied by a range of symptoms reflective of frontotemporal dysfunction, including behavioral and cognitive deficits and a dysexecutive syndrome, and the anatomical substrate of CTE is a FTLD characterized by superficial spongiosis, atrophy and neuronal loss with astrocytic and neuronal deposition of tau and TDP-43, CTE is increasingly categorized as an acquired FTLD."<sup>29</sup> Although we agree with most of the sentiments of this statement, the term "acquired" requires further study.

In the CTE study,<sup>1</sup> there was no study of genetic markers that are known to be causal in other neurodegenerative diseases,<sup>49</sup> such as *MAPT*, *C9ORF72*, and *GRN*, although *APOE* status was assessed and reported to be not statistically significant.

## COMMON NEURODEGENERATIVE DISEASES SEEN IN RETIRED ATHLETES

There are many causes for dementia and cognitive decline in retired athletes, including neurodegenerative dementias, dementia-plus diseases, leukodystrophies, lysosomal storage diseases, vascular diseases, brain tumors, hydrocephalus, severe brain injury, mitochondrial diseases, basal ganglia pathologies, prion diseases, infective dementias, inflammatory autoimmune disorders, and toxic-metabolic dementias.

In a recent study<sup>51</sup> of former NFL players, the mortality rate from neurodegenerative disease was reported as being 3 times greater than that of the general population. However, the sample size in this study was small, with only 2 cases of AD and 6 ALS cases in the total sample of 334 deaths, and the overall mortality rate of the cohort was half the expected value, with significantly low rates of death from cardiovascular disease compared with the general population. Although the results provide an intriguing observation, the study lacked power to be definitive.

A community-based study of high school students in Rochester, with a 50-year follow-up, demonstrated no significant difference in the incidence of dementia, Parkinson disease, or ALS in footballers and nonfootballers (band, glee club, or choir).<sup>52</sup>

The neurodegenerative category includes conditions such as Alzheimer disease, dementia with Lewy bodies, as well as tauopathies such as frontotemporal dementia, and corticobasal syndrome. The 2 major differential diagnoses are considered below.

## ALZHEIMER DISEASE

AD was originally described by Alois Alzheimer in 1906 and is the most common cause of dementia in adults. Clinically, AD is characterized by an insidious onset and progressive decline of cognitive function, usually beginning with impairment of short-term memory. As the disease progresses, patients depend heavily upon a caregiver and often require assistance maintaining their hygiene. At the end stages of the disease, patients are completely

dependent on others, may forget the identities of their closest friends and family members, and may become bed-bound.<sup>54</sup>

AD is characterized pathologically by 2 hallmark lesions, NFT and senile or amyloid plaques. NFT are comprised largely of hyperphosphorylated tau protein (phospho-tau), while the major protein component of senile plaques is amyloid beta (A $\beta$ ). Phospho-tau also accumulates as neurofibrillary threads (NT) and dystrophic neurites (DN) (Figure 1).

Subependymal, subpial, perivascular, and astrocytic accumulations of phospho-tau also occur in AD. A $\beta$  plaques may also have diverse morphologies, from diffuse, to cored, to neuritic, among other subtypes. The neuritic plaque (NP) is generally considered most relevant to AD in terms of diagnostic pathology, while diffuse plaques are considered age-related. Recent consensus guidelines for AD criteria encompass amyloid staging,<sup>55</sup> Braak neurofibrillary staging,<sup>56</sup> and assignment of CERAD (Consortium to Establish a Registry for AD<sup>57</sup>) NP frequency. Correlation between AD pathology and clinical disease is complex.<sup>58</sup>

Genetic causes for AD have been identified, especially in those presenting under 65 years of age (early-onset dementia). The causal genes identified are amyloid precursor protein (*APP* on chromosome 21 which codes for the APP cell surface receptor), presenilin 1 (*PSEN1* on chromosome 14 which codes for a protein involved in APP cleavage), and presenilin 2 (*PSEN2* on chromosome 1, which codes for a catalytic protein and may also be involved in

intracellular signalling).<sup>58</sup> There is variable clinical presentation associated with mutations in the AD causal genes. Mutations in *APP*, *PSEN1*, and *PSEN2* only account for 1.9% of patients with early-onset AD, with the remainder of cases probably due to multiple risk genes, which do not reliably cause the disease but increase an individual's susceptibility or predisposition to developing AD.<sup>59</sup> In addition to these causative genes, the  $\epsilon\epsilon$ -allele of the apolipoprotein E gene (*APOE* on chromosome 19) is associated with an increased risk of AD in sporadic cases and can be associated with earlier onset of disease. The risk of developing AD is increased approximately 4-fold in those with 1 *APOE* $\epsilon$  allele, and 15-fold in those with 2 *APOE* $\epsilon$  alleles, compared with the most common genotype (*APOE*  $\epsilon\epsilon$ ).<sup>61</sup> With genome-wide studies, many other genes have been associated with AD, and the interested reader is referred to Combarros.<sup>60</sup>

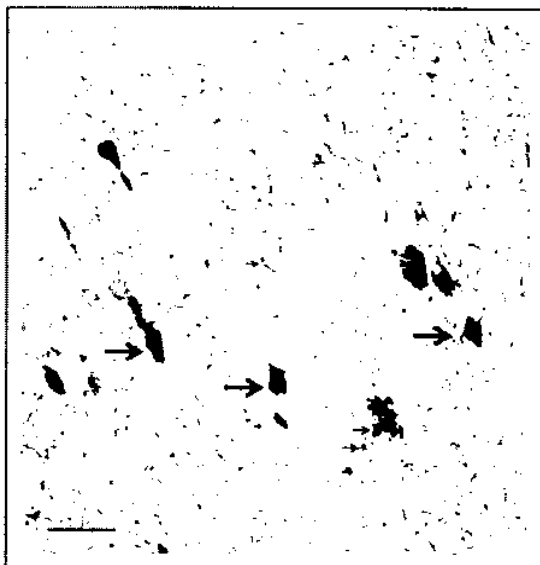
## FRONTOTEMPORAL DEMENTIA

FTD is a diverse group of non-AD dementias that are characterized by relatively focal and progressive atrophy of the frontal and/or temporal lobes in some cases.<sup>62</sup> Originally referred to as Pick disease, FTD now incorporates a group of diseases with diverse clinical, pathological, and genetic findings. FTD is the second most common neurodegenerative disease causing dementia in younger adults. The prevalence of FTD is 15 to 22/100,000, and the incidence is 2.7 to 4.1/100,000.<sup>63</sup>

Clinically, FTD is broadly divided into behavioral variant (bvFTD) and language decline (primary progressive aphasia, PPA), although there may be significant overlap within the individual patient. The PPA types are further classified as progressive nonfluent aphasia, semantic dementia, and logopenic progressive aphasia.<sup>62</sup> There are published international criteria to separate possible, probable and definite FTD.<sup>64</sup>

Motor presentations of FTD include FTD with motor neuron disease (FTD-MND), corticobasal degeneration (CBD; also sometimes referred to as corticobasal syndrome (CBS) and progressive supranuclear palsy (PSP). The term frontotemporal lobar degeneration (FTLD) is used to describe the specific pathological diseases that result in FTD syndromes. These too are united by their impact on frontal and temporal brain structures. Subtyping is based on the specific proteins found within neuronal inclusions. Most FTLD subtypes are either (a) FTLD-tau, which includes Pick disease, CBD and PSP, all of which show tau-containing inclusions or (b) FTLD-TDP, which includes several subtypes in which TDP-43 containing inclusions are seen.

Behavioral variant FTD is the predominant subtype occurring in approximately 60% of cases and is characterized by progressive change in personality, social emotional, and cognitive function and shares many similarities with the clinical features of modern CTE, including executive dysfunction, memory loss, explosivity, difficulty with attention and concentration, depression, mood swings, aggressive tendencies, paranoia, and visuospatial difficulties.<sup>65,66</sup>



**FIGURE 1.** *Phosphorylated tau photomicrograph of hippocampal formation in a patient with FTD.* The image was immunostained for phosphorylated tau protein (anti-P101, DSH). Showing neurofibrillary tangle (large arrow), dystrophic neurites (small black arrows) and neurofibrillary threads (small white arrows). Scale bar = 10  $\mu$ m.

The common findings in cases of FTLD are involvement of the frontal and/or temporal lobes, neuronal loss, gliosis, and microvacuolation of cortical layer 2. Associated with these changes is accumulation of proteins such as TDP-43, hyperphosphorylated tau, and FUS (fused in sarcoma protein). The nosology and nomenclature of FTLD has evolved as newer proteins are identified. The current pathological classification<sup>45,46</sup> is based upon these cellular inclusions such that the following types are recognized:

- FTLD-tau—up to 40% of FTLD
- FTLD-TDP—approximately 50% of FTLD
- FTLD-UPS—(ubiquitin proteasome system)
- FTLD-FUS—(the majority of tau-negative and TDP-43-negative cases)
- FTLD-ni—(no inclusions).<sup>45</sup>

The presence of these proteins in FTLD is considered a pathological finding and does not necessarily indicate that the proteins themselves are causative for the disease or reactive to the underlying disease process.

Although many FTLD cases are sporadic, up to 50% of patients have a family history.<sup>47</sup> A number of specific genes have been described that are associated with FTLD including *MAPT* (on chromosome 17 which encodes microtubule-associated protein tau), *GRN* (on chromosome 17, near *MAPT*, and encodes for growth regulation factor progranulin), *VCP* (on chromosome 9 and encodes for valosin containing protein which is involved in protein homeostasis), *CHMP2B* (charged multivesicular body protein 2B gene on chromosome 3 and encodes for a protein component involved in endosomal trafficking and degradation), and *C9ORF72* (Chromosome 9 Open Reading Frame 72).<sup>48</sup> The most frequent mutations associated with FTLD (>80%) are *MAPT*, *GRN*, and *C9ORF72*.<sup>49</sup>

The generic mutations described broadly correlate with the pathological findings such that *MAPT* is associated with FTLD-tau, *GRN*, *C9ORF72* and *VCP* with FTLD-TDP, and *CHMP2B* with FTLD-UPS.

## OTHER TAUOPATHIES

As discussed above, in addition to FTD there are a number of other distinct diseases associated with abnormal intracytoplasmic phosphorylated tau and as a group are referred to as tauopathies. While these conditions overlap with FTD, in broad terms they clinically differ from FTD and hence would be distinct from the reported CTE clinical features. These are listed in Table 2.<sup>49,50</sup>

## CEREBRAL PROTEIN FUNCTION

### Tau

Tau is one of many microtubule associated proteins and is normally expressed in the central and peripheral nervous system, as well as in systemic tissues including kidney, muscle, pancreas, heart, lung, testis, and fibroblasts.<sup>51,52</sup> The presence of tau in systemic tissues does limit its use as a serum biomarker of injury,

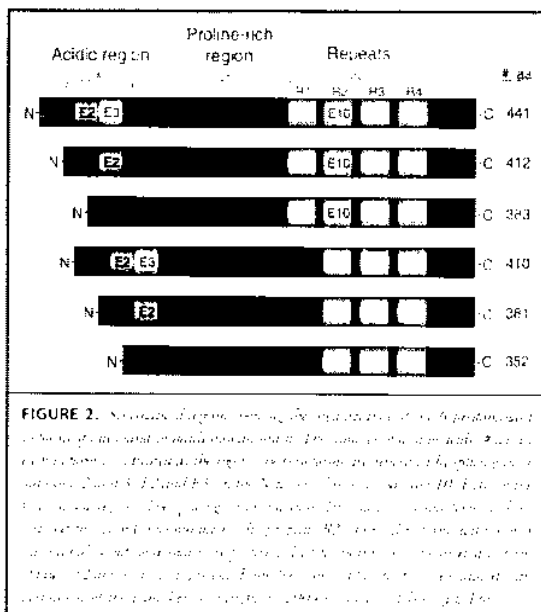
**TABLE 2. Tauopathies Other Than FTD Characterized by Abnormal Hyperphosphorylation of Tau<sup>49,50</sup>**

Alzheimer disease, including tangle only form of the disease
Corticobasal degeneration
Dementia pugilistica (Classical Chronic traumatic encephalopathy)
Dementia with argyrophilic grains
Diffuse neurofibrillary tangles with calcification
Down syndrome, adult cases
Familial British dementia
Familial Danish dementia
Fronto-temporal dementia
Gerstmann-Sträussler-Scheinker disease with tangles
Guadeloupean parkinsonism
Guam parkinsonism/Neurological Dementia Complex
Myotonic dystrophy
Niemann-Pick disease, type C
Non-Guamanian motor neuron disease with neurofibrillary tangles
Pallidoparkinsonism/degeneration
Pantothenate kinase associated neurodegeneration
Pink disease
Postencephalic parkinsonism
Pron protein cerebry amyloid angiopathy
Progressive supranuclear palsy
Progressive supranuclear palsy
SC94b-related fronto-reticular
Subacute sclerosing panencephalitis
Tangle only dementia
White matter neuropathy with glomerular glial inclusions

as tau in blood may have derived from these systemic sites and/or from the CNS.<sup>53</sup> Although tau in the CNS is predominantly located in axons, it is also found in neuronal somatodendritic compartments and in oligodendrocytes.<sup>52,55</sup>

Tau has many functions including microtubule stabilization, axonal transport regulation, actin filament binding, signal pathway regulation, facilitation of nerve growth factor signalling, phospholipase C binding, enzyme inhibition, and modulation of cellular response to heat shock. Tau also affects neurogenesis in adults.<sup>52</sup> The function of tau is regulated by phosphorylation of the protein, in addition to glycation, isomerization, nitration, sumoylation, O-GlcNAcylation, and ubiquitination.<sup>52</sup> Tau is a soluble protein in its functional form, but insoluble when hyperphosphorylated, resulting in formation of intracellular, and subsequently extracellular NFT (described below).

The human tau gene is located on chromosome 17 and contains 16 exons. Some exons are only transcribed in peripheral tissue. In adult human brain alternative splicing of exons E2, E3, and E10 generates 6 tau isoforms<sup>56</sup> (Figure 2) ranging from 352 to 441 amino acids in length. The different isoforms have 0, 1, or 2 N-terminal amino acids, each of which may have either 3 (3R) or 4 (4R) carboxy terminal random repeat sequences based on alternative splicing of E10. The ratio of 3R to 4R tau in adult human brain is 1:1, whereas in human fetal brain only the



shortest tau isoform (3R) is expressed, and in the peripheral nervous system transcription of additional exons results in a larger tau protein termed big tau.<sup>56</sup> Within the adult brain, tau isoforms are expressed differently within different brain regions and neuronal subpopulations, such as in the granular neurons of the dentate gyrus.<sup>57,58</sup>

While the tauopathies are associated with hyperphosphorylated tau, the tau isoform profile is different in different diseases. For example, AD is associated with all 6 tau isoforms, whereas 4R tau is characteristic of PSP and CBD, while 3R tau is characteristic of Pick disease.<sup>59</sup>

The importance of the different isoforms is also highlighted by the fact that different immunohistochemistry stains will only identify particular tau isoforms; in routine postmortem studies, AT8 and AT10 stains are the most commonly used stains. This in turn means that tau deposition with different isoforms or in different regions may be underestimated or missed entirely. In a brain autopsy study, Ramage et al.<sup>60</sup> identified more widespread immunoreactivity for AT180 than for AT8. The relationship of some of the anti-phospho-tau antibodies to phosphorylation sites along the tau isoform primary structure is shown in Figure 3.

Tau phosphorylation in and around the microtubule binding domain (MTBD) region alters the microtubule-binding function of tau. Tau phosphorylation is regulated by protein kinases and phosphatases, and phosphorylation typically occurs at serine and threonine residues that are usually followed by proline (proline-rich domains). There are 19 putative serine or threonine phosphorylation sites on the longest tau isoform and with phosphorylation-dependant monoclonal antibodies to tau,

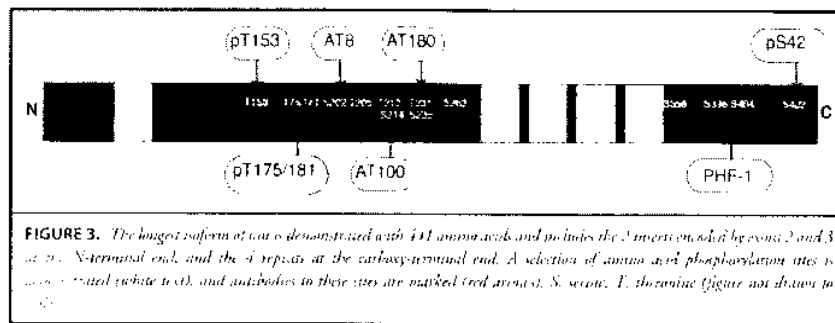
30 phosphorylation sites have been described.<sup>61</sup> Most of these phosphorylation sites surround the MTBD. The site of phosphorylation at individual serine or threonine residues follows a predictable sequence, and phosphorylation of one residue can affect subsequent phosphorylation of other residues.<sup>62</sup>

Phosphorylation of tau is known to regulate its function as a protein. Tau hyperphosphorylation is a known normal, physiological state, such as in the human fetus and in hibernating animals.<sup>63</sup> In fetal development, phosphorylated tau is high in the fetal state, and then with age, increasing phosphatase activity results in dephosphorylation.<sup>62</sup> Phosphatase activity can be reduced with lower temperature such as occurs during anaesthesia, which results in increased tau phosphorylation.<sup>64</sup> Hyperphosphorylation is also associated with neurodegenerative disease states (Figure 4).

The extent of phosphorylation in biopsy specimens and post-mortem examination is also affected by the time since tissue harvest and the temperature of the tissue/brain. At room temperature, phosphatase activity within the brain tissue results in dephosphorylation after 4 hours; however, this enzymatic activity is slowed if the tissue is cooled to  $-4^{\circ}\text{C}$ .<sup>65</sup> The practical implications of this are that brain specimens kept at room temperature for several hours before processing may underestimate the degree of tau phosphorylation, whereas a freshly acquired specimen that is immediately processed would more accurately reflect the degree of tau phosphorylation. Ramage et al.<sup>66</sup> suggest that any delay in postmortem may result in fewer cases with tau positivity, but were unable to quantify this further.

## Amyloid Beta

In the largest series of dementia pugilistica to date by Corsellis et al.,<sup>67</sup> the pathological findings were generally characterized as the presence of neurofibrillary degeneration out of proportion to amyloid plaque pathology, among other changes. Subsequent examination of this case series by others, however, demonstrated significant plaque pathology, in some cases qualifying for frank AD.<sup>68,69</sup> It should be noted that the original series used silver impregnation techniques and dyes, prior to the advent of immunohistochemistry. Amyloid- $\beta$  (A $\beta$ ) immunohistochemistry now involves more sensitive and specific methodologies, with antigen retrieval and antibody probes for a specific protein constituent of plaques. These analyses label not only neuritic plaques (A $\beta$  plaques containing dendritic and axonal swellings, generally viewed as more meaningful to the AD diagnosis, or more pathogenic<sup>70</sup>), but also diffuse A $\beta$  deposits (generally considered more age-related than pathogenic<sup>71</sup>) that lack fibrillarity and affinity for Congo red. Thus, the original hallmark of dementia pugilistica—neurofibrillary degeneration without plaques—is now amended to include diffuse plaques in a significant subset of cases.<sup>68,69,72</sup> Dementia pugilistica in its pure form is still said to lack the neuritic plaques more characteristic of AD, but the presence of diffuse A $\beta$  deposits along with studies showing increased A $\beta$  in the acute state after trauma,<sup>69</sup> has led some investigators to propose a role of the

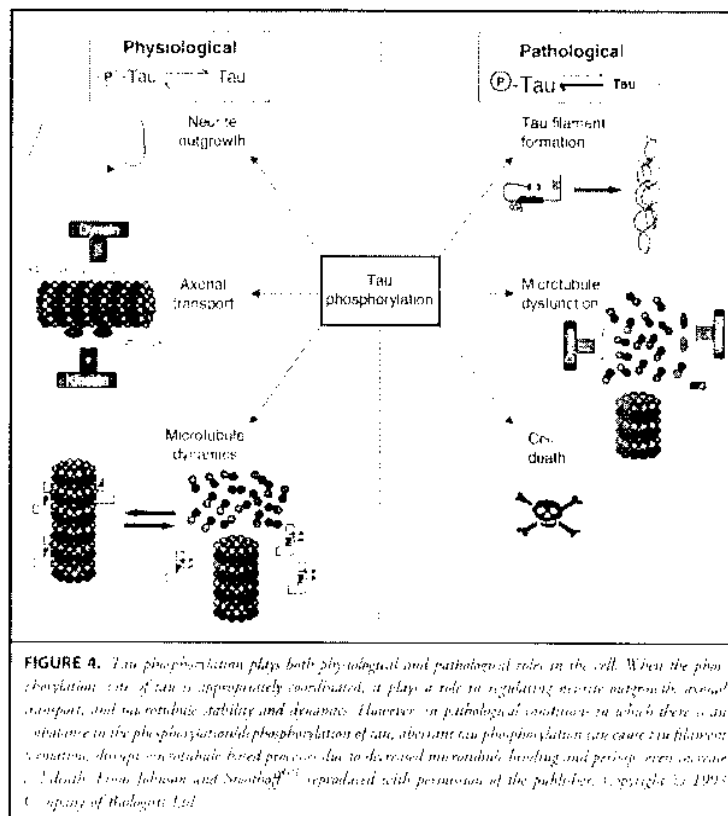


amyloid cascade in chronic sequelae of head trauma,<sup>30</sup> not unlike the proposed role for A $\beta$  precursor protein (APP) in AD pathogenesis.

In the Boston University case series,<sup>3</sup> 50 (63%) of the CTE subjects overall, and 2 % of the pure CTE subjects showed diffuse, neuritic, or vascular amyloid.<sup>3</sup> Of these, 7 subjects had sufficient A $\beta$  and tau pathology to carry the additional diagnosis of AD by 2012

National Institutes on Aging Alzheimer Association criteria.<sup>31</sup> Taken together, these findings also raise the issue of A $\beta$  plaque pathology and the role A $\beta$  metabolism in the putative disease process.

A role for APP metabolism in neurodegeneration (ie, the amyloid cascade hypothesis) is largely based on genetic data.<sup>32</sup> The initial identification of A $\beta$  in lesional tissue by Glenner and Wong<sup>33</sup> came from purification of vascular amyloid in Down





syndrome brains (which have an extra copy of chromosome 21 and therefore increased ABPP expression). Subsequent purification and linkage of amyloid plaque cores to AB, <sup>70</sup> and the identification of AB as a proteolytically cleaved product of ABPP, led initially to considerable enthusiasm for development of a serum diagnostic assay for AD and therapeutic intervention.<sup>71</sup> This was followed shortly thereafter by the identification of germline mutations in not only ABPP, but also the secretase complex (presenilin 1 and presenilin 2) involved in the elaboration of AB peptides, that produced familial early-onset AD and/or familial cerebral amyloid angiopathy. The support for the amyloid cascade hypothesis is thus consistent with central dogma of molecular biology from genetic lesions involving substrates and enzymes, to disease phenotype.

Diffuse amyloid plaques occur with age, beginning in middle age, with a possible influence of apolipoprotein E genotype,<sup>72</sup> and have not been shown to be increased in dementia pugilistica or CTE, relative to an age-matched population. Much like the issue of age-related tau deposits in middle age in CTE, diffuse AB deposits in a subset of boxers or other athletes is an expected finding. On the other hand, the presence of substantial AB deposits of diverse morphologies, along with cerebral amyloid angiopathy and abundant tau pathology, is indistinguishable from AD. Such pathology is described in a subset of dementia pugilistica and CTE cases as noted above. However, rather than conflating 2 separate processes, one being a well-defined neurodegenerative disease (AD) and the other (CTE) lacking well-defined clinical and pathological substrates, the presence of high-likelihood AD pathology should perhaps exclude such cases from the CTE category, unless and until a relationship is established.

### TDP43

TDP43 is a nuclear RNA binding protein that has been identified as a pathological aggregate in many neurodegenerative diseases.<sup>73</sup> TDP43 inclusions can also be found occasionally in normal aging brains.<sup>74</sup>

TDP43 is a 416 amino acid protein encoded by the *TARDDBP* gene on chromosome 1<sup>75</sup> and contains 2 RNA recognition motifs (RRM1 and 2) and a C-terminal glycine-rich region.<sup>76</sup> Structurally, TDP43 belongs to the very large family of nuclear factors known as heterogeneous nuclear ribonucleoproteins (hnRNPs), as does FUS.<sup>77</sup> As a member of the hnRNP family, TDP43 is involved in multiple steps of RNA processing, including transcription, splicing, transport, and translation.<sup>78</sup> The C-terminal region of TDP43, harboring most of the pathogenic disease mutations, is required for self-regulation. TDP43 has an intrinsic propensity to aggregate, and it is now widely accepted that its C-terminal tail is responsible for most of its tendency to aggregate.<sup>79</sup>

TDP43 inclusions are present in approximately 50% of cases of FTD, and is also the major inclusion in the majority of cases of ALS.<sup>82</sup> TDP43 proteinopathy is found in cases with mutations of *TARDDBP*, *C9orf72*, *GRN*, and sporadically. In a study of

single nucleotide polymorphisms (SNPs), McMillan et al.<sup>83</sup> identified the SNP rs690776 that conferred a 2-fold increased risk of FTD-TDP relative to FTD-tau. rs690776 is located near sortilin (*Sortin*) and has been associated with regulation of plasma progranulin levels. This SNP differs from rs8070723 associated with haplotypes *H1* and *H2* of *MAPT*, in which *H1* confers increased risk of FTD-tau and *H2* confers increased risk of FTD-TDP.

TDP43 inclusions have also been reported to occur in various forms of dementia, including approximately 30% of AD and various forms of synucleinopathies such as Parkinson disease. In these instances, TDP43 inclusions co-exist, but only partially colocalize with tau or alpha-synuclein aggregates. Variability in the extent of TDP43 pathology among different central nervous system regions is observed in the different TDP43 proteinopathies.<sup>84</sup>

In patients with FTD-TDP, Rohrer et al.<sup>85</sup> analyzed the cases with regard to neuropathological classification of TDP43 subtype,<sup>86</sup> in addition to antemortem MRI, and found that type 1 FTD-TDP is associated with Semantic Dementia, type 2 with bvFTD or FTD-MND, and type 3 with PNTA, CBI, bvFTD, and FTD-MND. The Boston group<sup>8</sup> identified TDP43 abnormalities in the majority of CTE cases, but further subtyping was not reported, and future research on TDP43 subtyping and CTE is required.

### Tau and Amyloid in Normal Aging

Tau hyperphosphorylation occurs in normal aging. In a study of 2332 nonselected autopsy cases ranging in age from 1 to 100 years, Braak et al.<sup>87</sup> identified abnormally phosphorylated tau protein (AT8 stain) within the brain in 2322 of 2332 cases (99.5%), including >90% of those over 10 years of age, and in 100% of cases in those aged over 30 years of age (Figure 5A). In the same autopsy series, extracellular AB deposits were identified in <4.2% of all brains, with the appearance of AB occurring later (in older individuals) than occurs with hyperphosphorylated tau (Figure 5B).

Similarly, Maysen et al.<sup>88</sup> identified phosphorylated tau in biopsy-derived brain samples at almost all of the sites tested, although in smaller quantities than found in disease, and Fisanowski et al.<sup>89</sup> identified phosphorylated tau in dystrophic neurites in olfactory epithelium in 6 out of 8 normal control adults.

The increased deposition of hyperphosphorylated tau has also been described due to exogenous substance abuse, such as opioid abuse. The Edinburgh group<sup>90-92</sup> performed autopsy studies in a series of HIV-negative opiate abusers, and found significant deposition of both 3R and 4R hyperphosphorylated tau in multiple brain regions of those with a history of opioid abuse compared with age-matched controls. They related this both to microglial activation and to breakdown of the blood-brain barrier, but found no correlation with deposition of amyloid beta. Furthermore, they found the "most significant correlate for hyperphosphorylated tau deposition proved to be the level of microglial activation. Whether changes in microglia are merely reactive to the rise in hyperphosphorylated tau, or to some other subtle pathology in drug-user brains, is unclear."<sup>92</sup> With regard to



In some pathologies (eg, PSP) it is considered that tau is composed of straight filaments rather than PHFs.<sup>10a</sup>

The insolubility of PHF has been thought to be related to the altered folding structure of hyperphosphorylated tau, although it may be due to glycation of tau.<sup>51</sup> The presence of hyperphosphorylated tau is a hallmark of the tauopathies; however, evidence suggests that it is not responsible for neuronal cell dysfunction. A series of animal experiments demonstrate that tau inclusions are not very toxic, and that toxicity is caused by smaller, soluble aggregates of tau oligomers.<sup>52</sup> It is unknown whether the presence of tau inclusions in tauopathies contributes to the pathogenesis of disease or whether it is an innocent or beneficial bystander.<sup>49</sup>

The distribution of hyperphosphorylated tau within the brain occurs in 3 stages: preNFT, iNFT (intraneuronal), and eNFT (extraneuronal).<sup>49</sup> PreNFT includes cells with normal cell and nucleus morphology, but contains cytoplasmic diffuse phospho-tau positive staining. iNFT contains aggregated cytoplasmic phospho-tau staining with some changes to cellular morphology. In eNFT there are extracellular phospho-tau fibrils after cell death. eNFT are commonly known as ghost tangles, in which the neuronal cell body has died, leaving the insoluble NFT, previously intracellular, in situ, and located in the extracellular space. The anti-tau antibodies used in staining brain specimens are each specific to a particular serine or threonine location, and different antibodies stain tau differently according to its stage (ie, pre-NFT, iNFT, or eNFT). For example, preNFT is stained predominantly with antibodies pT153, pS262 and TG3, iNFT with antibodies pT175/181, 12F8, pS422, pS214, and pS46, and eNFT with antibodies AT100, AT8, and PHF-1.<sup>49</sup> Whether or not a laboratory's choice of a particular antibody panel would affect the overall interpretation of tau deposition in an individual brain sample remains open to conjecture.

## CONCLUSION

The complex nature of neurodegenerative diseases in adults is underlined by the complex nature of some of the proteins involved (such as tau, amyloid beta, and TDP-43), the complex and incompletely understood genetics of these conditions, and the similarities between the clinical, pathological, and immunohistochemical findings in diseases as diverse as FTD, AD, and ALS.

When a previously undescribed condition, such as modern CTE in retired athletes, is proposed based on neuropathological findings in a small and potentially biased sample, then the complex genetic and environmental variables as well as the normal range of age-related brain degeneration implore us to cautiously review the data related to putative CTE.

The authors think that there is insufficient evidence to establish a causal relationship between sports participation and the existence of modern CTE. In the published CTE cases, there is a mixture of age-related tau hyperphosphorylation, which explains the majority of the pathological features and an overlap with the behavioral

variant FTD, which presents with an almost identical clinical phenotype. In some cases, the clinical features may reflect mental health issues, such as depression, which occur in adults unrelated to exposure to sport and/or repeated head trauma.

## Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials or devices described in this article.

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## COMMENTS

The authors have written a comprehensive and compelling article summarizing current neuropathological knowledge and applying it critically to what has been published by several research groups about chronic traumatic encephalopathy in sports. This is a timely, useful, and thought-provoking article. The authors demonstrate that degenerative disorders are multifactorial in nature and that at a scientific level, a simple linear relationship between concussion (or subconcussive impacts) and CTE is likely inadequate for causative explanation. This article is a well-earned addition to the literature, as it clearly makes a strong case for the multifactorial nature of neurodegenerative diseases, and in particular, the propositions that life, lifestyle, and genetic factors also must be considered in the determination of causation. The authors have provided scientific support for the conclusion of the 2012 Concussion in Sport Group that there remains no causative link between concussion or participation in contact sports and CTE.

Gary Solomon  
Nashville, Tennessee

The relationship between sports-related concussion (SRC) and chronic traumatic encephalopathy (CTE) are tenuous at best, with the most recent consensus statement reporting no scientific linkage between SRC and CTE. Furthermore, scientific investigations into SRC and modern CTE have been limited due to selection bias, lack of adequate control groups, and incomplete clinical data. Scientific discussion regarding SRC and CTE are highly pertinent topics at this time, given the media attention, public perceptions of SRC and CTE, potential implications for medical/legal consequences, and parents' child decisions regarding sport participation.

The current literature review is long overdue and presents a well-balanced and thorough review of previous literature, delineating potential relationships between sport concussion and long-term outcomes, namely, CTE. The authors critically evaluate the current research regarding proposed definitions of CTE and reiterate concerns regarding control groups in these studies. The authors poignantly review the heterogeneity of common neurodegenerative diseases that may develop in retired athletes, as well as tau and amyloid in normal aging. The authors also provide a compelling discussion of additional variables that need to be considered when evaluating for possible CTE, including depression, anxiety, suicidal behaviors, drug, and alcohol use/abuse, and chronic pain.

To further shed light on the relationship between sport-related concussion and long-term outcomes, multiple groups have identified specific subtypes of concussion. Targeting individualized problems has resulted in proposed treatments that have been shown to effectively facilitate recovery from SRC. While these models are certainly preliminary in nature and research validating proposed concussion subtypes is ongoing, expectations

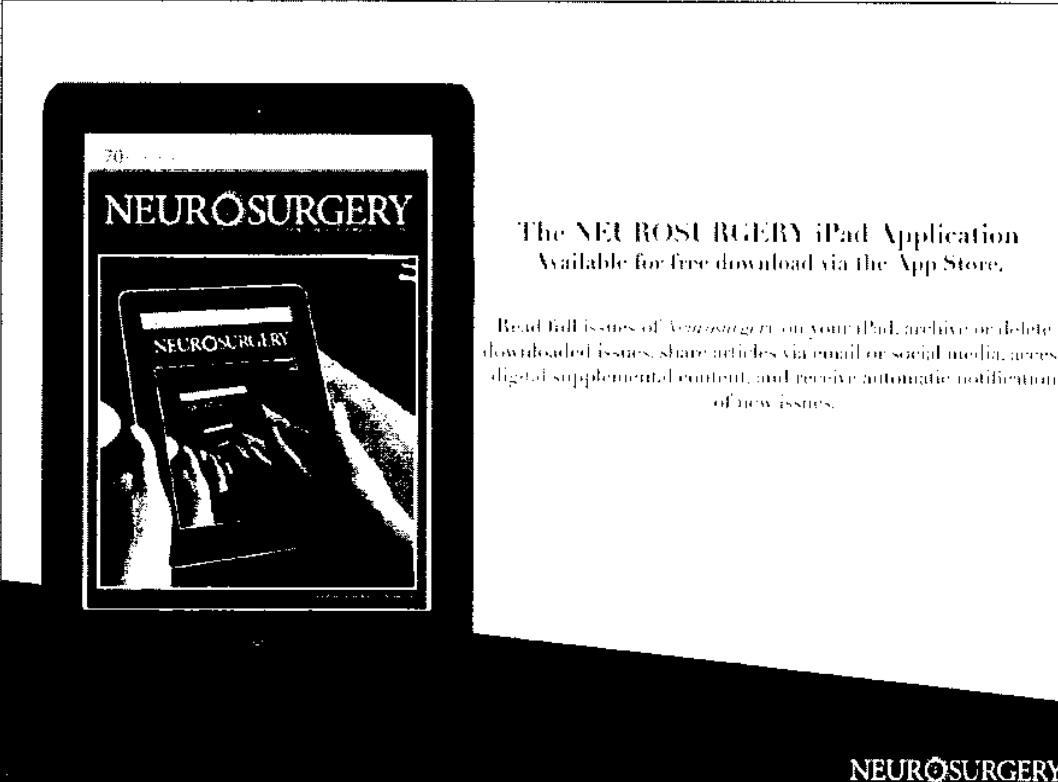
are that rehabilitation may mitigate potentially long-term risks and poor outcome in the future.

While absence of proof does not equate to proof of absence regarding proposed relationships between SRC and neurodegenerative conditions (eg, CTE), further study is indicated before policies are formed. The current review not only provides critical evaluation of current research and highlights the previously reported questionable relationship between SRC

and CTE, but also reiterates the ongoing need for additional studies further delineating associations between athletes with a history of concussion who develop CTE-like symptoms.

**Michael W. Collins**  
**Kelly L. Pearce**  
*Pittsburgh, Pennsylvania*

Commentary provided by Allen K. Sills on page 657.



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**NEUROSURGERY**

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 12 Nov 2015 12:15:25 -0500  
**To:** Lonser, Russell; 'Richard Ellenbogen'; 'Hunt Batjer'  
**Subject:** Re: brain bank stuides coming out with high frequency of finding CTE

Have seen P- tau in glia along the ventricles in aged folks.  
w

**From:** Russell Lonser <[Russell.Lonser@osumc.edu](mailto:Russell.Lonser@osumc.edu)>  
**Date:** Wednesday, November 11, 2015 at 9:07 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>, Richard Ellenbogen <[rge@neurosurgery.washington.edu](mailto:rge@neurosurgery.washington.edu)>, Hunt Batjer <[Hunt.Batjer@UTSouthwestern.edu](mailto:Hunt.Batjer@UTSouthwestern.edu)>  
**Subject:** RE: brain bank stuides coming out with high frequency of finding CTE

I have it on desktop (pdf). I'll send tomorrow. Just have my iphone with me.

Sent with Good ([www.good.com](http://www.good.com))

-----Original Message-----

**From:** Koroshetz, Walter (NIH/NINDS) [E] [[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)]  
**Sent:** Wednesday, November 11, 2015 08:45 PM Eastern Standard Time  
**To:** Lonser, Russell; 'Richard Ellenbogen'; 'Hunt Batjer'  
**Subject:** Re: brain bank stuides coming out with high frequency of finding CTE

Have never seen that from Braak. Do you have a reference?  
Walter

**From:** Russell Lonser <[Russell.Lonser@osumc.edu](mailto:Russell.Lonser@osumc.edu)>  
**Date:** Tuesday, November 10, 2015 at 10:22 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>, Richard Ellenbogen <[rge@neurosurgery.washington.edu](mailto:rge@neurosurgery.washington.edu)>, Hunt Batjer <[Hunt.Batjer@UTSouthwestern.edu](mailto:Hunt.Batjer@UTSouthwestern.edu)>  
**Subject:** RE: brain bank stuides coming out with high frequency of finding CTE

A large problem is that none of the studies have examined clinically normal individuals. Prior pathology studies (Braak) have shown that nearly every person (autopsy brain) older then 10 years of age (in age related amounts) has abnormal tau in brain but no clinical effect.

Sent with Good ([www.good.com](http://www.good.com))

-----Original Message-----

**From:** Koroshetz, Walter (NIH/NINDS) [E] [[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)]  
**Sent:** Tuesday, November 10, 2015 10:16 AM Eastern Standard Time  
**To:** Lonser, Russell; Richard Ellenbogen; Hunt Batjer

**Subject:** Re: brain bank studies coming out with high frequency of finding CTE

yes, it's really an unknown. From public health standpoint it really increases importance of careful longitudinal study to see what constellation of findings predicts progression to cognitive impairment, and when one can make that prediction accurately.

of note the early descriptions by Corsellis did include a behavioral syndrome before the cognitive decline.

if there is a behavioral syndrome that does not progress to cognitive impairment that would be tough to ID. would have to have unique features.

Would have to study high risk "normal" group prospectively with matched controls

walter

Walter

Sent from my iPhone

On Nov 10, 2015, at 5:20 AM, Lonser, Russell <[Russell.Lonser@osumc.edu](mailto:Russell.Lonser@osumc.edu)> wrote:

Thanks Walter. Does question the clinical significance of the pathologic findings.

**From:** Walter Koroshetz <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>

**Date:** Monday, November 9, 2015 at 10:49 AM

**To:** Jeffrey Miller <[Jeff.Miller@NFL.com](mailto:Jeff.Miller@NFL.com)>, "Ellenbogen, Richard (rge@neurosurgery.washington.edu)" <[rge@neurosurgery.washington.edu](mailto:rge@neurosurgery.washington.edu)>, Russell Lonser <[russell.lonser@osumc.edu](mailto:russell.lonser@osumc.edu)>, Hunt Batjer <[hunt.Batjer@UTSouthwestern.edu](mailto:hunt.Batjer@UTSouthwestern.edu)>, "Freire, Maria (FNIH) [T]" <[mfreire@fnih.org](mailto:mfreire@fnih.org)>

**Subject:** brain bank studies coming out with high frequency of finding CTE

FYI- The CTE consensus guidelines from the grantees allowed others to start looking in their brain banks. Attached two studies of reports of finding CTE in Brain Banks. These are not biased for professional athletes but are biased for people who die with neurological disorders.

But raises possibility that CTE may be relatively common in persons with history of various types of TBI. If so, then the clinical significance of the pathologic finding becomes the BIG question for the public health.

Walter

Walter Koroshetz, MD

Director, National Institute of Neurological Disorders and Stroke



**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 11 Nov 2015 20:37:53 -0500  
**To:** Ellenbogen, Richard  
**Cc:** Russ Lonser; Hunt Batjer  
**Subject:** Re: brain bank stuides coming out with high frequency of finding CTE

Right. And also would need long followup.  
walter

On 11/11/15, 5:36 PM, "Ellenbogen, Richard"  
<rge@neurosurgery.washington.edu> wrote:

>Walter:  
>I agree. But carefully collected population based longitudinal study  
>would really give us the public health info we need with matched  
>controls. The problem with high risk 'normal' group is the selection bias  
>inherent is the "high risk" and 'normal' group  
>On Nov 10, 2015, at 9:16 AM, Koroshetz, Walter (NIH/NINDS) [E]:  
><koroshetzw@ninds.nih.gov><mailto:koroshetzw@ninds.nih.gov>> wrote:  
>  
>yes. it's really an unknown. From public health standpoint it really  
>increases importance of careful longitudinal study to see what  
>constellation of findings predicts progression to cognitive impairment,  
>and when one can make that prediction accurately.  
>  
>of note the early descriptions by Corsellis did include a behavioral  
>syndrome before the cognitive decline.  
>  
>if there is a behavioral syndrome that does not progress to cognitive  
>impairment that would be tough to ID. would have to have unique features.  
>  
>Would have to study high risk "normal" group prospectively with matched  
>controls  
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>walter  
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>Walter  
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>Sent from my iPhone  
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>On Nov 10, 2015, at 5:20 AM, Lonser, Russell  
><Russell.Lonser@osumc.edu><mailto:Russell.Lonser@osumc.edu>> wrote:  
>  
>Thanks Walter. Does question the clinical significance of the pathologic  
>findings.  
>  
>From: Walter Koroshetz  
><koroshetzw@ninds.nih.gov><mailto:koroshetzw@ninds.nih.gov>>  
>Date: Monday, November 9, 2015 at 10:49 AM  
>To: Jeffrey Miller <Jeff.Miller@NFL.com><mailto:Jeff.Miller@NFL.com>>,  
>"Ellenbogen, Richard  
><rge@neurosurgery.washington.edu><mailto:rge@neurosurgery.washington.edu>>)"

>  
><orge@neurosurgery.washington.edu<mailto:orge@neurosurgery.washington.edu>>,  
> Russell Lonser  
><russell.lonser@osumc.edu<mailto:russell.lonser@osumc.edu>>, Hunt Batjer  
><hunt.Batjer@UTSouthwestern.edu<mailto:hunt.Batjer@UTSouthwestern.edu>>,  
>"Freire, Maria (FNIH) [T]" <mfreire@fnih.org<mailto:mfreire@fnih.org>>  
>Subject: brain bank stuides coming out with high frequency of finding CTE  
>  
>FYI- The CTE consensus guidelines from the grantees allowed others to  
>start looking in their brain banks. Attached two studies of reports of  
>finding CTE in Brain Banks. These are not biased for professional  
>athletes but are biased for people who die with neurological disorders.  
>  
>But raises possibility that CTE may be relatively common in persons with  
>history of various types of TBI. If so, then the clinical significance  
>of the pathologic finding becomes the BIG question for the public health.  
>Walter  
>  
>Walter Koroshetz, MD  
>Director, National Institute of Neurological Disorders and Stroke  
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>Privileged, confidential or patient identifiable information may be  
>contained in this message. This information is meant only for the use of  
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>copies of the message and any attachments.

**From:** Mona Hicks  
**Sent:** 11 Nov 2015 10:38:39 -0800  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Re: TBI neuropathology

Walter,

Coincidentally, yesterday at the TRACK/TED Investigator's meeting Geoff mentioned that accessing biopsy tissue for research was something that should be explored. I also heard that Ramon's research coordinator, Carol Moore, is going to try to figure out a way to get postmortem brains from people enrolled in TRACK - that would be extremely valuable. Lastly, it was encouraging to learn that Dan Perl had acquired and analyzed several brains and his presentation last week was even-handed and informative. At last we are getting some real data and moving beyond speculation.

Mona

On Wed, Nov 11, 2015 at 6:48 AM, Koroshetz, Walter (NIH/NINDS) [E]  
<[koroshetz@ninds.nih.gov](mailto:koroshetz@ninds.nih.gov)> wrote:

Dear Mona

neurosurgeons could access biopsy tissue, also brain autopsy from people who die after head trauma, usually brain death.

has there been call for this kind of tissue by TBI investigators?

Walter

Sent from my iPhone

On Nov 10, 2015, at 3:26 PM, Mona Hicks <[mona.hicks@onemind.org](mailto:mona.hicks@onemind.org)> wrote:

Hi Walter,

Pat and I met Gail Rosseau (copied on this email) last week at the Blast-related CTE meeting. Gail has been in a leadership role at AANS and has some ideas about how to enlist neurosurgeons in the effort to obtain TBI postmortem brains for research. This was once again highlighted as an important gap at the CTE meeting. Hope you are doing well.

Mona

--

## ONE MIND

**Ramona Hicks, Ph.D.**

*Chief Scientific Officer*

(o) 206.457.8403 (m) 206.799 (b) (6)

120 Lakeside Avenue, Suite 200, Seattle, WA 98122

"GLOBAL INNOVATION FOR BRAIN HEALTH"

--

## ONE MIND

**Ramona Hicks, Ph.D.**

*Chief Scientific Officer*

(o) 206.457.8403 (m) 206.799 (b) (6)

120 Lakeside Avenue, Suite 200, Seattle, WA 98122

"GLOBAL INNOVATION FOR BRAIN HEALTH"

**From:** Rosseau, Gail L.  
**Sent:** 10 Nov 2015 20:52:29 +0000  
**To:** Mona Hicks  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Re: TBI neuropathology

Thank you for introducing us, Mona.  
Walter and I are meeting at his office at 4pm this Thursday.

Great meeting you; hope to see you again soon.

Gail

Gail Rosseau, MD  
Associate Chairman, Neurosurgery Programs  
Department of Neurosciences  
Inova Fairfax Hospital  
3300 Gallows Rd  
Falls Church, VA 22042  
T: 703-776-6383 F: 703-776-4018

On Nov 10, 2015, at 3:26 PM, Mona Hicks <[mona.hicks@onemind.org](mailto:mona.hicks@onemind.org)> wrote:

Hi Walter,

Pat and I met Gail Rosseau (copied on this email) last week at the Blast-related CTE meeting. Gail has been in a leadership role at AANS and has some ideas about how to enlist neurosurgeons in the effort to obtain TBI postmortem brains for research. This was once again highlighted as an important gap at the CTE meeting. Hope you are doing well.

Mona

--

## ONE MIND

**Ramona Hicks, Ph.D.**  
*Chief Scientific Officer*  
(e) 206.457.8403 | (m) 206.79 (b) (6)  
120 Lakeside Avenue, Suite 200, Seattle, WA 98122

"GLOBAL INNOVATION FOR BRAIN HEALTH"

**From:** Walker, Paula (NIH/NINDS) [E]  
**Sent:** 10 Nov 2015 12:07:56 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E]; Mott, Meghan (NIH/NINDS) [E]  
**Subject:** Meeting to discuss CTE/Brain Injury w/Gail Rosseau

Hi Walter:

I just received another call from Gail Rosseau, Vice Chairman of Neurosciences at Inova Fairfax Hospital asking again to meet with you to discuss CTE/Brain Injury. Although she has already met with Pat Bellgowan, she would still like to meet with you.

I have scheduled the meeting for Thursday, November 12<sup>th</sup> at 4:00 p.m. in 31/8A52. She is fine if Pat joins the meeting.

Do you want to meet with her or should I reschedule? Should I moved the meeting to the NSC?

Thanks,

Paula Walker

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Thursday, November 05, 2015 2:28 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Walker, Paula (NIH/NINDS) [E]  
**Subject:** Re: Meeting Request to discuss CTE/Brain Injury

Dear Pat,  
Any idea what the Inova person wants to discuss?

Walter

**From:** Paula Walker <[walkerp@ninds.nih.gov](mailto:walkerp@ninds.nih.gov)>  
**Date:** Thursday, November 5, 2015 at 1:10 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Subject:** Meeting Request to discuss CTE/Brain Injury

Hi Walter:

Meghan took a call requesting a meeting with you and Dr. Rosseau, Vice Chairman of Neurosciences at Inova Fairfax Hospital. She would like to meet with you to discuss CTE/Brain Injury. She spoke with Pat Bellgowan yesterday.

Meghan offered her next Thursday, November 12<sup>th</sup> in the afternoon.

Do you want to meet with her and if so, who else would you like to invite?

Thanks.

Paula Walker

**From:** Mancini, Barbara (<mailto:Barbara.Mancini@inova.org>)  
**Sent:** Thursday, November 05, 2015 12:28 PM  
**To:** Walker, Paula (NIH/NINDS) [E]  
**Subject:** please schedule meeting with Dr.Koroshetz and Dr. Rosseau

Paula,

I just spoke with Meghan Mott about scheduling a meeting to discuss CTE/Brain Injury next Thursday at 230 with Dr Rosseau, who is our Vice Chairman of Neurosciences at Inova Fairfax Hospital and Dr. Koroshetz.

She is currently attending the DOD Blast Injury Research Program in Mclean VA and yesterday spoke to Patrick Belligowan about some important recommendations that she would like to discuss with Dr. Koroshetz.

Megan thought next Thursday, November 12 at 230 would be the best time for them to meet next week. Please confirm this appointment so I can add it to her calendar.

Thank you

Barbara Mancini

**Barbara Mancini**, RN, MBA, CNRN,FAHA

Director of Growth And Operations

Neurosciences

Inova Fairfax Medical Campus

Office 703-776-2692

Cell 571-237(b) (6)

Fax 703-776-4018

**To:** Babcock, Debra (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** FW: TBI/CTE Teleconference  
**Attachments:** Publication Agreement draft v1.docx

Attached is the publication agreement that Deb had set-up though I can't find any information about the final version of the "

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1417  
[psfb@marl.nih.gov](mailto:psfb@marl.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Babcock, Debra (NIH/NINDS) [E]  
**Sent:** Monday, November 10, 2014 1:22 PM  
**To:** wayne.gordon@mountsinai.org; Mckee, Ann C (amckee@bu.edu); Bellgowan, Patrick (NIH/NINDS) [E]; Michel, Mary Ellen (NIH/NICHD) [E]; Folkerth (rfolkerth@partners.org); Dams-o'connor, Kristen (kristen.dams-o'connor@mountsinai.org); Crane, Paul (pcrane@uw.edu); Perl, Daniel (daniel.perl@usuhs.edu); Keene, Dirk (cdkeene@uw.edu); Kowall, Neil W (nkowall@bu.edu); Steve Marshall (smarshall@unc.edu); Imurphy2@bu.edu; jessemez@bu.edu; chaisson@bu.edu  
**Subject:** TBI/CTE Teleconference

Hi Everyone,

It's that time again. Please let me know if you'd like to add other agenda items. I'll look forward to speaking with all of you this Thurs., November 13, at 3 pm.

Participant passcode: (b) (6)  
Dial in numbers: 888-455-(b) (6)

AGENDA

- 1) Update on consensus conference
- 2) Update on Neuropathology form/CDEs
- 3) Update on NBB
- 4) Follow-up on publication agreement (attached, with comments and personnel list)
- 5) Other items?

Best,

Deb and Patrick

Debra J. Babcock, Ph.D., M.D.  
Program Director, Behavioral & Cognitive Neuroscience  
NINDS/NIH  
6001 Executive Blvd., Room 2108, MSC 9521  
Bethesda, MD 20892-9521



Rockville, MD 20852 (for UPS, FedEx, etc.)  
Phone: 301-496-9964  
Fax: 301-402-2060  
Email: [dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)



---

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Monday, November 09, 2015 9:44 AM  
**To:** Chan, Leighton (NIH/CC/RMD) [E]  
**Subject:** RE: Mood disorders  
**Attachments:** Beiniek et al Acta Neuropathol 2015 - Mayo - CTE (3).pdf

Good point. That's really the big issue now.

The twist is new reports that pathological early CTE found in brain banks of people not professional athletes or even close (attached). 32% of people with brains in the Mayo brain bank in whom they could find history of contact sports had CTE! Mayo Brain Bank is biased toward neurologic disorders so may be less in a population study.

So more common than anyone guessed, not clear what the clinical relevance is which is the big question. Finding pathologic evidence of early stage CTE in brains of people who died elderly raises question of whether could be just a static injury that never worsens-- in some people.

Walter

-----Original Message-----

From: Chan, Leighton (NIH/CC/RMD) [E]  
Sent: Sunday, November 08, 2015 10:23 PM  
To: Koroshetz, Walter (NIH/NINDS) [E]  
Subject: Mood disorders

I would not agree to any collaborative agreement that did not assess mood disorders. Even if I were willing to ignore it, the IRB would require extensive testing to assess suicide risk.

On 11/8/15, 5:31 PM, "Koroshetz, Walter (NIH/NINDS) [E]"  
<koroshetzw@ninds.nih.gov> wrote:

(b) (5)



**From:** Chan, Leighton (NIH/CC/RMD) [E]  
**Sent:** 8 Nov 2015 22:23:07 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Mood disorders

I would not agree to any collaborative agreement that did not assess mood disorders. Even if I were willing to ignore it, the IRB would require extensive testing to assess suicide risk.

On 11/8/15, 5:31 PM, "Koroshetz, Walter (NIH/NINDS) [E]"  
<koroshetz@ninds.nih.gov> wrote:

>Thanks Leighton, will take a look. the only hing I could say to be aware

(b) (5)

[Redacted]

>

>-Walter

>

>Sent from my iPhone

>

>> On Nov 8, 2015, at 4:17 PM, Chan, Leighton (NIH/CC/RMD) [E]

>><chanle@cc.nih.gov> wrote:

>>

>>Hi Walter- This is what (b) (5)

(b) (5)

[Redacted]

>>

>>(b) (5)

[Redacted]

>>

>>LC

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>>Leighton Chan, MD, MPH

>>Chief, Rehabilitation Medicine Department, Clinical Center, National  
>>Institutes of Health

>>Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD  
>>20892-1604

>>

>>Phone: 301-496-4733

>> Fax: 301-402-0663  
>> Email: chanle@cc.nih.gov <<mailto:chanle@cc.nih.gov>>

>>

>>

>> -----Original Message-----

>> From: Guskiewicz, Kevin M [[mailto:gus\\_k\\_email@unc.edu](mailto:gus_k_email@unc.edu)]  
>> Sent: Friday, November 06, 2015 5:41 PM  
>> To: Chan, Leighton (NIH/CC/RMD) [E]; Lonser, Russell  
>> Cc: McCrea, Michael; Richard Ellenbogen; Jeffrey Miller; 'Armstrong,  
>> Regina'; 'Youngren, Kirsten'; Hassard, Samantha (NIH/CC/RMD) [C]; van  
>> der Merwe, Andre (NIH/CC/RMD) [V]; Hassard, Samantha (NIH/CC/RMD) [C];  
>> Clark, Michael  
>> Subject: RE: Draft Agenda

>>

>> Leighton,  
>> Thanks for sending the agenda for Monday. I just realized that you may  
>> not have received the slide set (attached). Looking forward to seeing  
>> you and your colleagues.

>> Best,

>> Kevin

>>

>> -----

>> Kevin Guskiewicz, PhD, ATC  
>> Kenan Distinguished Professor, Exercise and Sport Science Senior  
>> Associate Dean, Natural Sciences University of North Carolina at Chapel  
>> Hill

>>

>>

>>

>> -----Original Message-----

>> From: Chan, Leighton (NIH/CC/RMD) [E] [<mailto:chanle@cc.nih.gov>]  
>> Sent: Friday, November 06, 2015 10:53 AM  
>> To: Guskiewicz, Kevin M; Lonser, Russell  
>> Cc: McCrea, Michael; Richard Ellenbogen; Jeffrey Miller; 'Armstrong,  
>> Regina'; 'Youngren, Kirsten'; Hassard, Samantha (NIH/CC/RMD) [C]; van  
>> der Merwe, Andre (NIH/CC/RMD) [V]; Hassard, Samantha (NIH/CC/RMD) [C]  
>> Subject: Draft Agenda

>>

>> Folks- Here is a draft agenda. We are going to push back our start to  
>> 9:30am. We have the room until noon, but I am not sure that we will  
>> need that much time. Please send us your slides if you can. Samantha  
>> should have sent out dial in numbers for those calling in....

>>

>> Happy to make any changes to the agenda.

>>

>> L.C

>>

>>

>>

>> Leighton Chan, MD, MPH  
>> Chief, Rehabilitation Medicine Department, Clinical Center, National  
>> Institutes of Health Building 10, Room 1-1469 10 Center Drive, MSC 1604  
>> Bethesda, MD 20892-1604

>>

>> Phone: 301-496-4733

>> Fax: 301-402-0663

>> Email: chanle@cc.nih.gov <<mailto:chanle@cc.nih.gov>>  
>>  
>>  
>> -----Original Message-----  
>> From: Guskiewicz, Kevin M [<mailto:gus@email.unc.edu>]  
>> Sent: Thursday, November 05, 2015 5:30 PM  
>> To: Lonser, Russell  
>> Cc: Chan, Leighton (NIH CC/RMD) [E]; McCrea, Michael; Richard  
>> Ellenbogen; Jeffrey Miller  
>> Subject: Re: Monday  
>>  
>> Leighton- No. We are good. We will forward a slide set to you  
>> tomorrow and it would be good to have a projector.  
>> Thanks, kevin  
>>  
>> Sent from my iPhone  
>>  
>>> On Nov 5, 2015, at 8:45 AM, Lonser, Russell <[Russell.Lonser@osumc.edu](mailto:Russell.Lonser@osumc.edu)>  
>>> wrote:  
>>>  
>>> I don't need anything. Kevin might though.  
>>>  
>>>  
>>>  
>>> On 11/5/15 8:41 AM, "Chan, Leighton (NIH CC/RMD) [E]"  
>>> <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)>  
>>> wrote:  
>>>  
>>>> Russ et al- We are looking forward to meeting on Monday. If you  
>>>> have any slides to present, please forward them to us this week so  
>>>> that they can be uploaded. Beyond a slide projector, do you folks  
>>>> need anything  
>>>> else?  
>>>>  
>>>> LC  
>>>>  
>>>> \_\_\_\_\_  
>>>>  
>>>> Leighton Chan, MD, MPH  
>>>> Chief, Rehabilitation Medicine Department, Clinical Center, National  
>>>> Institutes of Health Building 10, Room 1-1469 10 Center Drive, MSC  
>>>> 1604 Bethesda, MD 20892-1604  
>>>>  
>>>> Phone: 301-496-4733  
>>>> Fax: 301-402-0663  
>>>> Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) / <mailto:chanle@cc.nih.gov>  
>>>>  
>>>>  
>>>> -----Original Message-----  
>>>> From: Guskiewicz, Kevin M [<mailto:gus@email.unc.edu>]  
>>>> Sent: Tuesday, October 27, 2015 8:32 AM  
>>>> To: Chan, Leighton (NIH CC/RMD) [E]; 'Lonser, Russell'; McCrea,  
>>>> Michael  
>>>> Cc: Richard Ellenbogen; Jeffrey Miller  
>>>> Subject: RE: Protocols  
>>>>

>>>> Leighton,  
>>>> Thanks for sending your project protocol. We will get up to speed on  
>>>> what your project before our Nov 9 meeting and look forward to the  
>>>> meeting to determine how we can begin a collaboration together. We  
>>>> will be sending you some additional materials regarding our project  
>>>> by week's end.

>>>> Best,  
>>>> Kevin

>>>>

>>>> -----

>>>> Kevin Guskiewicz, PhD, ATC  
>>>> Kenan Distinguished Professor, Exercise and Sport Science Senior  
>>>> Associate Dean, Natural Sciences University of North Carolina at  
>>>> Chapel Hill

>>>>

>>>>

>>>>

>>>>

>>>> -----Original Message-----

>>>> From: Chan, Leighton (NIH/CC RMD) [E] [<mailto:chanle@cc.nih.gov>]

>>>> Sent: Monday, October 26, 2015 11:33 AM

>>>> To: 'Lonser, Russell'; McCrea, Michael; Guskiewicz, Kevin M

>>>> Cc: Richard Ellenbogen; Jeffrey Miller

>>>> Subject: RE: Protocols

>>>>

>>>> Here is a recent version of our protocol. It needs to be updated,  
>>>> but it should give you a sense of the data we collect and the broad  
>>>> objectives of the project. I has been amended many times to deal  
>>>> with the shifting need of CNRM.

>>>>

>>>> LC

>>>>

>>>>

>>>>

>>>> Leighton Chan, MD, MPH

>>>> Chief, Rehabilitation Medicine Department, Clinical Center, National  
>>>> Institutes of Health Building 10, Room 1-1469 10 Center Drive, MSC  
>>>> 1604 Bethesda, MD 20892-1604

>>>>

>>>> Phone: 301-496-4733

>>>> Fax: 301-402-0663

>>>> Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>

>>>>

>>>> -----Original Message-----

>>>> From: Lonser, Russell [<mailto:Russell.Lonser@osumc.edu>]

>>>> Sent: Monday, October 26, 2015 10:30 AM

>>>> To: McCrea, Michael; Guskiewicz, Kevin M

>>>> Cc: Chan, Leighton (NIH/CC/RMD) [E]; Richard Ellenbogen; Jeffrey

>>>> Miller

>>>> Subject: Re: Protocols

>>>>

>>>> Michael,

>>>>

>>>> Sounds great.

>>>>

>>>> Thanks.

>>>>

>>>> Russ

>>>>

>>>>

>>>>> On 10/26/15, 1:56 PM, "McCrea, Michael" <mccrea@mew.edu> wrote:

>>>>>

>>>>> Russ and Leighton,

>>>>>

>>>>> Many thanks for building this bridge to us. I am in flight from

>>>>> London now and hope to convene with Kevin and Bruce on my return so

>>>>> we can discuss a few details related to our study design. We will

>>>>> then send Leighton the overview of our study proposal in

>>>>> anticipation of our meeting on November 9.

>>>>>

>>>>> We look forward to our upcoming discussion and to the prospect of

>>>>> our collaboration together.

>>>>>

>>>>> Michael McCrea, PhD, ABPP

>>>>> Professor & Director of Brain Injury Research Department of

>>>>> Neurosurgery Medical College of Wisconsin

>>>>> 9200 W. Wisconsin Avenue

>>>>> Milwaukee, WI 53226

>>>>>

>>>>> Office: 414-955-7302

>>>>> Fax: 414-955-0115

>>>>> Email: mccrea@mew.edu

>>>>>

>>>>>

>>>>>

>>>>>

>>>>>> On 10/25/15 5:13 AM, "Guskiewicz, Kevin M" <kgus@email.unc.edu>

>>>>>> wrote:

>>>>>>

>>>>>> Russ,

>>>>>> Sounds like a good plan. We will get these off to Leighton on

>>>>>> Monday.

>>>>>> Looking forward to the meeting.

>>>>>> Thanks,

>>>>>> Kevin

>>>>>>

>>>>>> Sent from my iPhone

>>>>>>

>>>>>>> On Oct 25, 2015, at 8:07 AM, Lonser, Russell

>>>>>>> <Russell.Lonser@osmnc.edu>

>>>>>>> wrote:

>>>>>>>

>>>>>>> Leighton/Mike/Kevin,

>>>>>>>

>>>>>>> Leighton would you be willing to send Mike/Kevin your natural

>>>>>>> history protocol? (and Mike/Kevin, could you send Leighton your

>>>>>>> proposed study/protocol? The study overview slides you showed

>>>>>>> yesterday were great).

>>>>>>>

>>>>>>> We would need keep all this confidential but seeing the protocols

>>>>>>> in advance of the meeting may help define areas of potential

>>>>>>> opportunity for collaboration. This would make the meeting more



>>>>>> efficient effective on 11-09.  
>>>>>>  
>>>>>> Thanks.  
>>>>>>  
>>>>>> Russ  
>>>>>>  
>>>>>>  
>>>>>>  
>>>>>> Sent with Good ([www.good.com](http://www.good.com))

(b) (4)



**From:** Chan, Leighton (NIH/CC/RMD) [E]  
**Sent:** 6 Nov 2015 17:03:35 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Re: NFL

I have spoken to M.Freire a couple of time about this, most recently this Thursday. (b) (5)  
(b) (5) Monday will be our first meeting. Just found out that Jeff Miller from NFL is not attending.

We will see how it goes. If it looks good from a science standpoint, I will tun the plans by you....

LC

---

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: 301-496-4733  
Fax: 301-402-0663  
Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>

**From:** Walter Koroshetz <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Date:** Friday, November 6, 2015 at 3:58 PM  
**To:** Leighton Chan <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)>  
**Subject:** Re: NFL

With this level of knowledge would (b) (5)  
(b) (5)

She has regular meetings with Francis.

Walter

Sent from my iPhone

On Nov 5, 2015, at 10:15 PM, Chan, Leighton (NIH/CC/RMD) [E] <[chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)> wrote:

The NFL Head and Neck Committee as well as the Guskiewicz, McCrea, and Jeff Miller from the NFL will be coming on Monday morning to meet with me. (b) (5)  
(b) (5)

(b) (5)



LC

---

Leighton Chan, MD, MPH Chief, Rehabilitation Medicine Department,  
Clinical Center, National Institutes of Health  
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20892-1604

Phone: 301-496-4733

Fax: 301-402-0663

Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>

**From:** Stern, Robert A  
**Sent:** 6 Nov 2015 16:15:26 +0000  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** U01 update and CTE neuropath paper from Mayo  
**Attachments:** Beiniek et al Acta Neuropathol 2015 - Mayo - CTE.pdf

Hi,

You probably have already seen this, but just in case, I thought I would send it to you.

And..Our updated JIT materials for the U01 should be uploaded later today or Monday. Once that is in the hands of the NINDS Administrative folks, is that the last step before NOGA??? Not that I am eager or anything...

Bob

Robert A. Stern, Ph.D.  
Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology  
Clinical Core Director, BU Alzheimer's Disease and CTE Center  
Boston University School of Medicine

72 East Concord Street, B7800  
Boston, MA 02118

Tel: 617-638-5678  
Fax: 617-638-5679

Email: [robstern@bu.edu](mailto:robstern@bu.edu)  
Web: [www.stern@uniofab.org](http://www.stern@uniofab.org)

**From:** Mack, Sarah H.  
**Sent:** 5 Nov 2015 15:34:33 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: Brain Series: updated outline, call next week, sample bio  
**Attachments:** Screen shot 2015-11-05 at 10.31.37 AM.png

Hi Walter,

Here is a rough mockup...

do you know the age/ history of the CTE subject? or should I just say "chronic traumatic encephalopathy"?

and I thought I would use generic arrow to the blowups since I don't know where exactly they came from.

let me know what you think.

best,

Sarah

---

From: Koroshetz, Walter (NIH/NINDS) [E] [koroshetzw@ninds.nih.gov]  
Sent: Thursday, November 05, 2015 9:19 AM  
To: Mack, Sarah H.  
Cc: margulie@seas.upenn.edu  
Subject: Re: Brain Series: updated outline, call next week, sample bio

Dear Sarah,

Here is a zoomed in panel for the image I sent yesterday. Use whichever one you think is best.  
Walter

On 11/5/15, 9:14 AM, "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzw@ninds.nih.gov> wrote:

>Dear Sarah,

>How about this one? Zoomed in image is at the bottom. Will also send a zoomed in image for the previous section that I sent yesterday.

>Walter

>

>On 11/4/15, 7:06 PM, "Mack, Sarah H." <shm1@cume.columbia.edu> wrote:

>

>>Hi Walter,

>>

>>1) The image looks great for the wide view. Do you have a zoomed in image that we could use with the others (see draft attached)? And is there a comparable label for the subject (age, history etc.)?

>>

>>2) The green line is synaptic density, added from a different slide that Susan provided (this came out of an early conference call). I am copying Susan on this in case you want to discuss the figure with her. I am getting worried about finishing up all of the figure changes at this

>>point so if, between you and Susan, you can provide clear directions on  
>>how to handle this figure that would be extremely helpful.

>>

>>3) Okay.

>>

>>4) Okay. I'll take out the trafficking. I do worry that the microglia  
>>activation portion might be confusing (switching from less green is bad,  
>>to less green is good, and apparently halting the "reaction" to the  
>>problem, if I read it correctly...?). But if you think you can explain  
>>it clearly I'll leave it in and we can discuss on Friday.

>>

>>Thanks so much -

>>

>>Sarah

>>

>>

>>

>>From: Koroshetz, Walter (NIH/NINDS) [E.] [koroshetzw@ninds.nih.gov]

>>Sent: Wednesday, November 04, 2015 5:59 PM

>>To: Mack, Sarah H.

>>Subject: Re: Brain Series: updated outline, call next week, sample bio

>>

>>Dear Sarah,

>>1) Attached photo of a late pathologic stage CTE brain slice. Look ok?

>>Not

>>sure if you want to add a 5th panel or could flip out one of the normal  
>>brain panels, and add this one as the 4th of 4.

>>

>>2) I tracked down the origin of the slide from Susan graphing the  
>>different regions. It just goes from one review article to another and so  
>>it is teaching slide not based on real data as is the Huttenlocher figure  
>>I sent. The IOM figure though is more artistically appealing. But in  
>>the

>>IOM report (see attached development in children....), there is not the  
>>green curve on top of the three curves for different brain regions that  
>>was present in Susan's slide. Not sure what the green curve refers to.  
>>It can't be the average of synaptic pruning. Can you take that out? Or  
>>just use the IOM figure?

>>

>>3) Think it is simpler to leave the blood vessels changes out of this  
>>presentation. The blood vessels don't get smaller with compression as  
>>far

>>as I know so this is likely sampling error.

>>

>>4) For time sake was thinking of leaving out the video of the  
>>myelomoneyte

>>trafficking. So that would leave the video of glial cell death in  
>>concussion vs. normal, then the video of microglia activation in  
>>concussion that is blocked by glutathione. Agree that keeping to the clip  
>>where microglia are green is best.

>>

>>

>>Walter

>>

>>

>>On 11-4-15, 3:49 PM, "Mack, Sarah H." <shm1@cumc.columbia.edu> wrote:

>>>  
>>>Hi Walter,  
>>>  
>>>Please let me know about these questions from Monday, and send me the  
>>>new  
>>>Tau images as soon as possible.  
>>>  
>>>Thanks!  
>>>  
>>>Sarah  
>>>  
>>>  
>>>  
>>>  
>>>From: Mack, Sarah H.  
>>>Sent: Monday, November 02, 2015 2:11 PM  
>>>To: Koroshetz, Walter (NIH/NINDS) [E]; Doyle, Christina;  
>>>margulie@seas.upenn.edu  
>>>Cc: Comstock, Dawn; McAllister, Thomas W; Mack, Sarah H.;  
>>>margulies@seas.upenn.edu; Walker, Paula (NIH/NINDS) [E];  
>>>jgillard@seas.upenn.edu; Martinez, Margaret J; Mott, Meghan (NIH/OD) [E]  
>>>Subject: Re: Brain Series: updated outline, call next week, sample bio  
>>>  
>>>Hi Walter,  
>>>  
>>>Thanks for sending the new graph. Since it shows Visual Cortex how  
>>>exactly would you like it to fit in with the other curves in the 'Course  
>>>of Brain Development figure'....?  
>>>And how do you think I should change the axis (or other) labels? The  
>>>ideal labeling was not clear to me from looking at the figure sources  
>>>(in  
>>>which the curves also differed - see sensorimotor ex in snapshot  
>>>attached).  
>>>  
>>>A couple of video questions:  
>>>  
>>>Regarding your first video, do we want them to see a difference  
>>>between the blood vessels in the control and compressed brains? (the  
>>>latter look much smaller but I don't know if that is significant).  
>>>  
>>>Eric and I talked about the second (treatment) video and were  
>>>concerned that the visuals may be confusing vis a vis the first video  
>>>(switching from less green is bad, to less green is good). What you  
>>>>would  
>>>think of using only the first video, and then talking about the  
>>>treatment  
>>>without showing the second video?  
>>>  
>>>Finally, when you send me the final CTE images, please let me know if  
>>>there is a  
>>>title that would be appropriate for the whole figure.  
>>>  
>>>Thanks a lot,  
>>>  
>>>Sarah  
>>>  
>>>



>>>

>>>

>>>

>>>

>>>From: Koroshetz, Walter (NIH/NINDS) [E] [koro@ninds.nih.gov]

>>>Sent: Monday, November 02, 2015 10:34 AM

>>>To: Doyle, Christina: margulie@seas.upenn.edu

>>>Cc: Comstock, Dawn; McAllister, Thomas W; Mack, Sarah H.;

>>>margulies@seas.upenn.edu; Walker, Paula (NIH/NINDS) [E];

>>>jgillard@seas.upenn.edu; Martinez, Margaret J; Mott, Meghan (NIH/OD) [E]

>>>Subject: Re: Brain Series: updated outline, call next week, sample bio

>>>

>>>I like the myelination curves.

>>>It want to complement with curves of synaptic density over time

>>>attached.

>>>From Huttenlocher.

>>>

>>>Walter

>>>

>>>

>>>

>>>On 11/2/15, 9:29 AM, "Doyle, Christina" <cad2012@cume.columbia.edu>

>>>wrote:

>>>

>>>Hi Susan,

>>>

>>>Yes, I believe she did - see the Google site, I see a new figure there.

>>>

>>>So, Walter and Susan, we will talk at 10:30? Here's the number:

>>>

>>>Dial-in number: 800-41 (b) (6)

>>>Passcode: (b) (6)

>>>

>>>Images:

(b) (6)

>>>

>>>For everyone else, I will see what Eric's schedule is when he's at the

>>>HHMI meeting, maybe we can do something before Friday. If not, though,

>>>he

>>>is free on Friday from 10:30am - 1pm.

>>>

>>>Thanks,

>>>Christina

>>>

>>>

>>>

>>>Christina A. Doyle, Ph.D.

>>>Lab Manager for Eric Kandel, Howard Hughes Medical Institute

>>>Administrative Coordinator, Kavli Institute for Brain Science

>>>Department of Neuroscience

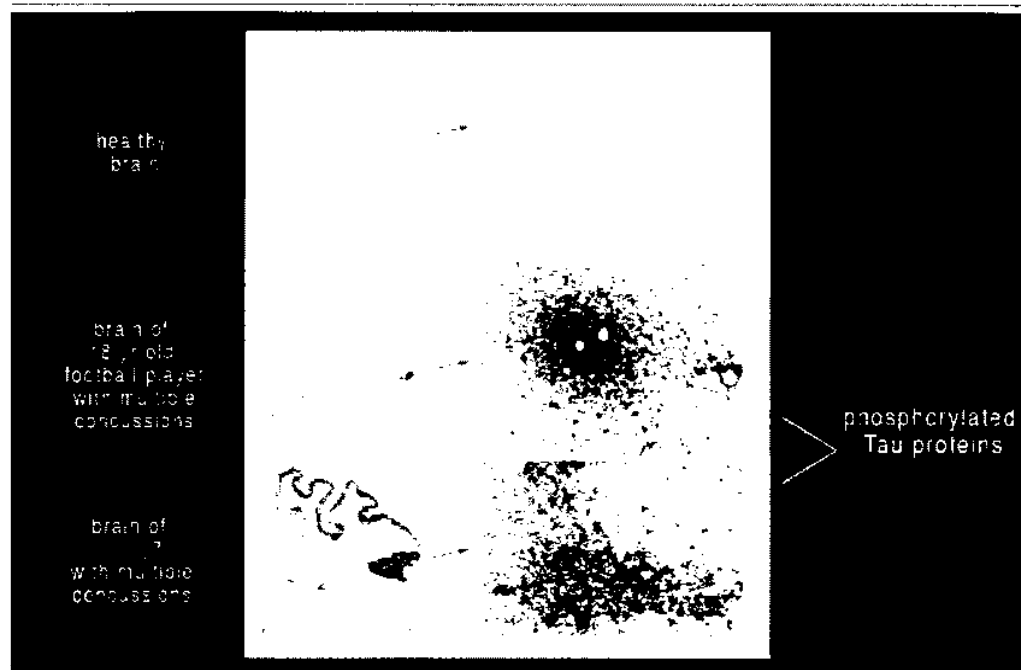
>>>Columbia University

>>>>1051 Riverside Drive  
>>>>New York, NY 10032  
>>>>  
>>>>\*\*PLEASE NOTE NEW NUMBERS\*\*  
>>>>(646) 774.6830 ph  
>>>>(646) 774.6812 fx  
>>>>  
>>>>  
>>>>  
>>>>  
>>>>  
>>>>On 11/1/15 4:09 PM, "Susan Margulies, Ph.D." <margulie@seas.upenn.edu>  
>>>>wrote:  
>>>>  
>>>>I can log in on Monday at 10:3am, but will Sarah have drafted the new  
>>>>figure yet?  
>>>>  
>>>>\_\_\_\_\_  
>>>>>Susan Margulies, Ph.D.  
>>>>>George H. Stephenson Professor of Bioengineering  
>>>>>University of Pennsylvania  
>>>>>Philadelphia, PA 19104-6321  
>>>>>  
>>>>>Mail: 240 Skirkanich Hall, 210 S. 33rd Street  
>>>>>Office: 1050 Hayden Hall, 3320 Smith Walk  
>>>>>  
>>>>>  
>>>>>On 2015-11-01 15:39, Doyle, Christina wrote:  
>>>>> Walter and Susan, if the two of you can call in then we can at least  
>>>>> work on your figures a bit more?  
>>>>>  
>>>>> Everyone else, we'll try for something on Friday. In the meantime,  
>>>>> Sarah will work with you via email on the figures.  
>>>>>  
>>>>> Thanks,  
>>>>> Christina  
>>>>>  
>>>>>  
>>>>>-----  
>>>>> From: Comstock, Dawn [DAWN.COMSTOCK@UCDENVER.EDU]  
>>>>> Sent: Sunday, November 01, 2015 7:15 AM  
>>>>> To: McAllister, Thomas W; <margulie@seas.upenn.edu>  
>>>>> Cc: Doyle, Christina; Koroshetz, Walter (NIH/NINDS) [E]; Mack, Sarah  
>>>>> H.; margulies@seas.upenn.edu; Walker, Paula (NIH/NINDS) [E];  
>>>>> jgillard@seas.upenn.edu; Martinez, Margaret J; Mott, Meghan (NIH/OD)  
>>>>> [E]  
>>>>> Subject: Re: Brain Series: updated outline, call next week, sample  
>>>>> bio  
>>>>>  
>>>>> Sorry, this Sun-Wed is APHA in Chicago. As ICEHS Chair I have many  
>>>>> duties  
>>>>> and am pretty booked.  
>>>>> Dawn  
>>>>>  
>>>>> On 10/31/15, 5:30 PM, "McAllister, Thomas W" <twmcallia@upui.edu>

>>>>>> wrote:  
>>>>>>  
>>>>>> Sorry- pretty much booked solid on Monday and can't make the 10:30  
>>>>>> slot.  
>>>>>> Tom  
>>>>>>  
>>>>>> Sent from my iPhone  
>>>>>>  
>>>>>> On Oct 31, 2015, at 6:16 PM, Susan Margulies, Ph.D.  
>>>>>> <margulie@seas.upenn.edu> wrote:  
>>>>>>  
>>>>>> 10:30-11:30 east coast time Monday works for me, too.  
>>>>>> Susan  
>>>>>>  
>>>>>> ---  
>>>>>> Susan Margulies, Ph.D.  
>>>>>> George H. Stephenson Professor of Bioengineering  
>>>>>> University of Pennsylvania  
>>>>>> Philadelphia, PA 19104-6321  
>>>>>>  
>>>>>> Mail: 240 Skirkanich Hall, 210 S. 33rd Street  
>>>>>> Office: 105D Hayden Hall, 3320 Smith Walk  
>>>>>>  
>>>>>>  
>>>>>> On 2015-10-31 17:58, Doyle, Christina wrote:  
>>>>>> Thanks, Walter. Would 10:30am work for anyone else?  
>>>>>> Christina  
>>>>>> -----  
>>>>>> FROM: Koroshetz, Walter (NIH/NINDS) [E]  
>>>>>> [koroshetzwa@ninds.nih.gov]  
>>>>>> SENT: Friday, October 30, 2015 7:59 PM  
>>>>>> TO: Doyle, Christina; Comstock, Dawn; Susan Margulies, Ph.D.;  
>>>>>> McAllister, Thomas W  
>>>>>> CC: Mack, Sarah H.; margulies@seas.upenn.edu; Walker, Paula  
>>>>>> (NIH/NINDS) [E]; jgillard@seas.upenn.edu; Martinez, Margaret J;  
>>>>>> Mott.  
>>>>>> Meghan (NIH/OD) [E]  
>>>>>> SUBJECT: Re: Brain Series: updated outline, call next week.  
>>>>>> sample  
>>>>>> bio  
>>>>>> Monday have free spot 10:30 to 11:30.  
>>>>>> Walter  
>>>>>> From: Christina Doyle <cad2012@cume.columbia.edu>  
>>>>>> Date: Friday, October 30, 2015 at 4:17 PM  
>>>>>> To: R Comstock <dawn.comstock@ucdenver.edu>, "Susan Margulies,  
>>>>>> Ph.D."  
>>>>>> <margulie@seas.upenn.edu>, Thomas McAllister  
>>>>>> <twmcallia@upui.edu>,  
>>>>>> "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzwa@ninds.nih.gov>  
>>>>>> Cc: Sarah Mack <shm1@cume.columbia.edu>,  
>>>>>> <margulies@seas.upenn.edu>  
>>>>>> <margulies@seas.upenn.edu>, Paula Walker <walkerpa@ninds.nih.gov>,  
>>>>>> "jgillard@seas.upenn.edu" <jgillard@seas.upenn.edu>,  
>>>>>> "majhugheta@upui.edu" <majhugheta@upui.edu>, "Mott, Meghan (NIH/OD)  
>>>>>> [E]"

<smottme@aol.nih.gov>  
 Subject: Brain Series: updated outline, call next week, sample  
 bio  
 Hello all,  
 Attached please find an updated outline (v21) with changes made  
 as  
 a  
 result of today's call with Susan and Tom. Walter, we added some  
 items  
 to your section, please let us know if you would be comfortable  
 addressing them - after Tom talks about what a concussion does to  
 the brain, the idea would be for you to go into why the young  
 brain  
 is  
 especially susceptible because of all the changes it is going  
 through.  
 There are some slides Sarah had already developed with Susan.  
 that  
 Susan thought you might want to use.  
 For next week, is it possible to have a call on Monday? Eric is  
 traveling so after Monday he can't talk again until Friday, and I  
 worry that is too much time to wait, given the episode should  
 tape  
 the  
 following week.  
 So, Monday Eric is free all morning, until 1:30pm. Please let me  
 know  
 when you might be free. I will check my email today/over the  
 weekend  
 so we can arrange the time.  
 I am trying my best to get confirmation from Charlie's producer  
 on  
 the  
 taping date/time, and will let you know as soon as I know so you  
 can  
 tell them your travel preferences. I apologize that it's still up  
 in  
 the air! They are very last-minute there.  
 Finally, for the short bio we need from each of you, an example  
 is  
 below. Particularly important is to let me know exactly how you  
 want  
 your name and institute to appear in the on-screen caption:  
 Janet Hyde  
 UNIVERSITY OF WISCONSIN-MADISON Janet Hyde is the Helen Thompson  
 Woolley Professor of Psychology and Gender & Women's Studies at  
 the  
 University of Wisconsin-Madison. Her research focuses on the  
 assessment of psychological gender differences and similarities.  
 She  
 has particular expertise on the questions of gender difference in  
 mathematics performance and the emergence of gender differences  
 in  
 depression in adolescence.  
 Thanks very much,  
 Christina

~~~~~  
~~~~~ Christina A. Doyle, Ph.D.  
~~~~~ Lab Manager for Eric Kandel, Howard Hughes Medical Institute  
~~~~~ Administrative Coordinator, Kavli Institute for Brain Science  
~~~~~ Department of Neuroscience  
~~~~~ Columbia University  
~~~~~ 1051 Riverside Drive  
~~~~~ New York, NY 10032  
~~~~~ \*\*PLEASE NOTE NEW NUMBERS\*\*  
~~~~~ (646) 774.6830 ph  
~~~~~ (646) 774.6812 fx  
~~~~~  
~~~  
~~~  
~~~  
~



**From:** McKee, Ann C  
**Sent:** 3 Nov 2015 23:13:13 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Re: Ann McKee sent you "IMAGES FOR WALTER"

Walter,  
You should receive another dropbox invitation to retrieve these images.  
Best,  
Ann

On Nov 3, 2015, at 5:35 PM, Koroshetz, Walter (NIH/NINDS) [E]  
<[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)> wrote:

Sorry to bug you. But would you be able to send me a ptau image showing stage 3 or 4 involvement. Would go with the stage 1 case of the 18 year old you sent so I can make the point about spread/progression.

Thanks  
Walter

**From:** Ann via Dropbox <[no-rec-p@dropbox.com](mailto:no-rec-p@dropbox.com)>  
**Reply-To:** ann McKee <[amckee@duke.edu](mailto:amckee@duke.edu)>  
**Date:** Monday, October 26, 2015 at 7:08 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Subject:** Ann McKee sent you "IMAGES FOR WALTER"



Ann shared some files with you on Dropbox

*Here are 2 images - 1 included a control case - as requested - as the case of the 18 year old.*

IMAGES FOR WALTER

[View files](#)

**From:** Stern, Robert A  
**Sent:** 3 Nov 2015 01:30:29 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: U01 Advisory Board Chair

Hi,  
Dave Knopman enthusiastically accepted the invitation to serve as Chair of the Advisory Board. Great news! I agree that he will be superb.  
Best,  
Bob

**From:** Koroshetz, Walter (NIH/NINDS) [E] [mailto:koroshetzw@ninds.nih.gov]  
**Sent:** Saturday, October 31, 2015 1:54 PM  
**To:** Stern, Robert A <bobstern@bu.edu>; Bellgowan, Patrick (NIH/NINDS) [E] <patrick.frostbellgowan@nih.gov>  
**Cc:** Babcock, Debra (NIH/NINDS) [E] <dbabcock@ninds.nih.gov>  
**Subject:** RE: U01 Advisory Board Chair

Dear Bob,  
Of course Bruce is wonderfully gifted behaviorally neurologist. As mentioned NINDS would strongly prefer David as chair because of his organizational skills.  
If group decides to appoint Bruce that's fine, but know it will cause NINDS to become more involved in the oversight of the research plan and progress.  
Best,  
Walter

**From:** Stern, Robert A [mailto:bobstern@bu.edu]  
**Sent:** Saturday, October 31, 2015 9:04 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: U01 Advisory Board Chair

Hi Pat,  
I have received feedback from my co-PIs regarding the Advisory Board Chair choice. Drs. Cummings and Reiman know both Drs. Miller and Knopman well (as do I) and feel that Dr. Miller would be a better choice for Chair; however, if he cannot take that on, Dr. Knopman would be a good choice. We would like to propose the following: I will first ask Dr. Miller to serve as Chair. If he agrees, I would then ask Dr. Knopman to become a member of the Advisory Board. If, however, Dr. Miller declines the role, I would invite Dr. Knopman to become a member of the board and to serve as its Chair.

Please let me know if this plan is okay with you all or if you still would rather me ask Dr. Knopman first.  
Thanks.

Bob



**From:** Bellgowan, Patrick (NIH/NINDS) [E] [mailto:patrick.frostbellgowan@nih.gov]  
**Sent:** Saturday, October 24, 2015 11:11 AM  
**To:** Stern, Robert A <bobstern@bu.edu>  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E] <patrick.frostbellgowan@nih.gov>; Koroshetz, Walter (NIH/NINDS) [E] <koroshetz@ninds.nih.gov>; Babcock, Debra (NIH/NINDS) [E] <dbabcock@ninds.nih.gov>  
**Subject:** Re: U01 Advisory Board Chair

Hi Bob

Will you ask Dr Knopman and if declines we can have Dr Miller chair and find another person to be a member.

Having Dr Cantu's involvement is very valuable I think the concern was only for having him on the SAB. So the role you suggest for Dr Cantu seems fine with me

Pat

Patrick SF Bellgowan, PhD  
Program Director  
NINDS / NIH  
301-496-1447  
Pat.bellgowan@nih.gov

On Oct 23, 2015, at 8:30 AM, "Stern, Robert A" <bobstern@bu.edu> wrote:

Walter and Pat,

Several weeks ago, Walter raised the issue that we should change the proposed chair of the U01 Advisory Board. I agreed that this should be done because the initially proposed chair, Dr. Cantu, has his primary faculty appointment at BU and, therefore, would not have the necessary "arm's length" requirement (either perceived or real) for an Advisory Board chair or member. I suggested Dr. Miller from UCSF since he had already agreed to serve on the proposed Advisory Board. Walter suggested Dr. Knopman from Mayo as another alternative, though he has not been involved with the project or included as a proposed Advisory Board member previously, and I do not know if he would even be interested in doing this. I believe we had left it that one of you was going to get back to me with a decision. I have not yet informed Dr. Cantu of the change. And, I would, of course, need to discuss with the other three PIs. I propose that Dr. continue as a consultant on the study, overseeing the "Neurological, Motor, and Headache" section of the Clinical Outcomes Team. So, prior to moving forward, could you please let me know whether you would like me to invite Dr. Knopman or Dr. Miller to serve as the chair of the Advisory Board.

Thanks very much.

Bob

Robert A. Stern, Ph.D.  
Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology  
Clinical Core Director, BU Alzheimer's Disease and CTE Center

Boston University School of Medicine

72 East Concord Street, B7800  
Boston, MA 02118

Tel: 617-638-5678

Fax: 617-638-5679

Email: [bobstern@bu.edu](mailto:bobstern@bu.edu)

Web: [www.sternneurolab.org](http://www.sternneurolab.org)

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** 2 Nov 2015 15:59:55 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Emr, Marian (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]  
**Subject:** TBI grantee publications

Hi Dr. Koroshetz,

Below are links to PubMed results showing recent publications by the NFL Sport & Health Research Program grantees:

Wayne Gordon, Mount Sinai  
Ann McKee, Boston University  
Jeffrey Ojemann, Seattle Children's Hospital \*\*Dr. Ojemann is a neurosurgeon and has no TBI-related publications  
Lara Beth McKenzie, Nationwide Children's Hospital  
Nicholas Port, Indiana University Bloomington  
Michael Whalen, Massachusetts General Hospital  
Jennifer Suskauer, Kennedy Krieger Institute  
Harvey Levin, Baylor

If Ms. Dodd would like to see specific articles, I would be happy to send them to her.

Thank you,  
Barbara

***Barbara L. McMakin***  
Science Writer  
Office of Communications and Public Liaison  
National Institute of Neurological Disorders & Stroke  
National Institutes of Health  
Building 31, Room 8A07  
31 Center Drive MSC 2540  
Bethesda, MD 20892-2540  
Main Office Line: (301) 496-5751  
Direct Line: (301) 435-7747  
Email: [memakinb1@ninds.nih.gov](mailto:memakinb1@ninds.nih.gov)

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** 2 Nov 2015 14:00:12 -0500  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** FW: Background info: NIH Foundation/NFL donation and Concussion research

Hi Dr. Koroshetz,

Below is the email I sent to Laura Dodd on Friday.

Thanks,  
Barbara

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** Friday, October 30, 2015 8:49 AM  
**To:** 'DoddL@cbsnews.com'  
**Cc:** Emr, Marian (NIH/NINDS) [E]; Walker, Paula (NIH/NINDS) [E]  
**Subject:** Background info: NIH Foundation/NFL donation and Concussion research

Hi Laura,

I've gathered some background information for you regarding research projects supported by the NFL donation. Below you will see links to our press release, meeting/workshop summaries and detailed information about the selected grants.

Dr. Koroshetz will respond to any other questions you may have when you speak to him on Monday afternoon. The interview needs to be pushed back to 4:15pm; please call 301-496-3167 at that time. If you need to change the interview time, contact Paula Walker (copied on this email).

[NINDS Press Release](#) announcing the grants

[Meeting Summary: Report from the First NIH Consensus Conference to Define the Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy](#)

[Workshop Summary: Report on the Neuropathology of Chronic Traumatic Encephalopathy Workshop](#)

[Workshop Summary: Report on the Brain Trauma-Related Neurodegeneration: Strategies to Define, Detect, and Predict Workshop](#)

For each of the grants below, you will find a project description, fiscal information for FY2014 and FY2015 and publications (a number of these grants have already started producing results):

#### CTE AND POSTTRAUMATIC NEURODEGENERATION: NEUROPATHOLOGY AND EX VIVO IMAGING

PI: Anne McKee, Boston University

[Project Description](#)

[Funding](#)

[Publications](#)

#### NEUROPATHOLOGY OF CTE AND DELAYED EFFECTS OF TBI: TOWARD IN-VIVO DIAGNOSTICS

PI: Wayne Gordon, Mount Sinai

[Project Description](#)

[Funding](#)

[Publications](#)

CORTICAL GABA IN PEDIATRIC SPORTS CONCUSSION

PI: George Ojemann, Seattle Children's Hospital

[Project Description](#)

[Funding](#)

[Publications](#)

EVALUATION OF SPOT LIGHT: A CONCUSSION INJURY MANAGEMENT APP FOR YOUTH SPORTS

PI: Lara Beth Trifiletti McKenzie, Nationwide Children's Hospital

[Project Description](#)

[Funding](#)

[Publications](#)

EYE MOVEMENT DYNAMICS: A RAPID OBJECTIVE INVOLUNTARY MEASURE OF CONCUSSION/MTBI

PI: Nicholas Port, Indiana University Bloomington

[Project Description](#)

[Funding](#)

[Publications](#)

CHARACTERIZATION OF THE BRAIN AND SERUM METABOLOME IN MOUSE MODELS OF CONCUSSION

PI: Michael Whalen, Massachusetts General Hospital

[Project Description](#)

[Funding](#)

[Publications](#)

SOMATOSENSORY PROCESSING-ASSESSING YOUTH SPORT-RELATED CONCUSSION AND RECOVERY

PI: Jennifer Suskauer, Kennedy Krieger Institute

[Project Description](#)

[Funding](#)

[Publications](#)

IMAGING AND BIOMARKERS IN ADOLESCENTS CLEARED FOR RETURN TO PLAY AFTER CONCUSSION

PI: Harvey Levin, Baylor College of Medicine

[Project Description](#)

[Funding](#)

[Publications](#)

Please let me know if I can be of further assistance.

Best,

Barbara

*Barbara L. McMakin*

Science Writer

Office of Communications and Public Liaison

National Institute of Neurological Disorders & Stroke

National Institutes of Health

Building 31, Room 8 A07  
31 Center Drive MSC 2540  
Bethesda, MD 20892-2540  
Main Office Line: (301) 496-5751  
Direct Line: (301) 435-1747  
Email: [memakinbj@ninds.nih.gov](mailto:memakinbj@ninds.nih.gov)

**From:** Stern, Robert A  
**Sent:** 31 Oct 2015 17:57:31 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]  
**Subject:** Re: U01 Advisory Board Chair

Thanks Walter. I am sure my colleagues will understand and be fine with David as Chair. I will contact him and hope that he agrees.

Bob

On Oct 31, 2015, at 1:54 PM, Koroshetz, Walter (NIH/NINDS) [E]  
<[koroshetzwa@ninds.nih.gov](mailto:koroshetzwa@ninds.nih.gov)> wrote:

Dear Bob,

Of course. Bruce is wonderfully gifted behaviorally neurologist. As mentioned NINDS would strongly prefer David as chair because of his organizational skills. If group decides to appoint Bruce that's fine, but know it will cause NINDS to become more involved in the oversight of the research plan and progress.

Best,  
Walter

**From:** Stern, Robert A [<mailto:robstern@biuedu>]  
**Sent:** Saturday, October 31, 2015 9:04 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: U01 Advisory Board Chair

Hi Pat,

I have received feedback from my co-PIs regarding the Advisory Board Chair choice. Drs. Cummings and Rerman know both Drs. Miller and Knopman well (as do I) and feel that Dr. Miller would be a better choice for Chair; however, if he cannot take that on, Dr. Knopman would be a good choice. We would like to propose the following. I will first ask Dr. Miller to serve as Chair. If he agrees, I would then ask Dr. Knopman to become a member of the Advisory Board. If, however, Dr. Miller declines the role, I would invite Dr. Knopman to become a member of the board and to serve as its Chair.

Please let me know if this plan is okay with you all or if you still would rather me ask Dr. Knopman first. Thanks.

Bob

**From:** Bellgowan, Patrick (NIH/NINDS) [E] [<mailto:patrick.frostbellgowan@nih.gov>]  
**Sent:** Saturday, October 24, 2015 11:11 AM

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 29 Oct 2015 15:48:00 +0000  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: Draft: Interview request: Concussion research

Looks good. Let's see what they say.  
Marian

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** Thursday, October 29, 2015 9:59 AM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** ACTION: Draft: Interview request: Concussion research

Hi Marian,

Below is a draft of the interview clearance for the CBS News concussion story. Do I need to add anything else before sending it to Building 1?

Thanks,  
Barbara

Reporter: Laura Dodd  
Organization: CBS News  
Phone/Email: [DoddL@cbsnews.com](mailto:DoddL@cbsnews.com)  
Subject: Concussion research  
Deadline: today for scheduling  
Spokesperson: Walter Koroshetz, M.D., Director, NINDS  
Expected place of publication (print, online, broadcast): online  
Expected date of publication/airing: unknown  
Expected prominence (e.g. front page, Sunday, evening/morning show, etc.): unknown

Key messages/talking points:

The reporter would like to interview Dr. Koroshetz about concussion research supported by a donation from the National Football League (see press release from December 2013 describing the funded projects: [http://www.ninds.nih.gov/news\\_and\\_events/news\\_articles/pressrelease\\_nfl\\_tbi\\_12162013.htm](http://www.ninds.nih.gov/news_and_events/news_articles/pressrelease_nfl_tbi_12162013.htm)). The reporter is gathering background information on these projects and Dr. Koroshetz will (b) (5)

*Barbara L. McMakin*  
Science Writer  
Office of Communications and Public Liaison  
National Institute of Neurological Disorders & Stroke  
National Institutes of Health  
Building 31, Room 8A07  
31 Center Drive MSC 2510  
Bethesda, MD 20892-2510  
Main Office Line: (301) 496-5751  
Direct Line: (301) 425-7747  
Email: [mcmakinb@ninds.nih.gov](mailto:mcmakinb@ninds.nih.gov)



**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 29 Oct 2015 18:36:26 +0000  
**To:** 'Dodd, Laura'  
**Cc:** McMakin, Barbara (NIH/NINDS) [E]  
**Bcc:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** RE: NIH Foundation / NFL donation and Concussion research

Dr. Koroshetz could speak with you at 4 pm on Monday. Does that work? Barbara is still gathering information re your questions.  
Marian

*Marian Emr  
Director, Office of Communications and Public Liaison-NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
marian.emr@nih.gov*

**From:** Dodd, Laura [mailto:DoddL@cbsnews.com]  
**Sent:** Thursday, October 29, 2015 2:26 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Cc:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** PRIORITY ACTION: NIH Foundation / NFL donation and Concussion research

Hi Marian,

Is Dr. Koroshetz available at any time Monday? If that's impossible I can move some things around and make Saturday work, but would prefer Monday if that's doable.

In the meantime, are you able to send over the answers to the questions below re: the funding?

Thanks for all of your help—  
Laura

**From:** Emr, Marian (NIH/NINDS) [E] [mailto:emr@ninds.nih.gov]  
**Sent:** Thursday, October 29, 2015 11:52 AM  
**To:** Dodd, Laura <DoddL@cbsnews.com>  
**Cc:** McMakin, Barbara (NIH/NINDS) [E] <mcmakin@ninds.nih.gov>  
**Subject:** RE: NIH Foundation / NFL donation and Concussion research

Good morning, Laura. I've asked my colleague, Barbara McMakin to gather some information about NIH concussion research and share it with you. In the meantime, I'm trying to see when we can connect you with Dr. Koroshetz, who I may have mentioned is travelling this week. Would you be willing to talk with him over the weekend, say Saturday, if that works for him?  
Marian

*Marian Emr  
Director, Office of Communications and Public Liaison-NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
marian.emr@nih.gov*

**From:** Dodd, Laura [mailto:DoddL@cnnnews.com]

**Sent:** Wednesday, October 28, 2015 6:27 PM

**To:** Emr, Marian (NIH/NINDS) [E]

**Subject:** ACTION: Hi Marian, re: NIH Foundation / NFL donation and Concussion research

Marian, hi –

Thanks for the quick call back and your time a moment ago. Just read the Twitter conversation ... very interesting.

As I mentioned, I'm working on a story about football safety, and the progress with concussion research is clearly appropriate. I want to be sure I've got all the numbers and dates, etc correct vis-à-vis funding, as well as the very latest re: scientific studies.

First, the funding ... I understand that in 2012, the NFL donated \$30 million to the Foundation for NIH for research studies on injuries affecting athletes, with brain trauma being the primary area of focus.

With that money, the FNIH funded:

- Two major studies (\$6 million each) looking at "long-term changes that occur in the brain years after a head injury or after multiple concussions." Boston University School of Medicine and U.S. Department of VA was one of the cooperative agreements.
- And "six pilot projects totaling just over \$2 million that will last up to two years and are designed to provide support for the early stages of sports-related concussion projects." These are at a variety of institutions across the country (Seattle's Children's Hospital, Baylor College of Medicine, etc).

A few questions:

1. So just so I'm clear, of the \$30 million the NFL donated to the FNIH, BU received \$6 million, yes?
2. When the NFL donated the money, did they have a say as to where it went / how it was distributed or was that solely at the Foundation's discretion?
3. Re: the six pilot projects that had two years of funding ... have any of them completed their studies since it's been just about two years?

Second topic: the latest in scientific research ... as you know more than most, there is no shortage of studies in this area and I want to be sure I'm referencing the very latest (hence curious if any of the six projects are done...). I realize we don't know more than we do know in the world of concussions and CTE but hoping you can provide a concise snapshot of where we stand today.

Look forward to hearing from you and many thanks,  
Laura

Laura Dodd  
Associate Producer  
60 Minutes  
O: 212-975-3614  
E: [doddla@cnnnews.com](mailto:doddla@cnnnews.com)

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** 29 Oct 2015 15:21:41 -0400  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: NFL concussion grants

Thanks for responding so quickly. Yes, (b) (5) that's why I wanted to clarify all of the information. I may have additional questions about these grants in the next day or two.

Best,  
Barbara

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Thursday, October 29, 2015 3:19 PM  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: NFL concussion grants

Those funds are through FNIH. Each FY FNIH asks the NFL for the funds so the money is not in the bank but is part of the agreement. (b) (5)

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** Thursday, October 29, 2015 3:08 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: NFL concussion grants

Are the funds for 2016 and 2017 guaranteed? And is that public knowledge?

Thanks,  
Barbara

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Thursday, October 29, 2015 3:05 PM  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: NFL concussion grants

Yes, they each have about \$1.5M per year for 4 years 2014-2017.

Patrick SF Bellgowan, PhD

Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** Thursday, October 29, 2015 3:00 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** NFL concussion grants

Hi Pat,

A reporter from CBS News is doing a segment on concussion research, focusing on the NFL-supported grants. I'm pulling together some information for her and had a question for you:  
I thought the two cooperative grants (McKee and Gordon) were to be worth \$6 million each. They have currently received \$3million (\$1.5mil/year for 2014 and 2015)--will they receive additional funding in FY2016 and FY2017?

Thanks,  
Barbara

***Barbara I. McMakin***

Science Writer  
Office of Communications and Public Liaison  
National Institute of Neurological Disorders & Stroke  
National Institutes of Health  
Building 31, Room 8A07  
31 Center Drive MSC 2840  
Bethesda, MD 20892-2540  
Main Office Line: (301) 496-5751  
Direct Line: (301) 435-7747  
E-mail: [memakinb@ninds.nih.gov](mailto:memakinb@ninds.nih.gov)

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 28 Oct 2015 18:32:02 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Re: aan research recommendations  
**Attachments:** image001.png

Hi Walter

FYI, the (b) (5), (b) (4) Maybe of interest to the SHRP/FNIHL. Though budget is ~\$500K/yr

Patrick SF Bellgowan, PhD  
Program Director  
NINDS / NIH  
301-496-1447  
[Pat.bellgowan@nih.gov](mailto:Pat.bellgowan@nih.gov)

On Oct 27, 2015, at 7:34 PM, "Koroshetz, Walter (NIH/NINDS) [E]"  
<[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)> wrote:

Dear Pat

FYI-- At my request the AAN sent along the research recommendations from their evidence based guideline process.

Walter

Walter Koroshetz, MD  
Director, National Institute of Neurological Disorders and Stroke

<image001.png>

<AAN evidence based guideline research recommendations.docx>

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** 28 Oct 2015 10:54:08 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Twitter chat on TBI today at 2pm

Hi Walter,

Today at 2pm NIMH is hosting a twitter chat on TBI and concussion. I would offer to tweet for you but will be speaking during that time. If you are on a computer between 2-3pm today and want to post a few tweets, below are some draft ones for you. Remember to use the hashtag #NIMHchats

**Role of key protein found in long-term complications from traumatic brain injury**  
<http://1.usa.gov/1GJ6SKu> #NIMHchats

**#NIH & @nfl are teaming up to tackle #concussion, #TBI and chronic traumatic encephalopathy**  
**w/@FNIH\_Org:** <http://1.usa.gov/1KQyueg> #NIMHchats

**March @NIH @FNIH\_Org @nfl Sports & Health Research Program meeting summary on #sports-related #concussion** <http://1.usa.gov/1HjxqBy> #NIMHchats

**Study shows young football players have most #concussions at practice, not games**  
<http://1.usa.gov/1FTNUyE> <http://bit.ly/1ihDXSp> #NIMHchats

**What is chronic traumatic encephalopathy? #NIH report guides pathologists' exam for CTE:**  
<http://1.usa.gov/1OP0IJG> Thanks @FNIH\_Org & @nfl

**What is chronic traumatic encephalopathy? #NIH report guides pathologists' exam:**  
<http://1.usa.gov/1OP0IJG> Thanks @FNIH\_Org & @nfl #NIMHchats

**From:** James, Stephanie (FNIH) [T]  
**Sent:** 27 Oct 2015 20:09:15 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Re: New SHRP strategy

That would be great. The only things I have on my calendar for Thursday are at noon and 4:00pm. I can be available anytime Friday. My number is 301-451-2810.

Thanks, Stephanie

Sent from my BlackBerry 10 smartphone.

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Tuesday, October 27, 2015 7:05 PM  
**To:** James, Stephanie (FNIH) [T]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: New SHRP strategy

Could fill you in on what I know. I can try to call at breaks on Thursday or Friday as I go to meetings in Philly Thurs AM.  
walter

**From:** James, Stephanie (FNIH) [T]  
**Sent:** Tuesday, October 27, 2015 6:23 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** New SHRP strategy

Dear Walter and Pat,

We understand that NFL is putting out some feelers about possibly funding research through an intramural mechanism. We know very little about their intentions so far, except that they have approached Leighton Chan. We were wondering if you have a better understanding of what they are thinking, and if so what your reaction is. We don't want to get caught flat footed if Jeff suddenly calls Maria with some new proposition.

Thanks for any advice you can give on this. I'm out of the office tomorrow but could be available for a call on Thursday or Friday if that would work better than email.

Best, Stephanie

Sent from my BlackBerry 10 smartphone.

**From:** Mckee, Ann C  
**Sent:** 26 Oct 2015 23:57:59 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/OD) [E]  
**Subject:** Re: Brain Series: concussion images

Hi Walter,

I tried to send higher res images earlier today and they keep getting stuck in the email - so I'm going to invite you to a dropbox to download the high res images. You probably will have to do this on a personal computer as I'm not sure the NIH can use dropbox. Please let me know if you have any trouble getting these- if so, I'll think of another way to send them.

Best,

Ann

On 10/26/15, 12:47 PM, "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetz@ninds.nih.gov> wrote:

~Dear Ann

>Sorry to bug you. Am going on Charlie Rose to talk about concussion. I

>wanted to show the pathology slides attached. The TV folks asked if I

>could get higher resolution images. These were in the kbyte range.

>Possible to send me these originals?

>

>Walter

>

>-----Original Message-----

>From: Muck, Sarah H. [mailto:shml@cumc.columbia.edu]

>Sent: Friday, October 23, 2015 9:24 AM

>To: Koroshetz, Walter (NIH/NINDS) [E]

>Subject: RE: Brain Series: concussion images

>

>Dear Walter,

>

>Thanks for getting back to me.

>

>I was thinking that something like the attached image might be clearest

>for a lay audience. For the healthy tissue I could use a blow up of the

>brain on the left (as I have done here, to show what it would look like),

>or use a separate sample. Let me know what you think.

>

>Do you have high resolution versions of the photos? These will look

>quite pixelated when blown up

>

>Also, can you tell me the main points you would want to convey with the 2

>images "Concussion : Scope of the issue" and "Pathology associated with

>"Compression...." (screenshot attached)? We will look at the videos

>together on the conference call but it would be good to know the main

>messages of the two slides.

>

>Many thanks.



>

>Sarah

>

>

>From: Koroshetz, Walter (NIH/NINDS) [E] [koroshetzw@ninds.nih.gov]

>Sent: Thursday, October 22, 2015 9:51 PM

>To: Mack, Sarah H.

>Subject: Re: Brain Series: concussion images

>

>Dear Sarah,

>The panels A-D show the dark dots on a pale background. The dots are the  
>abnormal part, rest is normal.

>Lower panels are the blow up of the dots.

>Walter

>

>On 10/22/15, 4:22 PM, "Mack, Sarah H." <shin1@cume.columbia.edu> wrote:

>

>>Hi Walter,

>>

>>If you look at the website I set up you will see that I put some of

>>your images on your page of the site:

(b) (6)

>>

>>I wondered - do you have a control brain for the Tau figure? I thought

>>that it might be best show a control with one or two of the two younger

>>subjects.

>>

>>Let me know if you see any changes you would like, or if you would like  
>>to discuss anything before the conference call.

>>

>>All the best,

>>

>>Sarah

>>

>>From: Koroshetz, Walter (NIH/NINDS) [E] [koroshetzw@ninds.nih.gov]

>>Sent: Friday, October 09, 2015 11:59 AM

>>To: Doyle, Christina; twincalli@iupui.edu; dawn.comstock@ucdenver.edu;

>>Mack, Sarah H.

>>Cc: Walker, Paula (NIH/NINDS) [E]; jgillard@seas.upenn.edu;

>>majhughe@iupui.edu

>>Subject: Re: Brain Series: Conference call tomorrow (Friday) 10:30am

>>EDT

>>

>>Dear Sarah and Eric,

>>Here are a few slides with the visual ideas. Slide 3 in the charlie

>>rose concussion file has two videos. Let me know your thoughts.

>>Best,

>>

>>Walter

>>

>>From: Christina Doyle

>>cc:ead2012@cume.columbia.edu; mailto:ead2012@cume.columbia.edu>>

>>Date: Thursday, October 8, 2015 at 3:10 PM

>>To: "Koroshetz, Walter (NIH/NINDS) [E]"  
>><koroshetzw@ninds.nih.gov<mailto:koroshetzw@ninds.nih.gov>>,  
>>"margulies@seas.upenn.edu<mailto:margulies@seas.upenn.edu>"  
>><margulies@seas.upenn.edu<mailto:margulies@seas.upenn.edu>>, Thomas  
>>McAllister <twmcalli@iupui.edu<mailto:twmcalli@iupui.edu>>, R Comstock  
>><dawn.comstock@ucdenver.edu<mailto:dawn.comstock@ucdenver.edu>>, "Mack,  
>>Sarah H." <shml@cume.columbia.edu<mailto:shml@cume.columbia.edu>>  
>>Cc: Paula Walker <walkerp@ninds.nih.gov<mailto:walkerp@ninds.nih.gov>>,  
>>"jgillard@seas.upenn.edu<mailto:jgillard@seas.upenn.edu>"  
>><jgillard@seas.upenn.edu<mailto:jgillard@seas.upenn.edu>>,  
>>"majhughe@iupui.edu<mailto:majhughe@iupui.edu>"  
>><majhughe@iupui.edu<mailto:majhughe@iupui.edu>>  
>>Subject: Brain Series: Conference call tomorrow (Friday) 10:30am EDT

>>

>>Hello all,

>>

>>First, just a reminder that we will speak tomorrow at 10:30am EDT. Here  
>>is the call-in number:

>>

>>Dial-in number: 800-41 (b) (6)

>>passcode (b) (6)

>>

>>I believe Eric already sent you this, but in case I have attached an  
>>extremely rough draft of the outline that we will prepare, just to give  
>>you an idea. Eric has a prepared introduction, but for the rest of it  
>>we will just have bullet points to keep track of who is going to do  
>>discuss what (and where the images will go).

>>

>>A few other scheduling items:

>>

>>1) You can release 10/26, that date is no longer an option for the  
>>taping. So we are holding 11/11 and 11/12. I will let you know the  
>>moment I get more info from the producer.

>>

>>2) We would like to have another call next week, to get a bit deeper  
>>into the topics and review any images that you start sending to Sarah.  
>>Is Tuesday (10/13) at 2pm possible for everyone?

>>

>>

>>Thanks,

>>Christina

>>

>>

>>

>>...

>>Christina A. Doyle, Ph.D.

>>Lab Manager for Eric Kandel, Howard Hughes Medical Institute

>>Administrative Coordinator, Kavli Institute for Brain Science

>>Department of Neuroscience Columbia University

>>1051 Riverside Drive

>>New York, NY 10032

>>

>>\*\*\*PLEASE NOTE NEW NUMBERS\*\*

>>(646) 774.6830 ph

>>(646) 774.6812 fx

**From:** Stern, Robert A  
**Sent:** 24 Oct 2015 15:11:46 +0000  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]  
**Subject:** Re: U01 Advisory Board Chair

Great. Will do. Thanks much.  
Bob

On Oct 24, 2015, at 11:11 AM, Bellgowan, Patrick (NIH/NINDS) [E]  
<patrick.frostbellgowan@nih.gov> wrote:

Hi Bob

Will you ask Dr Knopman and if declines we can have Dr Miller chair and find another person to be a member.  
Having Dr Cantu's involvement is very valuable I think the concern was only for having him on the SAB. So the role you suggest for Dr Cantu seems fine with me

Pat

Patrick SF Bellgowan, PhD  
Program Director  
NINDS / NIH  
301-496-1447  
Pat.bellgowan@nih.gov

On Oct 23, 2015, at 8:30 AM, "Stern, Robert A" <rohsstern@bu.edu> wrote:

Walter and Pat,  
Several weeks ago, Walter raised the issue that we should change the proposed chair of the U01 Advisory Board. I agreed that this should be done because the initially proposed chair, Dr. Cantu, has his primary faculty appointment at BU and, therefore, would not have the necessary "arm's length" requirement (either perceived or real) for an Advisory Board chair or member. I suggested Dr. Miller from UCSF since he had already agreed to serve on the proposed Advisory Board. Walter suggested Dr. Knopman from Mayo as another alternative, though he has not been involved with the project or included as a proposed Advisory Board member previously, and I do not know if he would even be interested in doing this. I believe we had left it that one of you was going to get back to me with a decision. I have not yet informed Dr. Cantu of the change. And, I would, of course, need to discuss with the other three PIs. I propose that Dr. continue as a consultant on the study, overseeing the "Neurological, Motor, and Headache" section of

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** 21 Oct 2015 16:45:28 -0400  
**To:** Doyle, Christina; margulie@seas.upenn.edu; Thomas McAllister  
**Cc:** Mott, Meghan (NIH/OD) [E]  
**Subject:** Re: FNIH here is the summary - do you have the program?

Yes but I don't know the details. Do you want to follow up with him? Or want me to do this?  
There is another individual that presented her story at the Soc for Neuroscience meeting. A woman who was on the US national soccer team.

On 10/20/15, 5:54 PM, "Doyle, Christina" <cad2012@columbia.edu> wrote:

>Dear Walter,  
>  
>I have passed the info on to Eric, thanks. So, he suffered concussion  
>while at NYU?

>  
>Christina  
>  
>  
>Christina A. Doyle, Ph.D.  
>Lab Manager for Eric Kandel, Howard Hughes Medical Institute  
>Administrative Coordinator, Kavli Institute for Brain Science  
>Department of Neuroscience  
>Columbia University  
>1051 Riverside Drive  
>New York, NY 10032

>  
>\*\*PLEASE NOTE NEW NUMBERS\*\*  
>(646) 774 6830 ph  
>(646) 774 6812 fx

>  
>  
>  
>  
>  
>  
>On 10/19/15 12:14 PM, "Koroshetz, Walter (NIH/NINDS) [E]"  
><koroshetzwa@ninds.nih.gov> wrote:

>  
>>Dear Sue and Christine,  
>>  
>>See below. Laura Baleer at NYU cares for patients with depression and got  
>>permission for us to contact someone. I don't have information but could  
>>make contact if  
>>Dr. Kandel wishes to pursue.

>>  
>>  
>>"The athlete's name is (b) (6) I have already  
>>contacted him and he said he is willing to help. His cell # is (b) (6)  
>>(b) (6) and his email is (b) (6) graduated and is no  
>>longer an (b) (6) athlete but he is living in the NYC area."

>>  
>>  
>>Let me know.

>>  
 >>Walter  
 >>  
 >>On 10/15/15, 8:53 PM, "Susan Margulies, Ph.D." <smargulie@seas.upenn.edu">  
 >>wrote:  
 >>  
 >>>I agree.  
 >>>  
 >>>I have some names I am about to share with the group - a colleague  
 >>>recommended them, and I have asked Eric's team to check them out before  
 >>>extending an invitation. If you know some would be good for the  
 >>>program, please chime in!  
 >>>  
 >>>S  
 >>>  
 >>>---  
 >>>Susan Margulies, Ph.D.  
 >>>George H. Stephenson Professor of Bioengineering  
 >>>University of Pennsylvania  
 >>>Philadelphia, PA 19104-6321  
 >>>  
 >>>Mail: 240 Skirkanich Hall, 210 S. 33rd Street  
 >>>Office: 105D Hayden Hall, 3320 Smith Walk  
 >>>  
 >>>  
 >>>On 2015-10-15 14:08, Koroshetz, Walter (NIH/NINDS) [E] wrote:  
 >>>> Not sure this is best fit for the topic of kids and sports though  
 >>>> Walter  
 >>>>  
 >>>> Sent from my iPhone  
 >>>>  
 >>>> On Oct 15, 2015, at 11:05 AM, Mott, Meghan (NIH/OD) [E]  
 >>>> <mottmc@od.nih.gov> wrote:  
 >>>>  
 >>>>> Hi Susan,  
 >>>>>  
 >>>>> Looks like PETE DID SUSTAIN CONCUSSIONS IN COMBAT, and may have also  
 >>>>> sustained a few doing sports (he is also a professional skier) take  
 >>>>> a look at this article from 2013 -  
 >>>>>  
 >>>>>  
 >>>>>http://www.mensjournal.com/magazine/a-navy-seals-next-mission-skiing-20  
 >>>>1  
 >>>>3  
 >>>>0925  
 >>>> [1]  
 >>>>  
 >>>>> "Over the next decade, Scobell completed six combat deployments  
 >>>>> - two in Iraq, two in Afghanistan, and one that featured the now  
 >>>>> legendary rescue of the Maersk Alabama, a containership that was  
 >>>>> overtaken by Somali pirates. Scobell and his SEAL teammates fought  
 >>>>> during the bloody Shia uprising of 2005, hunted and killed Al Qaeda  
 >>>>> leaders in the Hindu Kush, escorted critical convoys, and were in  
 >>>>> close proximity to more explosions than he can recall."  
 >>>>>

**From:** C. D. KEENE  
**Sent:** 18 Oct 2015 18:48:39 +0000  
**To:** Mckee, Ann C; carins@wustl.edu; Dennis Dickson; Folkerth, Rebecca Dunn, M.D.; Irene Litvan; daniel Perl; Stein, Thor; Jean Paul Vonsattel; william.stewart@glasgow.ac.uk; Tripodis, Yorghos; Crary, John; Bieniek, Kevin F.; Dams-o'connor, Kristen; Alvarez, Victor E; Gordon, Wayne  
**Cc:** Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: CTE consensus manuscript

Thanks Ann. Best wishes.

Dirk

-----Original Message-----

From: Mckee, Ann C [mailto:amckee@bu.edu]  
Sent: Sunday, October 18, 2015 4:18 AM  
To: carins@wustl.edu; Dennis Dickson; Folkerth, Rebecca Dunn, M.D.; C. D. KEENE; Irene Litvan; daniel Perl; Stein, Thor; Jean Paul Vonsattel; william.stewart@glasgow.ac.uk; Tripodis, Yorghos; Crary, John; Bieniek, Kevin F.; Dams-o'connor, Kristen; Alvarez, Victor E; Gordon, Wayne  
Cc: debra [E] Babcock; Patrick Bellgowan; Koroshetz, Walter (NIH/NINDS) [E]  
Subject: CTE consensus manuscript

All,

I'm just letting you know that the manuscript was submitted to Acta Neuropathologica last Thursday. I will keep you updated as the review process unfolds.

Thank you for all your help and best regards,

Ann

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** 15 Oct 2015 11:05:25 -0400  
**To:** 'margulie@seas.upenn.edu'  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: FNIH here is the summary - do you have the program?  
**Attachments:** SHRP 7.25.2013 (FINAL guest list).xlsx, Workshop Draft Agenda.pdf

Hi Susan,

Looks like **Pete did sustain concussions in combat**, and may have also sustained a few doing sports (he is also a professional skier) take a look at this article from 2013 -

<http://www.mensjournal.com/magazine/a-navy-seals-next-mission-skiing-20130925>

*"Over the next decade, Scobell completed six combat deployments – two in Iraq, two in Afghanistan, and one that featured the now legendary rescue of the Maersk Alabama, a containership that was overtaken by Somali pirates. Scobell and his SEAL teammates fought during the bloody Shia uprising of 2005, hunted and killed Al Qaeda leaders in the Hindu Kush, escorted critical convoys, and were in close proximity to more explosions than he can recall.*

*Knee pads aren't the only extra body protection Scobell incorporates into his ski ensemble; he also employs a set of Kevlar helmet inserts designed to reduce shock by 50 percent. That reduction in impact trauma is especially important, since Scobell has only recently recovered from a debilitating case of traumatic brain injury caused by all those years of training and combat. Some of it, he says, is from blast exposure, but the bulk of the damage may come from the incessant pounding of hours in skiffs and speedboats. For a period in 2011, Scobell's symptoms were so bad that he checked himself into a facility that specializes in traumatic brain injury. The last of many wake-up calls, he says, was when he found himself behind the wheel of his car in a parking lot with no idea how he'd gotten there."*

Pete was diagnosed and treated for TBI at NICoE. He speaks frequently on behalf of the Center for Brain Health at the University of Texas at Dallas and also presents to SEALs and their families at retreats when they return from deployment. His lecture is titled "The Blast Affect" and centers on blast exposures, concussions, and PTSD: <http://teamneverquit.com/tmq-members/pete-scobell/>

He was on the Glen Beck radio show in 2012 discussing ex-NFL suicides, specifically Junior Seau's: <http://www.glennbeck.com/2012/05/03/navy-seal-pete-scobell-discusses-junior-seau-the-latest-in-string-of-ex-nfl-suicides/>

The workshop agenda and guest list are attached from the 2013 SHRP meeting on Neurodegeneration. Of the other attendees who have ties to the navy, it looks like it could have been:

- **Dr. Rene Hernandez** ([rene.s.hernandez.mjl@mail.mil](mailto:rene.s.hernandez.mjl@mail.mil)), Commander, Medical Service Corps at the US Navy <http://www.vetsfwd.org/site/downloads/Hernandez%20VMF%20BIO.pdf>
- **Dr. Tom DeGraba** ([Thomas.j.degraba.civ@health.mil](mailto:Thomas.j.degraba.civ@health.mil)), Deputy Director and Chief of Medical Operations at NICoE. <http://www.nicoe.capmed.mil/Lists/Leadership/DispForm.aspx?ID=3>

Thanks,  
Meghan

-----Original Message-----

From: Susan Margulies, Ph.D. [mailto:margulie@seas.upenn.edu]  
Sent: Thursday, October 15, 2015 10:20 AM  
To: Mott, Meghan (NIH/OD) [E]  
Cc: Koroshetz, Walter (NIH/NINDS) [E]  
Subject: RE: FNIH here is the summary - do you have the program?

Possibly...did he sustain concussions? only in combat? If so, he is not ideal for the Charlie Rose show.

Later today, I could check my hard drive for any draft programs from that FNIH session.

Let me know if Pete had concussions or if his symptoms are stress-related. If not TBI, I'll keep looking.

s

---

Susan Margulies, Ph.D.  
George H. Stephenson Professor of Bioengineering  
University of Pennsylvania  
Philadelphia, PA 19104-6321

Mail: 240 Skirkanich Hall, 210 S. 33rd Street  
Office: 105D Hayden Hall, 3320 Smith Walk

On 2015-10-15 10:07, Mott, Meghan (NIH/OD) [E] wrote:

> Susan,  
>  
> Was it Lt. Pete Scobell? (Intrepid Fallen Heroes Fund; Naval Special  
> Warfare Command)  
>  
> <http://knowhow.napaonline.com/intrepid-fallen-heroes-fund-an-organization-that-walks-the-talk/>  
> [1]  
>  
> Thanks,  
>  
> Meghan  
>  
> -----Original Message-----  
> From: Susan Margulies, Ph.D. [mailto:margulie@seas.upenn.edu]  
> Sent: Wednesday, October 14, 2015 6:23 PM  
> To: Koroshetz, Walter (NIH/NINDS) [E]  
> Subject: FNIH here is the summary - do you have the program?  
>



> [http://www.ninds.nih.gov/news\\_and\\_events/proceedings/TBI-related\\_neurodegeneration\\_workshop\\_report.htm](http://www.ninds.nih.gov/news_and_events/proceedings/TBI-related_neurodegeneration_workshop_report.htm)

> [2]

>

> ---

>

> Susan Margulies, Ph.D.

>

> George H. Stephenson Professor of Bioengineering University of

> Pennsylvania Philadelphia, PA 19104-6321

>

> Mail: 240 Skirkanich Hall, 210 S. 33rd Street

>

> Office: 105D Hayden Hall, 3320 Smith Walk

>

> On 2015-10-14 16:29, Koroshetz, Walter (NIH/NINDS) [E] wrote:

>

>> Your memory is better than mine. Can't blame it on concussion

> though.

>

>> We will go back to our notes.

>

>> Walter

>

>>

>

>> On 10/14/15, 4:09 PM, "Susan Margulies, Ph.D."

>

>> <[margulie@seas.upenn.edu](mailto:margulie@seas.upenn.edu)>

>

>> wrote:

>

>>

>

>>> Walter - a year or 2 ago, you hosted an strategy session to

> generate

>

>>> human subject study ideas for the NFL funding to the FNIH. My role

>

>>> was to synthesize the workout group ideas (you may recall lots of

> big

>

>>> post-it flip chart pages on a wall). At that event, Pat LaFontaine

>

>>> spoke and a Navy Seal. Both were great. Who was the Navy Seal?

>

>>>

>

>>> S  
>  
>>>  
>  
>>> ---  
>  
>>> Susan Margulies, Ph.D.  
>  
>>> George H. Stephenson Professor of Bioengineering University of  
>  
>>> Pennsylvania Philadelphia, PA 19104-6321  
>  
>>>  
>  
>>> Mail: 240 Skirkanich Hall, 210 S. 33rd Street  
>  
>>> Office: 105D Hayden Hall, 3320 Smith Walk  
>  
>>>  
>  
>>>  
>  
>>>  
>  
>>> On 2015-10-14 15:45, Koroshetz, Walter (NIH/NINDS) [E] wrote:  
>  
>>>> Dear Christina,  
>  
>>>> We just got notice from NHL contact that Pat LaFontaine will not  
> be  
>  
>>>> able to join. No other info given.  
>  
>>>> Tom or Susan have thoughts on bringing someone with a good story  
> of  
>  
>>>> concussions?  
>  
>>>>  
>  
>>>> Best,  
>  
>>>> Walter  
>  
>>>>  
>  
>>>> From: Christina Doyle <[cad2012@cumc.columbia.edu](mailto:cad2012@cumc.columbia.edu)>  
>

>>>> Date: Wednesday, October 14, 2015 at 3:37 PM  
>  
>>>> To: "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
>  
>  
>>>> Cc: Paula Walker <[walkerp@ninds.nih.gov](mailto:walkerp@ninds.nih.gov)>  
>  
>>>> Subject: Re: Brain Series: call this Friday afternoon?  
>  
>>>>  
>  
>>>> Of course - I will keep you informed about what time we end up  
>  
>>>> having the call, if it turns out you can join us for part of it.  
>  
>>>>  
>  
>>>> --  
>  
>>>>  
>  
>>>> Christina A. Doyle, Ph.D.  
>  
>>>> Lab Manager for Eric Kandel, Howard Hughes Medical Institute  
>  
>>>> Administrative Coordinator, Kavli Institute for Brain Science  
>  
>>>> Department of Neuroscience Columbia University  
>  
>>>> 1051 Riverside Drive  
>  
>>>> New York, NY 10032  
>  
>>>>  
>  
>>>> \*\*PLEASE NOTE NEW NUMBERS\*\*  
>  
>>>> (646) 774.6830 ph  
>  
>>>> (646) 774.6812 fx  
>  
>>>>  
>  
>>>> From: "Koroshetz, Walter (NIH/NINDS) [E]"  
>  
>>>> <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
>  
>>>> Date: Wednesday, October 14, 2015 2:57 PM


>  
>>>> To: Christina Doyle <[cad2012@cumc.columbia.edu](mailto:cad2012@cumc.columbia.edu)>  
>  
>>>> Cc: "Walker, Paula (NIH/NINDS) [E]" <[walkerp@ninds.nih.gov](mailto:walkerp@ninds.nih.gov)>  
>  
>>>> Subject: Re: Brain Series: call this Friday afternoon?  
>  
>>>>  
>  
>>>> Tough to know about Friday as the meeting is with the Secretary of  
>  
>  
>>>> the Department of Energy.  
>  
>>>> Walter  
>  
>>>>  
>  
>>>> From: Christina Doyle <[cad2012@cumc.columbia.edu](mailto:cad2012@cumc.columbia.edu)>  
>  
>>>> Date: Wednesday, October 14, 2015 at 2:25 PM  
>  
>>>> To: "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
>  
>  
>>>> Cc: Paula Walker <[walkerp@ninds.nih.gov](mailto:walkerp@ninds.nih.gov)>  
>  
>>>> Subject: Re: Brain Series: call this Friday afternoon?  
>  
>>>>  
>  
>>>> Hello Walter,  
>  
>>>>  
>  
>>>> We had not realized that Meghan was on the call, or we would have  
>  
>>>> relayed any questions we had about your section to her. In the  
>  
>>>> future, could you ask her to say hello so we know who is on the  
>  
>>>> line?  
>  
>>>>  
>  
>>>> Unfortunately, Eric's schedule is packed except for Friday. Do you  
>  
>

>>>> have an idea of a time Friday that might be the best shot of you  
>  
>>>> being able to step out and join us? If not, we will continue to  
> work  
>  
>>>> via email, and we will have a call when Eric returns from Vienna.  
>  
>>>> Looking forward to then, how's Monday 10/26 for you?  
>  
>>>>  
>  
>>>> Thanks  
>  
>>>> Christina  
>  
>>>>  
>  
>>>> --  
>  
>>>>  
>  
>>>> Christina A. Doyle, Ph.D.  
>  
>>>> Lab Manager for Eric Kandel, Howard Hughes Medical Institute  
>  
>>>> Administrative Coordinator, Kavli Institute for Brain Science  
>  
>>>> Department of Neuroscience Columbia University  
>  
>>>> 1051 Riverside Drive  
>  
>>>> New York, NY 10032  
>  
>>>>  
>  
>>>> \*\*PLEASE NOTE NEW NUMBERS\*\*  
>  
>>>> (646) 774.6830 ph  
>  
>>>> (646) 774.6812 fx  
>  
>>>>  
>  
>>>> From: "Koroshetz, Walter (NIH/NINDS) [E]"  
>  
>>>> <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
>  
>>>> Date: Tuesday, October 13, 2015 7:47 PM

>  
>>>> To: Christina Doyle <[cad2012@cumc.columbia.edu](mailto:cad2012@cumc.columbia.edu)>,  
>  
>>>> "[margulies@seas.upenn.edu](mailto:margulies@seas.upenn.edu)" <[margulies@seas.upenn.edu](mailto:margulies@seas.upenn.edu)>,  
>  
>>>> "[twmcalli@iupui.edu](mailto:twmcalli@iupui.edu)" <[twmcalli@iupui.edu](mailto:twmcalli@iupui.edu)>,  
>  
>>>> "[dawn.comstock@ucdenver.edu](mailto:dawn.comstock@ucdenver.edu)" <[dawn.comstock@ucdenver.edu](mailto:dawn.comstock@ucdenver.edu)>, "Mack,  
>  
>>>> Sarah H." <[shm1@cumc.columbia.edu](mailto:shm1@cumc.columbia.edu)>  
>  
>>>> Cc: "Walker, Paula (NIH/NINDS) [E]" <[walkerp@ninds.nih.gov](mailto:walkerp@ninds.nih.gov)>,  
>  
>>>> "[jgillard@seas.upenn.edu](mailto:jgillard@seas.upenn.edu)" <[jgillard@seas.upenn.edu](mailto:jgillard@seas.upenn.edu)>,  
>  
>>>> "[majhughe@iupui.edu](mailto:majhughe@iupui.edu)" <[majhughe@iupui.edu](mailto:majhughe@iupui.edu)>  
>  
>>>> Subject: RE: Brain Series: call this Friday afternoon?  
>  
>>>>  
>  
>>>> Thanks. Meghan was on the call and gave me an update. Friday I am  
> at  
>  
>>>> Argonne National Lab discussing BRAIN initiative with Dept of  
> Energy  
>  
>>>> folks. I could try to step out but couldn't be counted on to do  
> so.  
>  
>>>> Would depend on how the meeting was going.  
>  
>>>>  
>  
>>>> Walter  
>  
>>>>  
>  
>>>> FROM: Doyle, Christina [<mailto:cad2012@cumc.columbia.edu>]  
>  
>>>> SENT: Tuesday, October 13, 2015 5:04 PM  
>  
>>>> TO: Doyle, Christina; Koroshetz, Walter (NIH/NINDS) [E];  
>  
>>>> [margulies@seas.upenn.edu](mailto:margulies@seas.upenn.edu); [twmcalli@iupui.edu](mailto:twmcalli@iupui.edu);  
>  
>>>> [dawn.comstock@ucdenver.edu](mailto:dawn.comstock@ucdenver.edu); Mack, Sarah H.  
>

>>>> CC: Walker, Paula (NIH/NINDS) [E]; [jgillard@seas.upenn.edu](mailto:jgillard@seas.upenn.edu);  
>  
>>>> [majhughe@iupui.edu](mailto:majhughe@iupui.edu)  
>  
>>>> SUBJECT: Brain Series: call this Friday afternoon?  
>  
>>>>  
>  
>>>> Hello all,  
>  
>>>>  
>  
>>>> We missed Walter and Dawn on today's call, but were able to work a  
>  
>  
>>>> bit on Susan and Tom's sections. We had a good discussion about  
> the  
>  
>>>> second round - after talking about treatments, we could turn to  
> the  
>  
>>>> bigger picture of what parents should do. It might be particularly  
>  
>  
>>>> interesting if Charlie were to ask all of you, personally, would  
> you  
>  
>>>> (or have you) let your children participate in sports, knowing  
> what  
>  
>>>> you know. We could also talk about which sports are 'worse.' The  
>  
>>>> topic of soccer came up, and how people assume heading is the  
> cause  
>  
>>>> of many concussions but that it really is not, if done correctly.  
>  
>>>>  
>  
>>>> An updated outline is attached. Sarah will continue to work with  
> you  
>  
>>>> directly on images.  
>  
>>>>  
>  
>>>>  
>

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(b) (6)



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>>>> [1]  
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>  
>>>> Unfortunately, Eric is in Europe all next week. So it would be  
> great  
>  
>>>> if we could have one more call this week to have everyone  
> together.  
>  
>>>> Could you let me know your availability for Friday afternoon  
> (10/16)?  
>  
>>>> Eric is free from 2pm onward.  
>  
>>>>  
>  
>>>> Thanks,  
>  
>>>>  
>  
>>>> Christina  
>  
>>>>  
>  
>>>> --  
>  
>>>>  
>  
>>>> Christina A. Doyle, Ph.D.  
>  
>>>> Lab Manager for Eric Kandel, Howard Hughes Medical Institute  
>  
>>>> Administrative Coordinator, Kavli Institute for Brain Science  
>  
>>>> Department of Neuroscience Columbia University  
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>>>> 1051 Riverside Drive  
>  
>>>> New York, NY 10032



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>>>> \*\*PLEASE NOTE NEW NUMBERS\*\*  
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>>>> (646) 774.6812 fx  
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>  
>>>> FROM: Christina Doyle <[cad2012@cumc.columbia.edu](mailto:cad2012@cumc.columbia.edu)>  
>  
>>>> DATE: Tuesday, October 13, 2015 10:36 AM  
>  
>>>> SUBJECT: Re: Brain Series: updated outline, next call Tuesday 2pm  
>  
>>>> EDT  
>  
>>>>  
>  
>>>> One other thing - here is the link to the website where we will  
>  
>>>> organize the images:  
>  
>>>>  
>  
>>>> You'll see that Sarah has already started to upload some of the  
>  
>>>> images you are sending in. So if you can be near a computer for  
> the  
>  
>>>> call later, you can pull that site up and we can discuss.  
>  
>>>>  
>  
>>>> FROM: Christina Doyle <[cad2012@cumc.columbia.edu](mailto:cad2012@cumc.columbia.edu)>  
>  
>>>> DATE: Monday, October 12, 2015 4:30 PM  
>  
>>>> TO: Christina Doyle <[cad2012@cumc.columbia.edu](mailto:cad2012@cumc.columbia.edu)>,  
>  
>>>> "[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>,  
>  
>>>> "[margulies@seas.upenn.edu](mailto:margulies@seas.upenn.edu)" <[margulies@seas.upenn.edu](mailto:margulies@seas.upenn.edu)>,  
>  
>>>> "[twmcalli@iupui.edu](mailto:twmcalli@iupui.edu)" <[twmcalli@iupui.edu](mailto:twmcalli@iupui.edu)>,  
>

>>>> "[dawn.comstock@ucdenver.edu](mailto:dawn.comstock@ucdenver.edu)" <[dawn.comstock@ucdenver.edu](mailto:dawn.comstock@ucdenver.edu)>, "Mack,  
>  
>>>> Sarah H." <[shm1@cumc.columbia.edu](mailto:shm1@cumc.columbia.edu)>  
>  
>>>> CC: "[walkerp@ninds.nih.gov](mailto:walkerp@ninds.nih.gov)" <[walkerp@ninds.nih.gov](mailto:walkerp@ninds.nih.gov)>,  
>  
>>>> "[jgillard@seas.upenn.edu](mailto:jgillard@seas.upenn.edu)" <[jgillard@seas.upenn.edu](mailto:jgillard@seas.upenn.edu)>,  
>  
>>>> "[majhughe@iupui.edu](mailto:majhughe@iupui.edu)" <[majhughe@iupui.edu](mailto:majhughe@iupui.edu)>  
>  
>>>> SUBJECT: Re: Brain Series: updated outline, next call Tuesday 2pm  
>  
>>>> EDT  
>  
>>>>  
>  
>>>> Hello all,  
>  
>>>>  
>  
>>>> Here is an updated version of the outline (v9) with any edits you  
>  
>>>> sent me today incorporated. Eric thanks you for your thoughts on  
> his  
>  
>>>> intro.  
>  
>>>> He realized he wants to begin his intro by talking generally about  
>  
>  
>>>> adolescence - what's going on in the developing brain, etc. So in  
>  
>  
>>>> this version he's started to flesh that out a bit, but he ran out  
> of  
>  
>>>> time before he had to go a meeting. So you'll see that it's not  
>  
>>>> complete, but it's just some initial brainstorming.  
>  
>>>>  
>  
>>>> We look forward to speaking tomorrow!  
>  
>>>>  
>  
>>>> Tuesday, October 13th  
>

>>>>  
>  
>>>> 2:00pm EDT (12 noon MDT)  
>  
>>>>  
>  
>>>> Dial-in number: 800-411 (b) (6)  
>  
>>>>  
>  
>>>> passcode (b) (6)  
>  
>>>>  
>  
>>>> Thanks,  
>  
>>>>  
>  
>>>> Christina  
>  
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>  
>>>> --  
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>>>>  
>  
>>>> Christina A. Doyle, Ph.D.  
>  
>>>> Lab Manager for Eric Kandel, Howard Hughes Medical Institute  
>  
>>>> Administrative Coordinator, Kavli Institute for Brain Science  
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>>>> Department of Neuroscience Columbia University  
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>>>> New York, NY 10032  
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>>>> (646) 774.6812 fx  
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>>>> Links:

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(b) (6)



> Links:

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> [1]

> <http://knowhow.napaonline.com/intrepid-fallen-heroes-fund-an-organization-that-walks-the-talk/>

> [2]

> [http://www.ninds.nih.gov/news\\_and\\_events/proceedings/TBI-related\\_neurodegeneration\\_workshop\\_report.htm](http://www.ninds.nih.gov/news_and_events/proceedings/TBI-related_neurodegeneration_workshop_report.htm)

> [3]

(b) (6)



**From:** Folkerth, Rebecca Dunn, M.D.  
**Sent:** 14 Oct 2015 13:23:46 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Walker, Paula (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]  
**Subject:** RE: Invitation to speak at American Association of Neuropathologists Annual Meeting, Symposium on TBI/CTE - June 16, 2016

Fantastic! Your perspective will really round out the content. So far, I have confirmed that Wayne (schedule permitting), Ann McKee, and Willie Stewart will be participating, and I am still waiting to hear from the others (topics: neuroimaging, military TBI. I believe it will be of great interest to the Association).

I will forward info regarding travel expenses, honorarium, etc, as it becomes available to me.

Best, Rebecca

**From:** Koroshetz, Walter (NIH/NINDS) [E] [mailto:koroshetzw@ninds.nih.gov]  
**Sent:** Tuesday, October 13, 2015 7:43 PM  
**To:** Folkerth, Rebecca Dunn, M.D.  
**Cc:** Walker, Paula (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]  
**Subject:** RE: Invitation to speak at American Association of Neuropathologists Annual Meeting, Symposium on TBI/CTE - June 16, 2016

Thanks Rebecca. I would be happy to join this meeting. Give my thanks to Wayne for suggesting it. I cc'ed Ms. Paula Walker who controls my calendar and travel.  
walter

**From:** Folkerth, Rebecca Dunn, M.D. [mailto:RFOLKERTH@PARTNERS.ORG]  
**Sent:** Tuesday, October 13, 2015 5:42 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Invitation to speak at American Association of Neuropathologists Annual Meeting, Symposium on TBI/CTE - June 16, 2016

Dear Dr. Koroshetz –

I am a member of Wayne Gordon's U01 group and have been deputized to develop a symposium on TBI/CTE for the AANP next June. I would be most honored and thrilled if you would be willing and able to come to the meeting in Baltimore on Thursday, June 16, 2016, to participate in this half-day symposium. While the details are still being ironed out, I anticipate that you would have approximately 30 minutes to discuss "The NIH Perspective on TBI and CTE Research Opportunities". (We are of course open to alternative topics, if you prefer.) Let me know what you think!

Thanks and best regards,  
Rebecca

**Rebecca D. Folkerth, M.D.**  
Director, Division of Neuropathology  
Department of Pathology  
Brigham and Women's Hospital  
75 Francis Street

Boston, MA 02115  
Phone: 617-732-7532  
Pager: 617-732-(b) (6)  
Fax: 617-975-0911  
rfoleth@partners.org

The information in this e-mail is intended only for the person to whom it is addressed. If you believe this e-mail was sent to you in error and the e-mail contains patient information, please contact the Partners Compliance HelpLine at <http://www.partners.org/compliance>. If the e-mail was sent to you in error but does not contain patient information, please contact the sender and properly dispose of the e-mail.

**From:** William Stewart  
**Sent:** 12 Oct 2015 13:23:50 +0000  
**To:** McKee, Ann C; Cairns, Nigel; Dennis Dickson; rfolkerth@partners.org; Keene, Dirk (cdkeene@uw.edu); Irene Litvan; Jean Paul Vonsattel; Perl, Daniel (daniel.perl@usuhs.edu); Stein, Thor; Tripodis, Yorghos; Crary, John; bieniek.kevin@mayo.edu; Dams-o'connor, Kristen; Alvarez, Victor E; wayne.gordon@mssm.edu  
**Cc:** Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]; Murphy, Lauren Elizabeth; Kiernan, Patrick  
**Subject:** RE: MANUSCRIPT ON CTE CONSENSUS  
**Attachments:** CTE U01 Consensus 10.7.5ws.docx

Thanks Ann

a triumph of draft and collation of comments.

I have a very small number of small, but I think important, observations and comments in attached.

In essence:  
- couple of minor typos and citation comments

(b) (4)

A large black rectangular redaction box covering several lines of text.

(b) (6)

A large grey rectangular redaction box covering several lines of text.

WS

**Dr Willie Stewart**  
Consultant Neuropathologist  
Honorary Clinical Associate Professor

Department of Neuropathology  
Laboratory Medicine Building  
Queen Elizabeth University Hospital  
Glasgow, UK

+44(0)141 354 (8)9535  
<http://www.gla.ac.uk/schools/medicine/staff/williamstewart/>

---

**From:** McKee, Ann C [amckee@bu.edu]  
**Sent:** 07 October 2015 15:53  
**To:** Cairns, Nigel; Dennis Dickson; rfolkerth@partners.org; Keene, Dirk (cdkeene@uw.edu); Irene Litvan; Jean Paul Vonsattel; Perl, Daniel (daniel.perl@usuhs.edu); Stein, Thor; William

Stewart; Tripodis, Yorghos; Crary, John; bieniek.kevin@mayo.edu; Dams-o'connor, Kristen; Alvarez, Victor E; wayne.gordon@mssm.edu  
**Cc:** debra [E] Babcock; Patrick Bellgowan; Koroshetz, Walter (NIH/NINDS) [E]; Murphy, Lauren Elizabeth; Kiernan, Patrick  
**Subject:** MANUSCRIPT ON CTE CONSENSUS

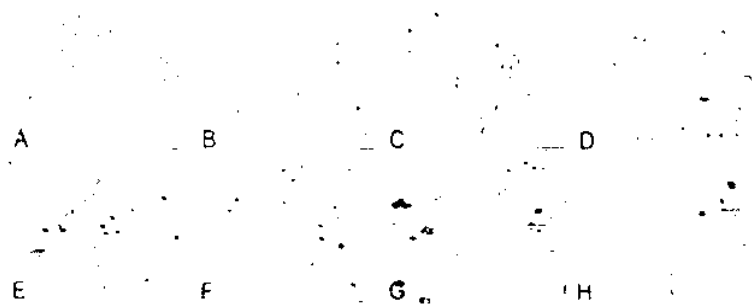
Dear Authors,

I've looked through your many insightful and important edits and comments to the paper very thoroughly and edited the manuscript accordingly. I wasn't able to make changes to the objectives of the meeting and study design, as the manuscript details the proceedings of a meeting that has already taken place, but other than that, I took great care to incorporate all suggestions (except for some very minor wording changes!). Please look through the manuscript and review your affiliations, funding and conflicts of interest. I plan to submit the manuscript to Acta Neuropathologica Thursday October 15. If I haven't heard from you by then, I will assume you are good to go with the manuscript as it stands.

I have taken the figures out of the manuscript so that it can be sent by email. The figures are the same except that I added a high magnification inset to Figure 2 to better show the size of the dot-like structures. I enclose a low res image of figure 2.

Thank you for your very thoughtful input and I look forward to hearing from you.

Ann







150 S. Huntington Avenue  
Boston, MA 02130  
Email: [amckee@bu.edu](mailto:amckee@bu.edu)  
Phone: 617-414-1188  
Fax: 617-638-5679



**From:** Patrick Kiernan  
**Sent:** 8 Oct 2015 09:18:30 -0400  
**To:** McKee, Ann C; Cairns, Nigel; Dennis  
Dickson; rfolkerth@partners.org; Keene, Dirk (cdkeene@uw.edu); Irene Litvan; Perl, Daniel  
(daniel.perl@usuhs.edu); Stein, Thor; Jean Paul  
Vonsattel; william.stewart@glasgow.ac.uk; Tripodis, Yorghos; Crary,  
John; bieniek.kevin@mayo.edu; Dams-o'connor, Kristen; Alvarez, Victor  
E; wayne.gordon@mssm.edu; Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS)  
[E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** CTE CONSENSUS MANUSCRIPT: UPDATED AFFILIATIONS LIST

Authors,

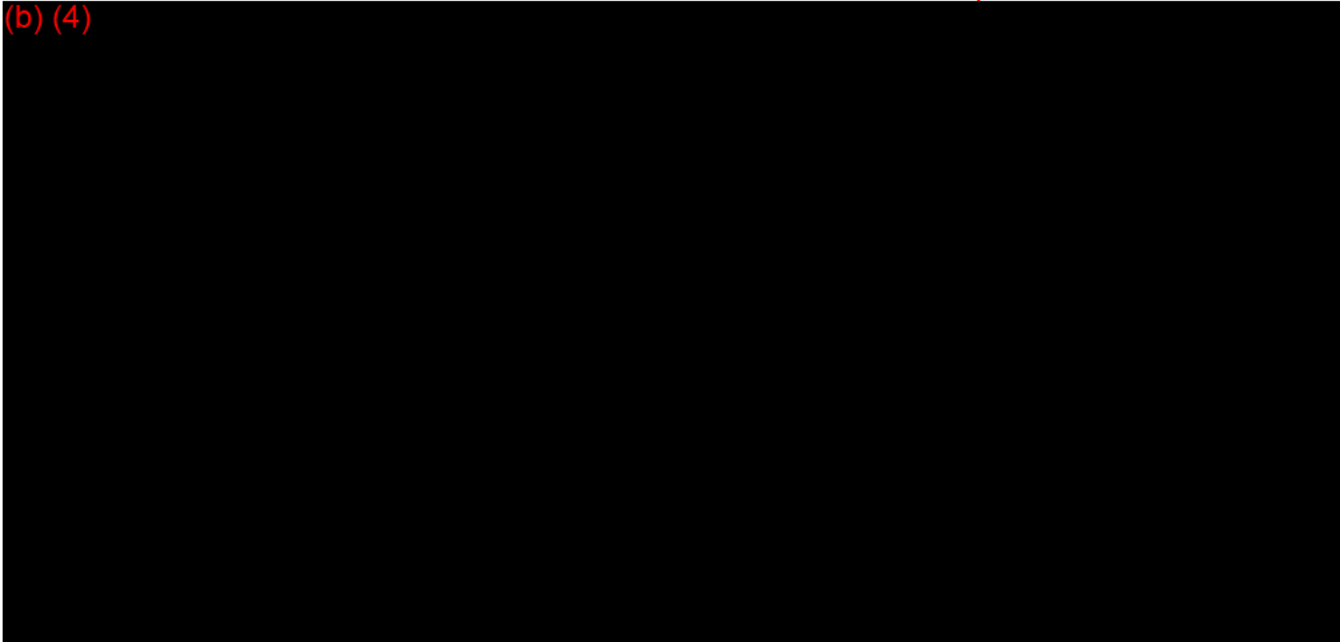
Please find the updated affiliations list below. Please reply directly to this email to add your departmental affiliations.

If there are any additional changes that need to be made please let me know.

Thank you,  
Patrick Kiernan

**The First NINDS/NIBIB Consensus Meeting to Define  
Neuropathological Criteria for the Diagnosis of Chronic Traumatic  
Encephalopathy**

(b) (4)





**From:** Raluca.PETRESCU@ec.europa.eu  
**Sent:** 6 Oct 2015 14:39:29 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Mark.GOLDAMMER@ec.europa.eu; Monica-Adriana.MARINESCU@ec.europa.eu  
**Subject:** Reminder - Annual meeting of the International Initiative for Traumatic Brain Injury Research (InTBIR), Brussels, 13-14 October 2015  
**Attachments:** Koroshetz Walter - Invitation ares.pdf, Draft Agenda TBI Research Meeting Brussels BLUE draft\_05\_10\_15\_V1.docx, building-map\_fr.pdf, CDMA transport map.pdf, rea\_hotel\_list\_2015\_012.pdf, Rue du Champ de Mars 21.png  
**Importance:** High

Dear Dr Koroshetz,

We are looking forward to welcoming you at the Annual Meeting of the International Initiative for Traumatic Brain Injury Research, which will take place in Brussels on the 13-14h October 2015. The latest provisional programme of the meeting is appended.

The registration of all our visitors in the e-Pass application (internal system) is mandatory. In order to allow a smooth management of the meeting, please send us by e-mail as soon as possible:

- the exact name (of the people attending the meeting)
- date of birth
- passport number
- nationality

*Please note that the processing operations on personal data for the organisation and management of meetings are necessary and lawfull under article 5 (a) of Regulation (EC) 45/2001.*

If you have not yet booked a hotel room, please note that we don't have a specific list of recommended hotels for events in our building. Yet, you find attached a list of hotels provided by the Research Executive Agency (REA), see in the attachment. The special prices are also valid for our event in October.

However, this is only indicative and you may book another hotel should you find it more convenient / closer than the listed ones.

The meeting will take place in our building, 21 rue du Champ de Mars, 21, 1050 Brussels. You will find the CDMA building location in the attached building map.

You will be able to find the nearest hotels to our premises through the different hotel searching engines with the areas keywords: "Champ de Mars," "Porte de Namur," "rue de Luxembourg," "rue du Commerce," "Place de Luxembourg," "Louise." In general you could also search by "European Parliament Brussels" or "European District Brussels."

Should you need any assistance or have additional questions, please do not hesitate to contact us.

Looking forward to welcoming you in Brussels!

Kind regards,

**Raluca PETRESCU**

Assistant



**European Commission**

DG Research & Innovation

E4

CDMA 02/108

1049 Brussels/Belgium

+32 229-59746

[raluca.petrescu@ec.europa.eu](mailto:raluca.petrescu@ec.europa.eu)

<http://ec.europa.eu/research>

on behalf of:

**Catherine BERENS, PhD**

**Head of Sector Neuroscience**



**European Commission**

**DG Research & Innovation**

**E4 Non-communicable diseases and the challenge of healthy ageing**

**CDMA 02/014**

**1049 Brussels/Belgium**

+32 229-50940

[catherine.berens@ec.europa.eu](mailto:catherine.berens@ec.europa.eu)

<http://ec.europa.eu/research>

**From:** EC ARES NOREPLY [mailto:DIGIT-NOREPLYARES@ec.europa.eu]  
**Sent:** Friday, September 11, 2015 12:23 PM  
**To:** walter.koroshetz@nih.gov  
**Cc:** MARINESCU Monica-Adriana (RTD); GOLDAMMER Mark (RTD)  
**Subject:** Ares(2015)3758989 - Invitation- Annual meeting of the International Initiative for Traumatic Brain Injury Research (InTBIR), Brussels, 13-14 October 2015

Ares(2015)3758989 - Invitation- Annual meeting of the International Initiative for Traumatic Brain Injury Research (InTBIR), Brussels, 13-14 October 2015

*Sent by PETRESCU Raluca (RTD) <[Raluca.PETRESCU@ec.europa.eu](mailto:Raluca.PETRESCU@ec.europa.eu)>. All responses have to be sent to this email address.*

*Envoyé par PETRESCU Raluca (RTD) <[Raluca.PETRESCU@ec.europa.eu](mailto:Raluca.PETRESCU@ec.europa.eu)>. Toutes les réponses doivent être effectuées à cette adresse électronique.*

Dear Dr Koroshetz,

We are delighted to send you the official invitation to the Annual Meeting of the International Initiative for Traumatic Brain Injury Research, which will take place in Brussels on the 13-14<sup>th</sup> October 2015.

The latest provisional programme of the meeting is also appended. You will receive more information on the meeting and the various sessions in due time.

The registration of all our visitors in the e-Pass application (internal system) is mandatory. In order to allow a smooth management of the meeting, please send us by e-mail:

- the exact name (of the people attending the meeting)
- date of birth
- passport number
- nationality



Should you need any assistance or have additional questions, please do not hesitate to contact us.

Looking forward to welcoming you in Brussels!

Kind regards,

**Raluca PETRESCU**

Assistant



**European Commission**

DG Research & Innovation

E4

CDMA 02/108

1049 Brussels/Belgium

+32 229-59746

[raluca.petrescu@ec.europa.eu](mailto:raluca.petrescu@ec.europa.eu)

<http://ec.europa.eu/research>

on behalf of:

**Catherine BERENS, PhD**

**Head of Sector Neuroscience**



**European Commission**

**DG Research & Innovation**

**E4 Non-communicable diseases and the challenge of healthy ageing**

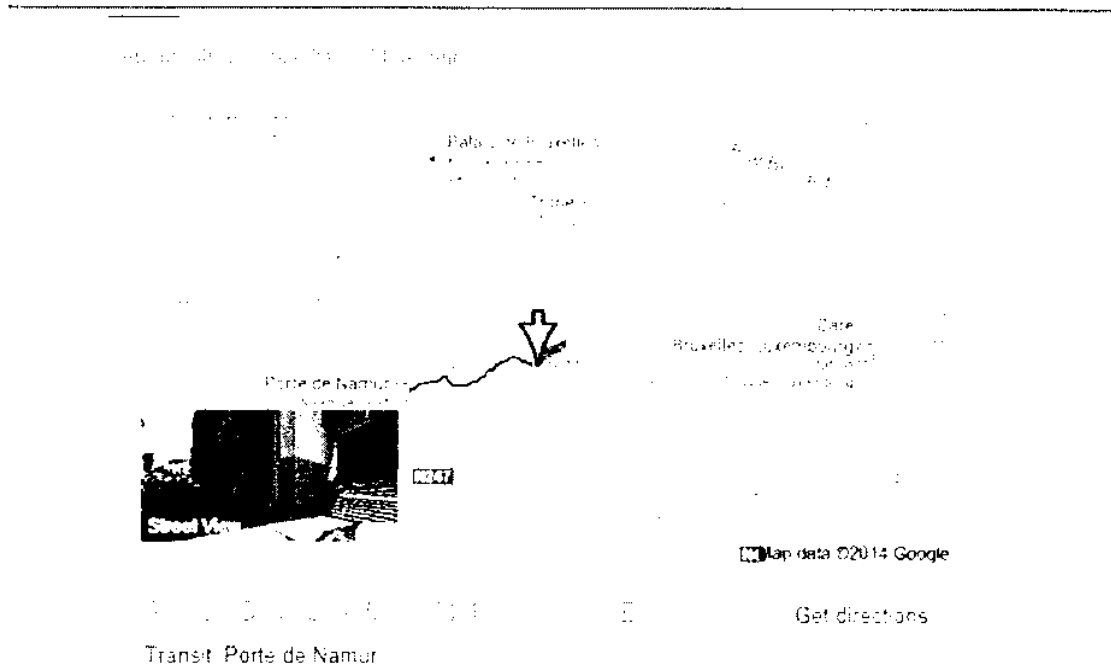
CDMA 02/014

1049 Brussels/Belgium

+32 229-50940

[catherine.berens@ec.europa.eu](mailto:catherine.berens@ec.europa.eu)

<http://ec.europa.eu/research>





**EUROPEAN COMMISSION**  
DIRECTORATE-GENERAL FOR RESEARCH & INNOVATION

Directorate E - Health  
The Director

Brussels, 07 September 2015  
rtd.ddg3.e.4(2015) 4081560

Dr Walter Koroshetz  
sent by email:  
[walter.koroshetz@nih.gov](mailto:walter.koroshetz@nih.gov)

**Subject: Annual meeting of the International Initiative for Traumatic Brain Injury Research (InTBIR), Brussels, 13-14 October 2015**

Dear Dr Koroshetz,

It is our great pleasure to hereby officially invite you to participate in the **Annual Meeting of the International Initiative for Traumatic Brain Injury Research (InTBIR)** to be held in **Brussels on 13-14 October 2015**, in building CDMA, rooms SDR1 and SDR2 located at rue du Champ de Mars, 21, 1050 Brussels.

I include for your early information the current draft agenda of the event. Should you have questions concerning the agenda, please do not hesitate to contact Dr Catherine Berens, Head of Sector Neuroscience (Tel. +32 2 2950940, email: [Catherine.BERENS@ec.europa.eu](mailto:Catherine.BERENS@ec.europa.eu)).

The objectives of this year's annual meeting are to:

- introduce OneMind as new InTBIR partner
- report on research advances under the different participating InTBIR projects
- highlight topical issues in TBI research, both breakthroughs and bottlenecks
- monitor harmonization/coordination efforts across the InTBIR projects
- report from working groups on thematic issues (data management and analysis, fluid biomarkers, neuroimaging)
- discuss safe clinical data sharing
- discuss expanded cooperation with relevant partners outside the InTBIR
- provide a venue for scientific exchange and networking among members of the funded international teams.

We hope you will be able to participate in this meeting and would be grateful for a confirmation of your participation by email to [Monica-Adriana.MARINESCU@ec.europa.eu](mailto:Monica-Adriana.MARINESCU@ec.europa.eu).

As discussed informally, the EC will not cover your travel or subsistence costs.

I look forward to meeting you in Brussels!

Yours sincerely,



Ruxandra Draghia-Akli

Enclosure: Draft agenda of the annual meeting

**08:15 – 8:45 Welcome & Opening Statements**

*Ruxandra Draghia-Akli, Director, Health Directorate,  
 European Commission, DG Research and Innovation*  
*Walter Koroshetz, Director, NIH/NINDS (video message)*  
*Anthony Phillips, Scientific Director CIHR-INMHA*  
*Mona Hicks, Chief Scientific Officer OneMind*

- Concept of the meeting, ways to work together - Ruxandra Draghia-Akli
- InTBIR new Member: One Mind – Mona Hicks
- ISAB recommendations from 2014 meeting - Sam Weiss

**09:00 Session I: Progress of the InTBIR Projects (per project: 5 min presentation + 5 min Q&A)**

- TRACK-TBI – Geoff Manley
- Managing severe TBI without ICP monitoring - guide lines development and testing – Randy Chesnut
- ADAPT – Mike Bell
- CENTER-TBI – Andrew Maas
- CREACTION – Guido Bertolini
- mTBI in youth ice hockey players – Kathryn Schneider
- Improving the diagnosis and treatment of mTBI in children and youth – Isabelle Gagnon
- Neurocare – Michelle Keightly
- Post-Concussive Syndrome in youth – Karen Barlow
- SP study – Roger Zemek
- TBI Prognosis Study – Alexis Turgeon

**11:00 Coffee Break**

**11:15 Session II – Working Groups: Priority Goals and Plans**

Keynote addresses: regulatory viewpoints (EMA (tbc), FDA (tbc) representatives)

- Data management, Data analysis & Clinical Endpoints - Steve Wisniewski & Lindsay Wilson

**13:15 Lunch**

**14:00 Session II – continued**

- Neuroimaging - Pratik Mukherjee & Pim Pullens
- Fluid Biomarkers - Ramon Diaz-Arrastia & Roberto Latini

**16:00 Coffee Break**

**16:15 Session III – Safe Common Clinical Data Sharing**

- Level(s) of aggregation/anonymization/access - Guido Bertolini
- Methodology panel discussion - Menon, Manley, Hill, Hicks, McAuliffe, Bertolini, Hutchison

**17:30 Day 1 Meeting Adjourns**

Cocktail: One Mind joining InTBIR

**9:15 Session IV – InTBIR and beyond – collaborations with partner initiatives and other funders (invited speakers from outside InTBIR, moderated discussion)**

**Collaboration with other funding agencies**

- NEURON Cofund – Upcoming opportunities within the first call – Marlies Dorlochter

**Collaboration in data management & analysis - infrastructure aspects**

- HBP – Opportunities for Collaborations - Sean Hill

**Collaboration with patient organisations – integrating patients' views**

- Patient organisation - Nikolaus Steinhoff

**Collaboration on TBI study design - clinical endpoint selection**

- Presentation on ongoing TED initiative on clinical endpoints (Geoff Manley)

**11:15 Coffee Break**

**11:30 Session IV (continued)**

**Collaboration - potential alignment/integration of projects/initiatives outside InTBIR**

- US Department of Defense - Presentation of the CENC project – Tammy Crowder
- Fédération Internationale de Football Association (FIFA) studies – Nina Feddermann-Demont
- National Collegiate Athletic Association (NCAA, USA) – Presentation of the CARE project – Steven Brogno

**12:15 What next - Final plenary**

(moderation by Kent Bassett-Spiers)

- Short feedback from the 3 Working Groups
- Observations by the ISAB
- Views and conclusions by InTBIR funders – Ruxandra Draghia-Akli (or EC representative, tbc), NIH representative tbc, Anthony Phillips, Mona Hicks

**13:00 Lunch**

**14:00 Parallel Meetings:**

- ➔ InTBIR Members Forum (closed session)
- ➔ ISAB Meeting (closed session)
- ➔ Followed by a joint meeting of InTBIR funders and ISAB – Progress in InTBIR (closed session)
- ➔ 3 Working groups follow-up meetings (closed s.)
  - Data management, Data analysis & Clinical Endpoints

- Neuroimaging
- Fluid Biomarkers

→ **Informal PIs Networking** (open for invited speakers from outside InTBIR)

**17:00** Day 2 Meeting Adjourns

**From:** Kandel, Eric  
**Sent:** 2 Oct 2015 20:10:28 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Walker, Paula (NIH/NINDS) [E]  
**Subject:** Re: Phone Call w/Walter Koroshetz Today  
**Importance:** High

Dear Walter,

I realize that we could talk today at 5:30pm, if I take the call from home. Would this still work for you? If so, please let me know what number at which to reach you.

Cheers,  
Eric

--

Eric R. Kandel, M.D.  
University Professor  
Kavli Professor and Director, Kavli Institute for Brain Science  
Co-Director, Mortimer B. Zuckerman Mind Brain Behavior Institute  
Senior Investigator, Howard Hughes Medical Institute  
Department of Neuroscience  
Columbia University  
1051 Riverside Drive, Box 87  
New York, NY 10032

\*NOTE NEW PHONE NUMBERS\*  
(646) 774.6825 ph  
(646) 774.6812 fx

**From:** "Walker, Paula (NIH/NINDS) [E]" <[walkerp@ninds.nih.gov](mailto:walkerp@ninds.nih.gov)>  
**Date:** Friday, October 2, 2015 1:05 PM  
**To:** "Kandel, Eric" <[erk5@cumc.columbia.edu](mailto:erk5@cumc.columbia.edu)>  
**Subject:** Phone Call w/Walter Koroshetz Today

Hi Dr. Kandel:

I understand you have a phone call with Dr. Koroshetz today at 4:00 p.m. Unfortunately, he now has a meeting that is scheduled to end at 4:30 p.m. but may possibly run over until 5:00 p.m. or 5:30 p.m. this evening.

Would you be available for a call after 5:30 p.m. today? If so, please let me know what number Dr. Koroshetz could reach you.

Thank you.

Paula Walker

---

**From:**Kandel, Eric [mailto:erk5@cumc.columbia.edu]  
**Sent:** Thursday, October 01, 2015 1:42 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Re: Brain Series

Dear Walter,

What about tomorrow (Friday) at 4pm?

Also, who is the best person to discuss the brain consequences of concussion in young people?

Cheers,  
Eric

--  
Eric R. Kandel, M.D.  
University Professor  
Kavli Professor and Director, Kavli Institute for Brain Science  
Co-Director, Mortimer B. Zuckerman Mind Brain Behavior Institute  
Senior Investigator, Howard Hughes Medical Institute  
Department of Neuroscience  
Columbia University  
1051 Riverside Drive, Box 87  
New York, NY 10032

\*NOTE NEW PHONE NUMBERS\*  
(646) 774.6825 ph  
(646) 774.6812 fx

**From:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzw@ninds.nih.gov>  
**Date:** Wednesday, September 30, 2015 3:55 PM  
**To:** "Kandel, Eric" <erk5@cumc.columbia.edu>  
**Subject:** RE: Brain Series

Sure thing. Let me know if want to set up time to talk. I think that Tom's questions get to the crux of the matter.

The problem is that there is some epidemiologic data, but little or nothing is known about what is going on in the brain. Show will present an interesting problem, interesting research going on at population level, will raise more questions than it answers, but hopefully it puts things in perspective for an audience faced with incomplete answers.

Could be worse, could be schizophrenia!  
walter

**From:**Kandel, Eric [mailto:erk5@cumc.columbia.edu]  
**Sent:** Wednesday, September 30, 2015 11:29 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Brain Series

McAllister makes some good suggestions. We should discuss.



Cheers,  
Eric

--

Eric R. Kandel, M.D.  
University Professor  
Kavli Professor and Director, Kavli Institute for Brain Science  
Co-Director, Mortimer B. Zuckerman Mind Brain Behavior Institute  
Senior Investigator, Howard Hughes Medical Institute  
Department of Neuroscience  
Columbia University  
1051 Riverside Drive, Box 87  
New York, NY 10032

\*NOTE NEW PHONE NUMBERS\*

(646) 774.6825 ph

(646) 774.6812 fx

**From:** "McAllister, Thomas W" <[twmcalli@iupui.edu](mailto:twmcalli@iupui.edu)>

**Date:** Tuesday, September 29, 2015 8:58 PM

**To:** "[erk5@columbia.edu](mailto:erk5@columbia.edu)" <[erk5@columbia.edu](mailto:erk5@columbia.edu)>

**Subject:** follow-up

Nice to speak with you yesterday Eric.

At your suggestion I watched the Transgender episode of the Brain Series. Great work!

I have been thinking about the show on concussion. In my many discussions with parents, kids, and colleagues, the most frequently asked questions seem to be:

"What is a concussion?"

"What is the mechanism of concussion?"

"How many concussions are too many?"

"If someone has a single concussion, are they going to be at risk for developing dementia?"

A follow up question of #3, "If my child has a concussion, is he or she going to develop chronic traumatic encephalopathy?"

"Are repetitive head impacts associated with some contact sports as bad for the brain as one or more concussions?"

"Are all athletes equally at risk for concussion, and/or developing the putative long-term sequelae of concussion such as CTE? Might there be subtypes of differing vulnerability?"

"We know some individuals get better quickly, some take a long time – what are the drivers of outcome variance?"

"Why does the relative risk of psychiatric illness go up when someone has a concussion (or brain injury more broadly)?"

"Are there sex differences in vulnerability to concussion and recovery from concussion?"

As with most controversial topics, there is a certain amount of popular belief about the topic that as of yet has not fully been substantiated by scientific data. These include:

- Brain "rest" is the best treatment for concussion

- All concussions lead to dementia/CTE

- When someone reports that they no longer have symptoms, their brain is "back to normal" and they can resume play/normal activities.

So with those thoughts in mind here are some folks that might have some interesting things to say on these topics:

Michael McCrea, Ph.D. – Neuropsychologist and concussion researcher from Medical College of Wisconsin. Mike and I, along with Steve Broglio, Ph.D. from University of Michigan, are PI's on what will be the largest study to date of concussion in collegiate athletes.

Chris Giza, M.D. – pediatric neurologist and concussion researcher from UCLA. Chris has done some work the pathophysiology of concussion. He is also a site PI in our collegiate NCAA concussion study.

Kevin Guskiewicz, Ph.D. – University of North Carolina. Kevin is an athletic trainer by training, and directs the Matthew Gfeller Sport-Related TBI research center.

Dawn Comstock, Ph.D. – you mentioned her on the phone. She is an epidemiologist specializing in youth sport injuries, particularly concussion.

Jim Kelly, MD – neurologist who I believe treated Pat LaFontaine in the past for concussion related issues.

As we discussed, my own interests have been in the neuropsychiatric sequelae of concussion/mild TBI. We have approached this with a variety of strategies including fMRI and diffusion tensor imaging in, looking at genetic predictors of outcome after injury, and using helmet sensors and modeling to look at biomechanical factors that might impact outcome and the effects of non-concussive repetitive head impacts.

Hope all this helps.

Best,

Tom

Thomas W. McAllister, M.D.  
Albert E. Sterne Professor and Chair  
Department of Psychiatry  
Indiana University School of Medicine

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**From:** Babcock, Debra (NIH/NINDS) [E]  
**Sent:** 2 Oct 2015 15:43:19 -0400  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Happy to provide reinforcement.

**From:** Stern, Robert A [mailto:bobstern@bu.edu]  
**Sent:** Friday, October 02, 2015 3:40 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Thanks Pat. I just tried calling you but it went to voice mail and messages could not be received. If you can, please call me at 781-453-2336. I will be available until 4:00.  
Bob

**From:** Bellgowan, Patrick (NIH/NINDS) [E] [mailto:patrick.frostbellgowan@nih.gov]  
**Sent:** Friday, October 02, 2015 3:28 PM  
**To:** Stern, Robert A <bobstern@bu.edu>  
**Cc:** Babcock, Debra (NIH/NINDS) [E] <dbabcock@ninds.nih.gov>  
**Subject:** RE: U01 Award

Hi Bob,

I'm happy to speak with you now. If you want Walter and Deb on the call that may take a bit to coordinate.

Pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Stern, Robert A [mailto:bobstern@bu.edu]  
**Sent:** Friday, October 02, 2015 3:23 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Thanks on all accounts. I will be able to sleep this weekend! I would very much like to arrange a call, however. Please let me know what works for you all. Thanks, Pat.  
Bob

**From:** Bellgowan, Patrick (NIH/NINDS) [E] [<mailto:patrick.frostbellgowan@nih.gov>]  
**Sent:** Friday, October 02, 2015 3:15 PM  
**To:** Stern, Robert A <[robstern@bu.edu](mailto:robstern@bu.edu)>  
**Cc:** Babcock, Debra (NIH/NINDS) [E] <[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)>  
**Subject:** RE: U01 Award

Hi Bob,

Yes, I was talking about the advisory committee. As for Dr. Knopman, I think he is a fine choice but will confirm with Walter.

I'm sure we can arrange a call but I want to clarify that NINDS is committed to fully funding all 7 years of this proposal regardless of what happens with the FNIH. As for the partners commitment we just don't know at this point.

Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

I would VERY much like to request a phone call with you, Debra, Walter, and me as soon as possible to discuss this. As you can imagine, this is incredibly distressing and I feel completely in the dark as to what has been going on. If there is no commitment for future funding after NINDS FY16, there would be many issues to be faced and many individuals and groups (IRBs, Sponsored Project Offices, partnering industry collaborators, not to mention the study investigators and consultants) who may have serious problems. In addition, in order to truly succeed in the initiation of subject recruitment efforts, there would need to be a clear message to all concerned that this was, indeed, a fully-funded, 7-year project. The FNIH website, the partner's own website, and national media all clearly stated that the partner committed the full amount back in 2012. The entire FNIH/NINDS process, including the July 2013 NINDS workshop, the resulting RFP, the subsequent multiple grant submissions, the peer-review process, and the initial Council decision, was all based on that commitment. I also made some very strong and honest statements during a lengthy on-camera interview for a prominent television news program earlier this week about what I viewed (at the time of the interview) as the partner's commitment to funding this type of research through its FNIH donation (there was no mention of this specific grant). If the partner has revoked its pledge or will be revoking its pledge, I would need to make sure that those comments not be included when the program airs.

In other words, this is very serious and I would very much like the opportunity to speak with you all to get more information.

Bob

**From:** Bellgowan, Patrick (NIH/NINDS) [E] [<mailto:patrick.frostbellgowan@nih.gov>]  
**Sent:** Friday, October 02, 2015 2:25 PM  
**To:** Stern, Robert A <[robstern@bu.edu](mailto:robstern@bu.edu)>  
**Cc:** Babcock, Debra (NIH/NINDS) [E] <[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)>  
**Subject:** RE: U01 Award

Hi Bob,

Walter and I were on a call today with the FNIH and their partner. Unfortunately, nothing was resolved and no commitments were made regarding funds. Because we don't know their decision timeline, I think it is most prudent for us to proceed under the assumption that only NINDS FY16 funds will be used for starting this grant. I know that this is not great news but this way we can get the paperwork done and waiting for the new budget. Unfortunately, FY15 wasn't an option because NINDS hadn't made financial plans to pay this grant with NINDS monies in FY15.

If the situation changes we will be able to move more quickly. Please remember that at this point no decision has been made by that partner and thus this is just our contingency plan. Finally, as usual, nothing is done until the NOA comes out.

Action Items:

1. We will need to settle on Executive committee membership
2. We need to finalize the Milestones (pretty much done)

Best wishes,  
Pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

-----Original Appointment-----

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Monday, September 21, 2015 8:59 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; 'Stern, Robert A'  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** U01 Award  
**When:** Tuesday, September 29, 2015 12:00 PM-1:00 PM (UTC-05:00) Eastern Time (US & Canada).  
**Where:** 1-866-624-(b) (6) passcode (b) (6)

Hi Bob,

We can use may TC number

1-866-62 (b) (6) passcode (b) (6)

Thanks  
pat

---

**From:** Stern, Robert A [mailto:robstern@bu.edu]  
**Sent:** Monday, September 21, 2015 7:30 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** Re: U01 Award

Woohoo!  
Thanks. Should I set up a conference call number?  
Bob

On Sep 21, 2015, at 7:27 PM, Bellgowan, Patrick (NIH/NINDS) [E] <patrick.frostbellgowan@nih.gov> wrote:

Book it, Dan-O

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
psfb@mail.nih.gov

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Stern, Robert A [mailto:robstern@bu.edu]  
**Sent:** Monday, September 21, 2015 4:57 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Hi Pat,

I had not heard back from you about potential time slots that you and Dr. Babcock may be free to go over milestones for the U01. However, knowing how difficult it is to try to get availability for Drs. Cummings, Reiman, Shenton, and myself, we went back to the drawing board to come up with times that the four of us would be free between now and October 6. Alas, the only time slot we all have available (and one of the four may have to leave after 30 minutes) is:

Tuesday, September 29, 11:00-12:00 noon (Eastern).

I am crossing my fingers that that works for the two of you.

Please let me know.

Regards,

Bob

**From:** Bellgowan, Patrick (NIH/NINDS) [E] [<mailto:patrick.frostbellgowan@nih.gov>]  
**Sent:** Thursday, September 17, 2015 3:04 PM  
**To:** Stern, Robert A <[bobstern@bu.edu](mailto:bobstern@bu.edu)>  
**Cc:** Babcock, Debra (NIH/NINDS) [E] <[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)>  
**Subject:** RE: U01 Award

Hi Bob,

I think an hour should be sufficient but we will need to wait until I hear from Dr. Koroshetz to get started.

Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Stern, Robert A [<mailto:bobstern@bu.edu>]  
**Sent:** Thursday, September 17, 2015 11:34 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Hi,

We are working on finding slots of time for the four co-PIs to have a conference call with you regarding milestones. Could you please give me a ballpark estimate on how long you expect the call to take, e.g., 60 min, 90 min, 120 min, less than 60 min. In addition, if there are blocks of time over the next week that you know will not work for you, please let me know. Thanks very much. I look forward to the call and to moving forward on this exciting project.

Regards,  
Bob

**From:** Bellgowan, Patrick (NIH/NINDS) [E] [<mailto:patrick.frostbellgowan@nih.gov>]  
**Sent:** Friday, September 11, 2015 12:33 PM  
**To:** Stern, Robert A <[bobstern@bu.edu](mailto:bobstern@bu.edu)>

**Cc:** Babcock, Debra (NIH/NINDS) [E] <[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)>  
**Subject:** RE: U01 Award

Hi Bob,

The milestone development will be for your project as proposed.

Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Stern, Robert A [<mailto:robert.stern@bu.edu>]  
**Sent:** Friday, September 11, 2015 12:30 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Hi Pat,

Thanks for the update. Great news that we have the go ahead to discuss Milestones. I will look through the Rigor guidelines. I will also provide you and Dr. Babcock with some times for my three co-PIs and I to have a conference call. In the meantime, is it possible to let me know if there was any change to the overall picture, vis-à-vis the request to Council for additional funding for another project. That is, should we be expecting to move forward with our proposed U01 or will there be any important changes that came out of Council?

I look forward to hearing back from you and will be getting back to you with the available meeting times ASAP.

Regards,

Bob

Robert A. Stern, Ph.D.  
Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology  
Clinical Core Director, BU Alzheimer's Disease and CTE Center  
Boston University School of Medicine

72 East Concord Street, B7800  
Boston, MA 02118

Tel: 617-638-5678  
Fax: 617-638-5679



Email: bobstern@bu.edu  
Web: www.bu.edu/alzresearch

**From:** Bellgowan, Patrick (NIH/NINDS) [E] [<mailto:patrick.frostbellgowan@nih.gov>]  
**Sent:** Friday, September 11, 2015 11:26 AM  
**To:** Stern, Robert A <[bobstern@bu.edu](mailto:bobstern@bu.edu)>  
**Cc:** Babcock, Debra (NIH/NINDS) [E] <[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)>; Koroshetz, Walter (NIH/NINDS) [E] <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Subject:** U01 Award

Hi Bob,

Now that Council has finished up, we have the go ahead to meet regarding the Milestones. Once we agree on the Milestones we can get the NOA out the door. Before we speak we will need to make sure your study will be consistent with the new NIH emphasis on Rigor (e.g. blinded assessment, independent validation and reporting of negative results. (see attached)) as those components will need to be included in your Milestones. It will be important to have all of the PIs available for the call so that they all are aware of the Milestones and can have input. Can you provide Dr. Babcock and me with some times that may be convenient for all of us to get on a Teleconference together?

Thanks  
Pat

Patrick SF Bellgowan PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Chan, Leighton (NIH/CC/RMD) [E]  
**Sent:** 1 Oct 2015 09:11:41 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Walker, Paula (NIH/NINDS) [E]  
**Subject:** Re: NFL funds

In a meeting. 9:45 ok

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: 301-496-4733  
Fax: 301-402-0663  
Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov)

On Oct 1, 2015, at 9:05 AM, Koroshetz, Walter (NIH/NINDS) [E]  
<[koroshetzwa@ninds.nih.gov](mailto:koroshetzwa@ninds.nih.gov)> wrote:

Give a call. I am at 301 496 3167 for a while. Will ask Paula Walker to put you through if I am on another call.

best  
walter

**From:** Chan, Leighton (NIH/CC/RMD) [E]  
**Sent:** Thursday, October 01, 2015 8:44 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** NFL funds

Hi Walter- I got a call from Russ Lonser about the NFL resources at the FNIH and the possibility of using some of them to expand the civilian TBI natural history study at NIH to focus on athletes. Do you have time to chat about this? Sounds like an interesting opportunity, but I feel like I walking into a hornets nest....

LC

---

Leighton Chan, MD, MPH  
Chief, Rehabilitation Medicine Department, Clinical Center, National Institutes of Health  
Building 10, Room 1-1469 10 Center Drive, MSC 1604 Bethesda, MD 20892-1604

Phone: 301-496-4733  
Fax: 301-402-0663  
Email: [chanle@cc.nih.gov](mailto:chanle@cc.nih.gov) <<mailto:chanle@cc.nih.gov>>

**From:** Rieff, Heather (NIH/NINDS) [E]  
**Sent:** 30 Sep 2015 17:25:18 -0400  
**To:** Scott, Paul (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/OD) [E]  
**Subject:** RE: prep for cong hearing  
**Attachments:** Potential Questions for Senate LHHS hearing.docx

Walter:—In preparation for our meeting tomorrow, here are some questions to start thinking about. The first two (easy!) ones are ones that Anne Houser has passed on to Senator Moran's office, so there's a decent chance you might get asked at least one of those. The trick of course is answering them in about 60 seconds or less.

The others on the list are ones that Paul and I and others in OSPP brainstormed. Happy to discuss more tomorrow- I am sure there are lots of potential questions we haven't thought of yet.

Heather

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Wednesday, September 30, 2015 4:40 PM  
**To:** Scott, Paul (NIH/NINDS) [E]  
**Subject:** RE: prep for cong hearing

Sure, we can start at 11:30. I have to leave to arrive at the BRAIN event downtown so probably need to finish up by 12:30.

walter

**From:** Scott, Paul (NIH/NINDS) [E]  
**Sent:** Wednesday, September 30, 2015 4:36 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/OD) [E]; Walker, Paula (NIH/NINDS) [E]; Rieff, Heather (NIH/NINDS) [E]  
**Subject:** prep for cong hearing

Hi Walter, Heather and I are on your calendar for tomorrow at noon for 30 minutes to discuss/start practicing for the cong hearing next week, and more immediately the mock hearing with FC on Friday. Would it be ok to expand this meeting to a full hour? I think we need to maximize the amount of prep time given that this will be your first hearing as Director, and I believe that FC will expect some well-developed answers at the mock hearing on Friday. Along those lines, we may want to consider some additional time either tomorrow or Friday before the mock hearing in the afternoon.

Also looking at early next week may be good to see about additional prep sessions to work on your answers. Perhaps Paula can see what your schedule looks like next week?

Thanks.

Paul

Paul A. Scott, Ph.D.  
Director  
Office of Science Policy and Planning

National Institute of Neurological Disorders and Stroke  
National Institutes of Health  
Department of Health and Human Services  
31 Center Drive, Room 8A03  
Bethesda, MD 20892-2540  
301-496-9271 (phone)  
301-480-9172 (fax)  
[scottp@ninds.nih.gov](mailto:scottp@ninds.nih.gov)

## Potential Questions for Senate L-HHS Appropriations Subcommittee Hearing (Oct 7)

Sent to Anne Houser (Anne passed them on to Senator Moran's office):

- **What would be the biggest impact of a shortfall in the projected funding for the BRAIN Initiative?**
- **Recent budgets have included money to expand research efforts related to Alzheimer's Disease. Can you tell me about some of those efforts and things you hope to achieve in the next few years?**

### **Other Potential Questions:**

- Strategic Planning: Tell me how your institute does strategic planning? What processes do you use to prioritize areas of research? How closely do you base that on disease burden and/or economic cost?
- Concussion: My grandson is interested in playing football. I'm really concerned about the risk neurological disease from concussions. What is NIH doing about this, and what's your advice?
- NFL Money for Concussion Research: Several years ago the NFL entered into an agreement with the NIH to provide \$30M for sports related health research, including research on the effects of concussion on the brain. Can you update us on how that money is being spent?
- ME/CFS: I've been hearing from the CFS community that this area of research is falling through the cracks at NIH – What is NIH doing to address this?
- ALS: Is there something beyond funding, for example a policy that Congress could change, that would facilitate advancing research on ALS? [In March 2014, WK and FC met with Senator Murkowski (on full Approps Committee) and her cousin, whose husband died of ALS]
- MS: My father has MS. What are the most exciting/promising avenues of research for curing this devastating disease? [Note: Senator Murray's father has MS]
- Fetal Tissue: Does NINDS fund research using fetal tissue? Is it being used to treat/cure diseases like Parkinson's?
- AD Funding:
  - In the FY 2017 AD Bypass Budget, NIH estimates we will need an additional \$323 million above the estimated base budget in FY 2017 toward the goal of preventing and treating Alzheimer's disease and related dementias by 2025. Is this an adequate increase? What is level of funding that will be needed to reach the goal of preventing and treating Alzheimer's disease and related dementias by 2025?
  - In the FY 2016 appropriations bill, we increased the NIA budget because they are the lead Institute for Alzheimer's research -- Should we increase the budget of other ICs if

we are going to reach the goal of preventing and treating AD and related dementias by 2025?

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 29 Sep 2015 17:42:37 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** SHRP Call today

Hi Walter,

I had another call with FNIH today to discuss the oversight strategy for the U01 (general terms) and other funding scenarios.

It seems Maria had a short conversation with Jeff M. and was told that the NFL may partially fund the Stern proposal (not sure why only partially). FNIH seemed to think that they may wish to partially fund Stern and then use remaining monies to fund the other projects or write a new RFA. We discussed that a new RFA was considered by Council but only if the NFL paid the first grant and put money in the bank before the review of the RFA. They seemed to think that this was putting a negative spin on the situation but they know that any smorgasbord option is going to depend upon your approval. We also discussed that the study could get up and running faster if the NFL were to fund the study due to the NINDS end of the fiscal year complications.

For the call on Friday they asked that I explain:

- 1) How NINDS oversight of U01s works.
  - a) Two PD's
  - b) Monthly calls
  - c) Milestone driven
- 2) What the structure (no BU persons) and function of the U01 Steering Committee
- 3) Required datasharing
  - a. FITBIR for behavioral and neuroimaging
  - b. NINDS Bio-repository for biofluids
- 4) Annual PI meetings
- 5) Multiple CTE diagnostic Consensus conferences (after years 2 & 7)
- 6) Use of blinding / Rigor during analysis
- 7) Open to suggestions for the u01 steering committee
- 8) If they were to fund a 2<sup>nd</sup> study for 5-years, that study would be used to replicate the Stern Criteria
- 9) Advisory Council felt that (b) (5) grant had significant design flaws hence the (b) (5)
- 10) Describe TRACK-TBI and ADAPT.

It won't be dull,  
Pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS

301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>



**From:** Stern, Robert A  
**Sent:** 29 Sep 2015 01:11:38 +0000  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** CTE U01 Milestones - Updated Draft for 9-29-15 discussion  
**Attachments:** Milestones for CTE U01 - September 28 2015.docx

Hi all,

It was great speaking with you today. I have edited the previous draft Milestones based on our discussion (see attached). I will be sending this out to the other three PIs' for their review prior to our conference call tomorrow (Tuesday). I think this should go pretty smoothly. If you have any word on the timing of the NoGA per our earlier discussion, it would be great to get that update during the call tomorrow.

I am thrilled to be working on this with you all. Thanks for everything.

Regards,

Bob

Robert A. Stern, Ph.D.  
Professor of Neurology, Neurosurgery, and Anatomy & Neurobiology  
Director, Clinical Core, BU Alzheimer's Disease and CTE Center  
Boston University School of Medicine

72 East Concord Street, B7800  
Boston, MA 02118

Tel: 617-638-5678  
Fax: 617-638-5679  
Email: [bobstern@bu.edu](mailto:bobstern@bu.edu)

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 29 Sep 2015 10:06:06 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** CTE U01 question

Hi Walter,

If NINDS is going to fund the BU U01 will there be a 17.5% budget cut??

Pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 28 Sep 2015 13:19:08 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** CTE TC

1-866-622-6222 (b) (6)  
(b) (6)

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-498-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 28 Sep 2015 13:10:48 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** U01 Award  
**Attachments:** Milestones for STERN U01b.docx

Hi Bob,

Here is a draft of the proposed milestones. Walter suggested we add a milestone that apriori defines "progression" of disease. That Milestone is a bit awkward as is but we can adjust it. We also would like to discuss holding an annual consensus conference similar to the one that Ann & Wayne have been holding. Finally, we will also need to discuss membership of the executive committee. NINDS is concerned about the perception of having Dr. Cantu as the lead of the executive committee. Clearly he is among the foremost experts but it may be better to include someone who is not associated with the lead institution.



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**From:** Stern, Robert A [mailto:robstern@bu.edu]  
**Sent:** Tuesday, September 22, 2015 5:11 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** Re: U01 Award

Great idea. Yes, I could do 1:15-2:00.  
Bob

On Sep 22, 2015, at 4:57 PM, Bellgowan, Patrick (NIH/NINDS) [E] <patrick.frostbellgowan@nih.gov> wrote:

Hi Bob,

Deb and I were thinking that it might be more efficient if the three of us have a "draft" Milestone call first. This would make the second call with all PIs more efficient and let you know some of the issues that need to be tweaked in the Milestones

DO either of you have 1/2 hour on Monday? I'm free noon-2:30pm on Monday?

Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
psfba@mail.nih.gov

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

---

**From:** Stern, Robert A [mailto:robstern@bu.edu]  
**Sent:** Tuesday, September 22, 2015 11:51 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]

**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

I am so sorry to have to do this, but one of the PIs discovered a conflict after the time slot was confirmed. Would you both possibly be able to change the time to noon-1PM on that same day???

Bob

**From:** Bellgowan, Patrick (NIH/NINDS) [E] [<mailto:patrick.frostbellgowan@nih.gov>]  
**Sent:** Monday, September 21, 2015 7:27 PM  
**To:** Stern, Robert A <[robstern@bu.edu](mailto:robstern@bu.edu)>  
**Cc:** Babcock, Debra (NIH/NINDS) [E] <[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)>  
**Subject:** RE: U01 Award

Book it, Dan-O

Patrick SE Bellgowan, PhD  
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301-496-1447  
[psfbt@mail.nih.gov](mailto:psfbt@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Stern, Robert A [<mailto:robstern@bu.edu>]  
**Sent:** Monday, September 21, 2015 4:57 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Hi Pat,

I had not heard back from you about potential time slots that you and Dr. Babcock may be free to go over milestones for the U01. However, knowing how difficult it is to try to get availability for Drs. Cummings, Reman, Shenton, and myself, we went back to the drawing board to come up with times that the four of us would be free between now and October 6. Alas, the only time slot we all have available (and one of the four may have to leave after 30 minutes) is:

Tuesday, September 29, 11:00-12:00 noon (Eastern).

I am crossing my fingers that that works for the two of you.

Please let me know.

Regards,

Bob

**From:** Bellgowan, Patrick (NIH/NINDS) [E] [<mailto:patrick.frostbellgowan@nih.gov>]  
**Sent:** Thursday, September 17, 2015 3:04 PM  
**To:** Stern, Robert A <[robstern@bu.edu](mailto:robstern@bu.edu)>  
**Cc:** Babcock, Debra (NIH/NINDS) [E] <[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)>  
**Subject:** RE: U01 Award

Hi Bob,

I think an hour should be sufficient but we will need to wait until I hear from Dr. Koroshetz to get started.

Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Stern, Robert A [<mailto:robstern@bu.edu>]  
**Sent:** Thursday, September 17, 2015 11:34 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Hi,  
We are working on finding slots of time for the four co-PIs to have a conference call with you regarding milestones. Could you please give me a ballpark estimate on how long you expect the call to take, e.g., 60 min, 90 min, 120 min, less than 60 min. In addition, if there are blocks of time over the next week that you know will not work for you, please let me know. Thanks very much. I look forward to the call and to moving forward on this exciting project.

Regards,  
Bob

**From:** Bellgowan, Patrick (NIH/NINDS) [E] [<mailto:patrick.frostbellgowan@nih.gov>]  
**Sent:** Friday, September 11, 2015 12:33 PM  
**To:** Stern, Robert A <[robstern@bu.edu](mailto:robstern@bu.edu)>  
**Cc:** Babcock, Debra (NIH/NINDS) [E] <[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)>  
**Subject:** RE: U01 Award

Hi Bob,

The milestone development will be for your project as proposed.

Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Stern, Robert A [<mailto:robstern@bu.edu>]  
**Sent:** Friday, September 11, 2015 12:30 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Hi Pat,



**From:** Francis, Tiffany (FNIH) [T]  
**Sent:** 25 Sep 2015 10:06:51 -0400  
**To:** Mott, Meghan (NIH/OD) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: Projects

Good Morning,

I would like to confirm the call for Monday, 9/28 at 12pm. I will follow-up with the calendar invitation and dial-in information.

Thank you,

Tiffany Francis  
(301) 443-1598  
[tfrancis@fnihi.org](mailto:tfrancis@fnihi.org)

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** Friday, September 25, 2015 9:04 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E] <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>; Francis, Tiffany (FNIH) [T] <[tfrancis@fnihi.org](mailto:tfrancis@fnihi.org)>  
**Subject:** RE: Projects

Hi Tiffany,

I could do Monday noon-1pm or 10/1 noon-1pm. Not sure if it would be wise to schedule on 10/1 though.

Thanks,  
Meghan

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Friday, September 25, 2015 8:58 AM  
**To:** Francis, Tiffany (FNIH) [T]; Mott, Meghan (NIH/OD) [E]  
**Subject:** RE: Projects

Hi Tiffany,

I am available  
9/28 Monday 11:30am -1pm  
9/29 9-10 am; 1-2pm  
9/30 Not available  
10/1 anytime after 11am

thanks  
Pat

---



**From:** Freire, Maria (FNIH) [T]  
**Sent:** 24 Sep 2015 17:33:06 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Fw: NHL CTE article mentions Stern, McKee (Boston University)

Just FYI, M.

**From:** Meltzer, Abbey (FNIH) [T] <ameltzer@fnihi.org>  
**Sent:** Thursday, September 24, 2015 5:00 PM  
**To:** Freire, Maria (FNIH) [T]; James, Stephanie (FNIH) [T]; Wolf-Rodda, Julie (FNIH) [T]; Baruchin, Andrea (FNIH) [T]  
**Subject:** NHL CTE article mentions Stern, McKee (Boston University)

Dr. Freire, Stephanie, Julie and Andrea,

I just wanted to alert you to this article mostly about the NHL (not NFL) that mentions Boston University (Stern and McKee both issued subpoenas) and CTE.

Best,  
Abbey

<http://www.tsn.ca/nhl-demands-boston-university-researchers-hand-over-concussion-documents-1.365922>

## NHL demands Boston U researchers hand over concussion documents

The National Hockey League, which is battling a high-stakes lawsuit filed by former players who charge the league put profits ahead of their health, is going after a group of influential medical researchers who have drawn a link between playing in the NHL and a degenerative brain disease.

The league has demanded documents and correspondence from Chris Nowinski, a co-director of the Centre for the Study of Traumatic Encephalopathy at Boston University. Nowinski has pressured the NFL, NHL and other leagues to acknowledge that there is a connection between their sports and brain disease. The league has also issued subpoenas to Dr. Ann McKee and Dr. Robert Stern, both of whom work at Boston University.

The subpoenas, which were issued Sept. 1 and obtained by TSN, demand Nowinski, McKee and Stern hand over research related to concussions, as well as any communications with NHL officials, current and former NHL players, NHL player agents, and the family members of players. The researchers have been given an Oct. 1 deadline to comply.

NHL deputy commissioner Bill Daly said the subpoenas were sought because the researchers are fact witnesses with relevant information.

Neither Nowinski nor a Boston University spokeswoman returned phone calls or emails for comment.

The university's researchers have studied the brains of several deceased NHL players, and have reported that players including Derek Boogaard, Reggie Fleming, Rick Martin and Bob Probert each suffered from chronic traumatic encephalopathy, or CTE, a brain disease linked to Alzheimer's.

CTE is believed to be caused by repeated head trauma and can only be diagnosed after death. Scientists say its symptoms include memory loss, mood swings, addictive behaviour and angry outbursts.

Boston University in conjunction with the U.S. government reported last week that its latest studies show the brains of 87 out of 91 former NFL players had signs of CTE. Establishing a closer link between the NFL, NHL and CTE has been a key factor in lawsuits filed by groups of players in both leagues.

In the NHL, a group of about 80 former players is suing the league in U.S. federal court in Minnesota, charging the league knew or ought to have known that players with head injuries should have been examined by independent doctors and been fully healed before they were permitted to return to play.

The NHL has said players know the risks of hockey or could have educated themselves about the sport's dangers.

The subpoenas come months after Nowinski was critical of NHL commissioner Gary Bettman on social media.

In May, referring to the alleged link between concussions and CTE, Bettman told reporters in Chicago that "from a medical science standpoint, there is no evidence yet that one leads to the other..."

"I know there are a lot of theories, but if you ask people who study it, they tell you there is no statistical correlation that can definitely make that conclusion," Bettman said at the time.

Nowinski responded on his Twitter account, writing, "If 'necessarily' means 'always,' fine. If not then 'no evidence' is untrue. We have 'some' pretty good evidence."

It's unclear how much communication Boston University staff has had with former NHL players, player agents, and their families. Stern told TSN on Sunday that the school does not disclose details of its communications with possible brain donors or their families.

Also this week, the NHL asked a judge in its concussion lawsuit to dismiss the claims brought by former players Dan Fritsche, German Titov and Bob Bourne. The players have refused to fill out fact sheets detailing their medical and employment histories as required by the court.

"The NHL has sent multiple letters to plaintiffs' counsel addressing the missing fact sheets in an effort to resolve this problem," a lawyer for the NHL wrote in a court motion. "In response to these letters, plaintiffs' counsel advised during a Sept. 18, 2015, meet-and-confer call that the three plaintiffs have ceased communicating regarding their fact sheet obligations and are therefore not expected to provide fact sheets."

"The complete failure of these plaintiffs to respond to court-ordered discovery requests, or even attempt to explain why they have not responded to the NHL's repeated requests, warrants dismissal of their claims without prejudice."

**Abbey Meltzer**

Director of Communications

Foundation for the National Institutes of Health

[ameltzer@fnih.org](mailto:ameltzer@fnih.org) | 301-435-4103

[www.fnih.org](http://www.fnih.org)



*For eleven consecutive years, Charity Navigator has rated the FNIH as an organization that exceeds industry standards.*

**From:** Francis, Tiffany (FNIH) [T]  
**Sent:** Thursday, September 24, 2015 12:26 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]  
**Subject:** FW: Projects

Good Afternoon, Patrick and Meghan,

I would like to arrange a one-hour call in preparation for the NFL meeting next Friday. Here are some suggested dates/times for your consideration:

Friday, September 25 – 10-11am, 1-3pm

Monday, September 28 – open

Tuesday, September 29 – 9-10am, 11am-12pm, 1-3pm

Wednesday, September 30 - 11am-12pm, 1-3pm

Thursday, October 1 - open

Please suggest any other possible dates/times that work best for you, and I will confirm the availability of the other participants.

Thank you,

**Tiffany Francis**

Executive Assistant, Science Division

Foundation for the National Institutes of Health

9650 Rockville Pike | Bethesda, MD 20814 | [www.fnih.org](http://www.fnih.org)

Direct (301) 443-1598 | Fax (301) 480-0186 | Email [tfrancis@fnih.org](mailto:tfrancis@fnih.org)

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*Combined Federal Campaign (CFC) #29165*

*For eleven consecutive years, Charity Navigator has rated the FNIH as an organization that exceeds industry standards.*



**From:** James, Stephanie (FNIH) [T]  
**Sent:** Thursday, September 24, 2015 10:56 AM  
**To:** Freire, Maria (FNIH) [T] <[freiremc@od.nih.gov](mailto:freiremc@od.nih.gov)>; Mott, Meghan (NIH/OD) [E] <[mottmc@od.nih.gov](mailto:mottmc@od.nih.gov)>; Bellgowan, Patrick (NIH/NINDS) [E] <[patrick.frost@bellgowan.nih.gov](mailto:patrick.frost@bellgowan.nih.gov)>; Wolf-Rodda, Julie (FNIH) [T] <[jwolf-rodga@fnih.org](mailto:jwolf-rodga@fnih.org)>  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E] <[koroshetz@ninds.nih.gov](mailto:koroshetz@ninds.nih.gov)>; Francis, Tiffany (FNIH) [T] <[tfrancis@fnih.org](mailto:tfrancis@fnih.org)>; Gray, Felicia (FNIH) [T] <[fgray@fnih.org](mailto:fgray@fnih.org)>  
**Subject:** RE: Projects

Good idea. I will ask my assistant, Tiffany Francis, to work with all of you to find a time for a pre-meeting to discuss the options for presentation to NFL. Patrick, would you like us to come over to your office for this?

Best, Stephanie

**From:** Freire, Maria (FNIH) [T]  
**Sent:** Thursday, September 24, 2015 10:41 AM  
**To:** Mott, Meghan (NIH/OD) [E] <mottmc@od.nih.gov>  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E] <koroshetzwa@ninds.nih.gov>; Bellgowan, Patrick (NIH/NINDS) [E] <patrick.frostbellgowan@nih.gov>; James, Stephanie (FNIH) [T] <sjames@fnihi.org>  
**Subject:** Re: Projects

Ah, great! Yes, happy to do that. I will be traveling too but I can join by phone as well. In any event, this is terrific and we will start working with Pat ASAP. Thank you and thank you, Walter. Onward!

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** Thursday, September 24, 2015 10:34 AM  
**To:** Freire, Maria (FNIH) [T]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: Projects

Hi Maria,

Walter will be out of town at meetings in Ann Arbor and Chicago starting today until Wednesday next week. He suggested it may be best for you and Pat to go ahead and organize a meeting and he can try to call in if his schedule allows. I will also try to call in.

Thanks,  
Meghan

**From:** Freire, Maria (FNIH) [T]  
**Sent:** Tuesday, September 22, 2015 10:51 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Projects

Hi, Walter. Would it be helpful if we met with you and Patrick (or only with Patrick given your crazy schedule) to look over possible projects before the NFL folks come to see you? Best, M.

**From:** Freire, Maria (FNIH) [T]  
**Sent:** 24 Sep 2015 10:58:15 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E]; James, Stephanie (FNIH) [T]  
**Subject:** Re: Projects

Thanks for this, Walter. We should consider all of these.

Further, is the idea of having more than one group work on CTE completely off the table? The logic you and I discussed still holds so I wonder if there is a way to follow-up with that without thwarting Council's recommendations. You were very persuasive and it would be worth thinking more on this, perhaps?

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Thursday, September 24, 2015 10:48 AM  
**To:** Freire, Maria (FNIH) [T]; Mott, Meghan (NIH/OD) [E]  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E]; James, Stephanie (FNIH) [T]  
**Subject:** RE: Projects

Thanks Maria. Patrick and I discussed showing our going major TBI projects which will go to year 4/5 and 5/5. There will be applications for continuation of these great projects and likely the NCAA concussion project as well. But can not be sure which ones will actually come through at this point in time.

Starting the other key project focused on concussion in kids could be entertained—process would be sequential—first a workshop, then an rfa, fund grant in 1 and half years. Would want to include NICHD. Worried that to go down this road again especially with another IC that FNIH would have to secure conditional gift funds in advance.

Walter

**From:** Freire, Maria (FNIH) [T]  
**Sent:** Thursday, September 24, 2015 10:41 AM  
**To:** Mott, Meghan (NIH/OD) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; James, Stephanie (FNIH) [T]  
**Subject:** Re: Projects

Ah, great! Yes, happy to do that. I will be traveling too but I can join by phone as well. In any event, this is terrific and we will start working with Pat ASAP. Thank you and thank you, Walter. Onward!

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** Thursday, September 24, 2015 10:34 AM  
**To:** Freire, Maria (FNIH) [T]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: Projects

Hi Maria,

Walter will be out of town at meetings in Ann Arbor and Chicago starting today until Wednesday next week. He suggested it may be best for you and Pat to go ahead and organize a meeting and he can try to call in if his schedule allows. I will also try to call in.

Thanks,  
Meghan

**From:** Freire, Maria (FNIH) [T]  
**Sent:** Tuesday, September 22, 2015 10:51 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Projects

Hi, Walter. Would it be helpful if we met with you and Patrick (or only with Patrick given your crazy schedule) to look over possible projects before the NFL folks come to see you? Best, M.

**From:** Stern, Robert A  
**Sent:** 18 Sep 2015 12:35:06 +0000  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Hi,

It turns out that Jeff Cummings is unavailable for that Thursday afternoon time slot. So, we will be working on providing you with the groups' availability for the following week.

Bob

**From:** Bellgowan, Patrick (NIH/NINDS) [E] [mailto:patrick.frostbellgowan@nih.gov]  
**Sent:** Thursday, September 17, 2015 3:04 PM  
**To:** Stern, Robert A <bobstern@bu.edu>  
**Cc:** Babcock, Debra (NIH/NINDS) [E] <dbabcock@ninds.nih.gov>  
**Subject:** RE: U01 Award

Hi Bob,

I think an hour should be sufficient but we will need to wait until I hear from Dr. Koroshetz to get started.

Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Stern, Robert A [mailto:bobstern@bu.edu]  
**Sent:** Thursday, September 17, 2015 11:34 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Hi,

We are working on finding slots of time for the four co-PIs to have a conference call with you regarding milestones. Could you please give me a ballpark estimate on how long you expect the call to take, e.g., 60 min, 90 min, 120 min, less than 60 min. In addition, if there are blocks of time over the next week that you know will not work for you, please let me know. Thanks very much. I look forward to the call and to moving forward on this exciting project.

Regards,  
Bob



**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 18 Sep 2015 12:04:46 -0400  
**To:** Babcock, Debra (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Frontline

Just in case you've been watching how FRONTLINE tracks concussion in football. Here is its latest release.

<http://www.pbs.org/wgbh/pages/frontline/sports/concussion-watch/new-87-deceased-nfl-players-test-positive-for-brain-disease/>

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Folkerth, Rebecca Dunn, M.D.  
**Sent:** 18 Sep 2015 15:17:22 +0000  
**To:** 'William Stewart'; Dams-o'Connor, Kristen; 'McKee, Ann C'; Cairns, Nigel; Dennis Dickson; Keene, Dirk (cdkeene@uw.edu); Irene Litvan; Perl, Daniel (daniel.perl@usuhs.edu); Stein, Thor; Tripodis, Yorghos; Jean Paul Vonsattel; Crary, John; Bieniek, Kevin F.; Alvarez, Victor E; Gordon, Wayne; Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: Rebecca Folkerth shared "CTE U01 Consensus 9.2acm RF edits.docx" with you

(b) (4)

Probably worth a few sentences.

**From:** William Stewart [mailto:William.Stewart@glasgow.ac.uk]  
**Sent:** Friday, September 18, 2015 9:47 AM  
**To:** Dams-o'Connor, Kristen; Folkerth, Rebecca Dunn, M.D.; 'McKee, Ann C'; Cairns, Nigel; Dennis Dickson; Keene, Dirk (cdkeene@uw.edu); Irene Litvan; Perl, Daniel (daniel.perl@usuhs.edu); Stein, Thor; Tripodis, Yorghos; Jean Paul Vonsattel; Crary, John; Bieniek, Kevin F.; Alvarez, Victor E; Gordon, Wayne; Debra [E] Babcock; Patrick Bellgowan; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: Rebecca Folkerth shared "CTE U01 Consensus 9.2acm RF edits.docx" with you

Ann

Thanks for bringing this draft together. Quite a task

I made a start on editing and commenting, but to do it justice will require more effort, and I wonder now whether it is worth highlighting a few recurring observations you might like to look at before I get too far into it. The part-edited file is at

(b) (4)

Observations:

(b) (4)

WS

Dr Willie Stewart  
Consultant Neuropathologist  
Honorary Clinical Associate Professor

Dept of Neuropathology  
Laboratory Medicine Building  
Queen Elizabeth University Hospital  
Glasgow G51 4TF

+44(0)141 354 (8)9535

<http://www.gla.ac.uk/researchinstitutes/neurosciencepsychology/staff/williamstewart/#tabs=0>

-----Original Message-----

From: Dams-o'Connor, Kristen [mailto:kristen.dams-o'connor@mountsinai.org]

Sent: 16 September 2015 21:43

To: Folkerth, Rebecca Dunn, M.D.; 'McKee, Ann C'; Cairns, Nigel; Dennis Dickson; Keene, Dirk (cdkeene@uw.edu); Irene Litvan; Perl, Daniel (daniel.perl@usuhhs.edu); Stein, Thor; William Stewart; Tripodis, Yorghos; Jean Paul Vonsattel; Crary, John; Bieniek, Kevin F.; Alvarez, Victor E; Gordon, Wayne; Debra [E] Babcock; Patrick Bellgowan; Koroshetz, Walter (NIH/NINDS) [E]  
Subject: RE: Rebecca Folkerth shared "CTE U01 Consensus 9.2acm RF edits.docx" with you

I've added minor comments and suggestions to the version Rebecca edited. Link to dropbox is below:

(b) (6)



---

From: Folkerth, Rebecca Dunn, M.D. [RFOLKERTH@PARTNERS.ORG]

Sent: Wednesday, September 16, 2015 2:23 PM

To: 'McKee, Ann C'; Cairns, Nigel; Dennis Dickson; Keene, Dirk (cdkeene@uw.edu); Irene Litvan; Perl, Daniel (daniel.perl@usuhhs.edu); Stein, Thor; William Stewart; Tripodis, Yorghos; Jean Paul Vonsattel; Crary, John; Bieniek, Kevin F.; Dams-o'Connor, Kristen; Alvarez, Victor E; Gordon, Wayne; Debra [E] Babcock; Patrick Bellgowan; Koroshetz, Walter (NIH/NINDS) [E]  
Subject: FW: Rebecca Folkerth shared "CTE U01 Consensus 9.2acm RF edits.docx" with you

Hi all -

Please see my edits to the manuscript and, in a separate link, (b) (4)

(b) (4) I feel very strongly that (b) (4)

(b) (4) but would like to see them, perhaps after Ann incorporates them and sends the final version around for approval before it is submitted.

Thanks.

Rebecca

P.S. let me know if you can't get to Dropbox – I am having trouble with firewall here at hospital so sent from my other email...

From: Rebecca Folkerth via Dropbox (<mailto:no-reply@dropbox.com>)

Sent: Wednesday, September 16, 2015 2:10 PM

To: Folkerth, Rebecca Dunn, M.D.

Subject: Rebecca Folkerth shared "CTE U01 Consensus 9.2acm RF edits.docx" with you

[Image removed by sender.]

Rebecca used Dropbox to share a file with you!

(b) (6)

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**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** 17 Sep 2015 12:55:43 -0400  
**To:** Babcock, Debra (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** CTE U01 Milestones  
**Attachments:** Milestones for STERN U01.docx

Hi Walter and Deb

Attached are an initial suggestion for the Milestones for the CTE U01 that Deb and I have developed.  
Please provide feedback.

Thanks  
pat

(b) (5)





From: (b) (6)  
Sent: 16 Sep 2015 00:04:31 -0700  
To: Koroshetz, Walter (NIH/NINDS) [E]  
Subject: (b) (6)

Dr. Koroshetz,

As a (b) (6) I believe that I engaged in more one on one devastating head-on collisions and trauma producing impacts with (b) (6) than any other single individual in their life long careers, or mine for that matter.

(b) (6)  
(b) (6) especially against one of the top defenses in the country led by two All-Americans, (b) (6). For three straight years it was an all-out head banging war. I had to show the staff I could dish it out just as much as I could take it. In fact, in my mind, I had to prove I could take it to make it. A determined walk-on has no other option. (b) (6) were equally determined to prove they would not lose the battle to a "walk-on" on any given play. As a result, we went head smacking against each other in every drill and every scrimmage play. I earned a football scholarship after just two years because of the tenacious blows we delivered to each other on a near daily basis. I earned my right of passage. But, we all paid a high price.

With the demise of (b) (6) and both death's showing signs of CTE, I live in fear today as I feel and show so many signs that a living former athlete can show. I don't know what I have or why I feel what I feel, but I live in fear that CTE is growing inside me.

My once overzealous desire for anything has subsided to a life of lackluster and lackadaisical lifestyle. That has never been me. But, my motivation to do much of anything has subsided into a state of some sort of depression.

I am living in fear now that my condition seems to grow worse on a monthly basis. I don't know if what I am dealing with has anything to do with CTE or if there is another reason I feel I am declining.

(b) (6) I fret I don't have the desire to play outside much at all. Yet, I really want to. I want to run and play with her but I feel sidelined and feel awful I can't get up and go.

When I read of symptoms of CTE, so many relate to me: apathy, depression, memory loss (both short term and long term), difficulty planning and carrying out tasks, weakness, rigidity, loss of attention and concentration, anxiety, and cognitive impairment. They all seem to apply to my everyday life these days and they never used to be part of who I was prior to my mid-20's.

I started this letter to you on September 8th, but ran out of steam to keep writing after just three paragraphs. I used to write for hours at a time. (b) (6)

(b) (6)

It took me five years to (b) (6) and my (b) (6) flowed as I got closer to the end. After just the past 2 and a half years, my desire to (b) (6) let alone (b) (6) anything has come to a screeching halt. I am so concerned with where I am going. I believe I need help. And I am very interested to see if any of your state-of-the-art testing can help diagnose my situation and see if CTE is growing inside my brain.

Please let me know your thoughts and or any advice you may wish to give. I am certainly open to your expertise as I feel like I am driving on a desolate road. I have not told my wife or my other family members how I have been feeling so I am definitely on a solo journey at the moment.

Hope to hear from you.

Regards,

(b) (6)

(b) (6)



## Porter, Kevin (NIH/OD) [E]

---

**From:** Jeff Miller <Jeff.Miller=NFL.com@cmail2.com> on behalf of Jeff Miller  
<Jeff.Miller@NFL.com>  
**Sent:** Wednesday, September 16, 2015 10:05 AM  
**To:** Collins, Francis (NIH/OD) [E]  
**Subject:** Dr. Betsy Nabel talks health and safety on ABC's "This Week"

**Follow Up Flag:** Follow up  
**Flag Status:** Completed

Good morning,

In case you missed the airing of ABC's "This Week" on Sunday, I wanted to share a segment that examined in detail what the league is doing to make the game safer. The show interviewed Dr. Betsy Nabel, the NFL's chief health and medical adviser, on the league's wide-ranging player health and safety efforts. A link to her interview is here: <http://bit.ly/1ih3jQt>

Here are a few highlights:

**On the need for more independent head health research:**

"The NFL can play a leadership role in understanding the scientific basis for acute and a chronic brain injury. Is there a protein that's secreted by the brain and into the blood that indicates injury? How are helmets constructed? Can you use materials that will absorb the shock of contact a bit better?"

**On the standardized concussion protocol – just one of the NFL's many new safety measures – which outlines concussion symptoms and asks players to perform simple cognitive tests to be allowed back in the game:**

"We have a standardized checklist that all 32 teams must comply with."

**On the dozens of rule changes that already are making the game safer with more to come:**

"There'll be rule changes regarding equipment, helmets, tackling."

**On a parent's decision to let their child play football:**

"We want our child to have rich life experiences. We want them to engage in activities that

have deep values and are character-building. Team sports can play that role. And this is where the NFL can play a leadership role and have a watershed effect on youth sports.”

Best,

Jeff

\*\*\*

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345 Park Ave, New York, NY 10154

**From:** Guskiewicz, Kevin M  
**Sent:** 15 Sep 2015 16:44:59 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Re: (b) (4)

Just left you a voice message.

Sent from my iPhone

On Sep 15, 2015, at 11:18 AM, Koroshetz, Walter (NIH/NINDS) [E]  
<[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)> wrote:

Dear Kevin,  
Give a call to my cell if you have a chance. 617 250-  
Best,  
Walter

(b) (6)

**From:** Kevin Guskiewicz <[gus@email.unc.edu](mailto:gus@email.unc.edu)>  
**Date:** Thursday, August 20, 2015 at 6:57 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Cc:** Michael McCrea <[mmccrea@mcw.edu](mailto:mmccrea@mcw.edu)>, Bruce Miller <[Bruce.Miller@ucsf.edu](mailto:Bruce.Miller@ucsf.edu)>, Michael McCrea <[mmccrea@mcw.edu](mailto:mmccrea@mcw.edu)>  
**Subject:** RE: (b) (4)

(b) (4)

Walter,  
Is there a chance that Bruce, Mike, and I could connect with you by phone in the next few days?  
Kevin

**From:** Koroshetz, Walter (NIH/NINDS) [E] [<mailto:koroshetzw@ninds.nih.gov>]  
**Sent:** Wednesday, July 29, 2015 1:14 PM  
**To:** Guskiewicz, Kevin M; Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Mike McCrea ([mmccrea@mcw.edu](mailto:mmccrea@mcw.edu)); Miller, Bruce; Marshall, Steve; Bellgowan, Patrick (NIH/NINDS) [E]; Freire, Maria (FNIH) [T]  
**Subject:** Re: (b) (4)

(b) (4)

Thanks Kevin. The documents were perfect. I sent them along to Dr. Betsy Nabel the CMO for NFL. I plan to make a proposal to our Sept Council, Sept 8/9.  
Best,  
Walter

**From:** Kevin Guskiewicz <[gus@email.unc.edu](mailto:gus@email.unc.edu)>  
**Date:** Wednesday, July 29, 2015 at 1:04 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>, Patrick Bellgowan

**From:** Walker, Paula (NIH/NINDS) [E]  
**Sent:** 15 Sep 2015 10:37:55 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Freire, Maria (FNIH) [T]; Jeff.Miller@nfl.com  
**Cc:** James, Stephanie (FNIH) [T]; Gray, Felicia (FNIH) [T]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Dates for Follow-up Meeting

Hello Everyone:

Walter is available to meet in the next week or so as listed below. Please let me know which date and time works best for you. The meeting will last for an hour and will take place at NIH in Walter's Office. A call-in number will be provided if you are unable to attend in person.

September 16 = 4:00 p.m.-5:00 p.m.  
September 17 = 11:00 a.m.-12:00 p.m.  
September 23 = 9:00 a.m.-10:00 a.m.  
September 30 = 9:00 a.m.-10:30 a.m.  
October 2 = Anytime from 11:00 a.m.-1:00 p.m.

Thank you.

Paula Walker

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Tuesday, September 15, 2015 10:29 AM  
**To:** Freire, Maria (FNIH) [T]; Jeff.Miller@nfl.com  
**Cc:** James, Stephanie (FNIH) [T]; Gray, Felicia (FNIH) [T]; Bellgowan, Patrick (NIH/NINDS) [E]; Walker, Paula (NIH/NINDS) [E]  
**Subject:** Re: Follow-up  
**Importance:** High

Thanks Maria. Yes Paula would be best contact in my office to set up time.  
Walter

**From:** Maria Freire <freirem@fnihi.org>  
**Date:** Tuesday, September 15, 2015 at 10:10 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetz@ninds.nih.gov>, Jeff Miller <Jeff.Miller@NFL.com>  
**Cc:** "James, Stephanie (FNIH) [T]" <james@fnihi.org>, "Gray, Felicia (FNIH) [T]" <gray@fnihi.org>  
**Subject:** Follow-up

Dear Walter and Jeff,

Thank you both for your flexibility and willingness to work to achieve a path forward that will benefit patients and science. To this end, it would be beneficial to find a time in the next week or so to meet to discuss options for projects that achieve this goal. An in-person meeting would be best, although it

might be difficult to achieve; a phone conversation is the next best option (but a second-best from my perspective).

Jeff, I understand that you would like to ask Betsey and perhaps one of two members of your Head, Neck and Spine Committee to join the discussion. Walter, I know you are looking at possible grants or topics that would nicely fit the purpose.

Walter, would you like Paula to try to set this up? I have copied Felicia Gray, my Assistant, on this note. She would be pleased to help coordinate this as well. Please let me know.

Best, Maria

**From:** Stern, Robert A  
**Sent:** 14 Sep 2015 22:17:25 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Hi Walter,

Checking in. I would love to be able to let my co-PIs know what is going on when I email them to set up a conference call to go over milestones.

Bob

**From:** Koroshetz, Walter (NIH/NINDS) [E] [<mailto:koroshetzw@ninds.nih.gov>]  
**Sent:** Friday, September 11, 2015 2:39 PM  
**To:** Stern, Robert A <[bobstern@bu.edu](mailto:bobstern@bu.edu)>  
**Subject:** RE: U01 Award

Hope to get things tied up today.

walter

**From:** Stern, Robert A [<mailto:bobstern@bu.edu>]  
**Sent:** Friday, September 11, 2015 2:36 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Thanks Walter. I would really appreciate that. Prior to my getting in touch with the co-PIs to work on scheduling, it would be great to give them a full update.

Bob

**From:** Koroshetz, Walter (NIH/NINDS) [E] [<mailto:koroshetzw@ninds.nih.gov>]  
**Sent:** Friday, September 11, 2015 12:38 PM  
**To:** Stern, Robert A <[bobstern@bu.edu](mailto:bobstern@bu.edu)>; Bellgowan, Patrick (NIH/NINDS) [E] <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Cc:** Babcock, Debra (NIH/NINDS) [E] <[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)>  
**Subject:** RE: U01 Award

Hi Bob. Let me dot a couple of I's and cross some t's and will then get back to you to answer questions below.

Walter

**From:** Stern, Robert A [<mailto:bobstern@bu.edu>]  
**Sent:** Friday, September 11, 2015 12:30 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Babcock, Debra (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: U01 Award

Hi Pat,

Thanks for the update. Great news that we have the go ahead to discuss Milestones. I will look through the Rigor guidelines. I will also provide you and Dr. Babcock with some times for my three co-PIs and I

**From:** Rieff, Heather (NIH/NINDS) [E]  
**Sent:** 14 Sep 2015 08:38:34 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Scott, Paul (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]  
**Subject:** FW: Summary of briefing: Peering into the brain: Public and private investment in the BRAIN Initiative

Walter-

Paul mentioned that you were curious how this briefing went. See below for a summary I sent on Friday. Had a chance to chat with Rep. Blumenauer's staffer and the ABC folks there, so glad I went.

Thanks,  
Heather

**From:** Rieff, Heather (NIH/NINDS) [E]  
**Sent:** Friday, September 11, 2015 1:54 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Adams, Amy (NIH/NINDS) [E]; Ramos, Khara (NIH/NINDS) [E]  
**Cc:** Scott, Paul (NIH/NINDS) [E]; Wong, Ling (NIH/OD) [E]  
**Subject:** Summary of briefing: Peering into the brain: Public and private investment in the BRAIN Initiative

Yesterday I attended the briefing: **Peering into the brain: Public and private investment in the BRAIN Initiative**, sponsored by the American Brain Coalition and the Congressional Neuroscience Caucus. A brief summary is below.

**Speakers**

**Moderator:** Robin Elliott; President, Parkinson's Disease Foundation; Chair, The American Brain Coalition  
Alan Gilbert, Director of Global Government and NGO Strategy, GE's healthymagination  
Pushkar Joshi, PhD, Director of Strategy & Business Development, Inscopix  
Jeffrey Borenstein, MD, President & CEO, The Brain & Behavior Research Foundation

Rep. Blumenauer, one of the co-chairs of the Neuroscience Caucus, made a very brief appearance.

The industry reps talked about how their research programs complement those of the BRAIN initiative. GE highlighted their partnerships with the NFL and Under Armour to develop optimized techniques for diagnosing concussion, and neurological disease in general. Mr. Gilbert also mentioned GE's collaborations with the Kavli Foundation to convene meetings focused on private investment in BRAIN. He talked about the importance of data sharing and a pilot they have sponsored with Kavli and the Allen Institute on sharing mouse data. The Inscopix representative gave an overview of the company and their technology, the nVista miniaturized microscope which has allowed imaging of the brain in action. He stressed how the company's goals align with the BRAIN initiative, particularly a new grant program they launched right after the BRAIN initiative was announced.

Dr. Bornestein talked about how the Foundation has provided seed funding for researchers who have gone on to make major advances relevant to the BRAIN initiative (e.g, Karl Deisseroth, Helen Mayburg), and the Foundation's focus on advancing research in mental illness.

Let me know if you have any questions.

Thanks,  
Heather

Heather Rieff, Ph.D.  
*Office of Science Policy and Planning*  
*National Institute of Neurological Disorders and Stroke (NINDS)*  
*National Institutes of Health/HHS*  
301-496-9271



**From:** Isabelle J. Gagnon, Dr.  
**Sent:** 11 Sep 2015 15:23:55 +0000  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Re: InTBIR Meeting 13/14th October

Hi Patrick,  
Would you happen to have any news as to when the pre-conference call will occur?  
Thanks  
Isabelle

*Isabelle Gagnon PhD*  
Assistant Professor  
School of Physical and Occupational Therapy/ Pediatrics McGill University  
3834 Promenade Sir-William-Osler Montreal, Qc H3A 1Y4  
☎ 514-398-4400 x099057  
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1001 Decarie, Montreal, Qc H4A 3J1  
☎ 514-412-4400 x23896  
Fax 514-412-4398

**From:** "Bellgowan, Patrick (NIH/NINDS) [E]" <patrick.frostbellgowan@nih.gov>  
**Date:** Wednesday, August 19, 2015 at 15:43  
**To:** 'Feddermann Nina' <Nina.Feddermann@usz.ch>, 'Jiri Dvorak' <jiri.dvorak@f-marc.com>, 'Steve Broglio' <broglio@umich.edu>, "McCrea, Michael" <mmccrea@mcw.edu>, "McAllister, Thomas W" <twmcalli@iupui.edu>, "Hainline, Brian" <bhainline@ncaa.org>, Isabelle Gagnon <isabelle.gagnon8@mcgill.ca>, Carolyn Emery <caemery@ucalgary.ca>  
**Cc:** "Stephenson, Shundel (NIH/NINDS) [E]" <stephes@od.nih.gov>  
**Subject:** RE: InTBIR Meeting 13/14th October

Hi All

As you all know InTBIR is trying to expand its mission to include sports-related concussion. To do this we have developed a section of the InTBIR meeting agenda to present and discuss your studies. One of the primary goals is to begin to harmonize both your data collection, analyses and possibly include data sharing among "like" studies. Drs Broglio and Dvorak will be presenting summaries of your studies and goals (I hope) to the InTBIR group in Brussels (Dr. Emery and Gagnon are already InTBIR studies). We hope that there will be time to discuss overlap and possibilities of collaboration. To foster this I would like to organize a teleconference, possibly in late September, so that you all will have a chance to discuss your projects overlap and missions ahead of the meeting.

Soon, Shundel will be sending out a Doodle poll to see what time will work for most of you. There is a huge timezone difference so we will try to accommodate.

Thanks  
pat

Patrick SF Bellgowan, PhD

Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

-----Original Message-----

From: Feddermann Nina [<mailto:Nina.Feddermann@usz.ch>]  
Sent: Tuesday, August 18, 2015 3:00 AM  
To: Belligowan, Patrick (NIH/NINDS) [E]  
Subject: AW: InTBIR Meeting 13/14th October

Dear Patrick,  
thanks for the information, I just wanted to let you know, that I did not receive another e-mail yesterday.

Kind regards, Nina

-----  
Dr. med. Nina Feddermann-Demont

Oberassistentin

Klinik für Neurologie, UniversitätsSpital Zurich

Frauenklinikstrasse 26

CH- 8008 Zürich

FIFA Medical Assessment and Research Centre (F-MARC)

Lengghalde 2

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Tel.: +41 44 255 4294

Mobil: +41 78 61 (b) (6)

[Nina.Feddermann@usz.ch](mailto:Nina.Feddermann@usz.ch)

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Von: Bellgowan, Patrick (NIH/NINDS) [E] [[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)]  
Gesendet: Montag, 17. August 2015 16:10  
An: Feddermann Nina; 'Jiri Dvorak'  
Betreff: RE: InTBIR Meeting 13/14th October

Hi All,

Sorry for the delay. Later today, I will get you in touch with the NCAA study and some of the Canadian studies. Hopefully, we can organize a teleconference before the October meeting where you can all discuss your projects and think about areas of shared interest and methods for collecting data that may allow for simpler collaborations

Best wishes  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

-----Original Message-----

From: Feddermann Nina [[ma.lto:Nina.Feddermann@usz.ch](mailto:ma.lto:Nina.Feddermann@usz.ch)]  
Sent: Monday, August 10, 2015 11:39 AM  
To: Bellgowan, Patrick (NIH/NINDS) [E]; 'Jiri Dvorak'  
Subject: InTBIR Meeting 13/14th October

Dear Patrick,  
thanks again for the kind invitation to your next InTBIR Meeting on 13th/14th of October. I was able to discuss with Jiri and as already stated in my previous mail we appreciate to participate and are very interested in establishing a collaboration and contribute to your program as proposed on your draft program.

How shall we proceed? Could you send more information with respect to your NCAA project to us, that we can "peruse" and make proposals of how we could make a contribution to your project or do you have already a precise project plan?

Thanks and kind regards, Nina

---

Dr. med. Nina Feddermann-Demont, MD

Neurologist

Department of Neurology, University Hospital Zurich

Frauenklinikstrasse 26

CH- 8008 Zurich

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[Nina.Feddermann@usz.ch](mailto:Nina.Feddermann@usz.ch) <<mailto:Nina.Feddermann@usz.ch>>3cmailto:Nina.Feddermann@usz.ch>

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Von: Bellgowan, Patrick (NIH/NINDS) [E] [[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)]

Gesendet: Freitag, 31. Juli 2015 20:02

An: 'Jiri Dvorak'

Cc: Feddermann Nina

Betreff: RE: Thank you from FNIH!

Hi Jiri and Nina,

Sorry for the long delay in communication. On behalf of the international TBI Research Consortium (InTBIR; <http://intbir.nih.gov/>) Executive Committee, we like to invite you to attend the 2015 InTBIR meeting will be hosted by the European Commission and held on 13-14 October 2015 in Brussels. As you may know InTBIR is an international collaboration among the EU, USA, Canada, and One Mind to bring together TBI research programs in an effort to accelerate the improvement of outcomes. To date, InTBIR has sister studies of TRACK-TBI and CENTER-TBI in the US and EU respectively. InTBIR also includes several other pediatric and sports-related (mostly from Canada studies). Part of the mission of InTBIR is to harmonize common data elements (measures) use across similar studies. As we spoke awhile ago, we would like to have FIFA join us along with the NCAA/ DOD study of collegiate athletes to more about your concussion studies. I realize this may be challenging with such a short timeframe but please let me know if you are interested.

I have attached information about the meeting.

Thank You  
Pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
psfb@mail.nih.gov<mailto:psfb@mail.nih.gov>

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

From: Jiri Dvorak [mailto:[jiri.dvorak@f-marc.com](mailto:jiri.dvorak@f-marc.com)]  
Sent: Wednesday, June 17, 2015 6:05 PM  
To: Wolf-Rodda, Julie (FNIH) [T]  
Cc: Nina Feddermann; James, Stephanie (FNIH) [T]; Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
Subject: Re: Thank you from FNIH!

Dear Julie,

we look forward

Greetings

Jiri

Prof Jiří Dvořák, MD  
FIFA Chief Medical Officer  
Chairman F-MARC  
Schulthess Clinic Zurich

+41 44 385 7415 Office direct  
+41 79 597 (b) FIFA mobile

Am 17 Jun 2015 um 23:38 schrieb Wolf-Rodda, Julie (FNIH) [T] <[jwolf-rodde@fnih.org](mailto:jwolf-rodde@fnih.org)<mailto:jwolf-rodde@fnih.org>>

Dear Jiri and Nina,

Thank you again for taking the time to speak with me, my FNIH colleagues, and Drs. Walter Koroshetz and Patrick Bellgowan of the NINDS. Everyone appreciated your overview of your

extensive research portfolio in TBI and the opportunity to begin to explore a possible path forward for scientific collaboration. There is great excitement about the potential for improving coordination, and NINDS is looking at various ways to introduce you to the Sports and Health Research Program (SHRP) grantees and collaborators. We will be back in touch within the next few weeks about next steps.

Best regards,  
Julie

Julie Wolf-Rodda  
Director of Development  
Foundation for the National Institutes of Health  
9650 Rockville Pike | Bethesda, MD 20814 | [www.fnih.org](http://www.fnih.org)<<http://www.fnih.org>> Direct (301) 402-6027 | Fax (301) 480-2752

-----Original Message-----

From: Wolf-Rodda, Julie (FNIH) [T]  
Sent: Monday, June 08, 2015 5:48 PM  
To: 'Feddermann Nina'  
Cc: 'Jiri.Dvorak@F-MARC.com'<<mailto:Jiri.Dvorak@F-MARC.com>>  
Subject: RE: Thank you from FNIH!

Dear Nina,

Thank you for your quick and encouraging reply! Dates and times that would work for FNIH and NINDS are below. All are Eastern US times that should be suitable for Zurich as well. Please let me know what might work, or feel free to suggest alternates if these do not agree with your schedule.

June 10 = 7:00 a.m.-8:00 a.m.

June 11 = 8:00 a.m.-9:00 a.m.

June 12 = 8:00 a.m.-9:00 am.

June 30 = 8:00 a.m.-9:00 a.m. and 10:00 a.m.-11:00 a.m.

Best regards,  
Julie

Julie Wolf-Rodda  
Director of Development  
Foundation for the National Institutes of Health  
9650 Rockville Pike | Bethesda, MD 20814 | [www.fnih.org](http://www.fnih.org)<<http://www.fnih.org>> Direct (301) 402-6027 | Fax (301) 480-2752

-----Original Message-----

From: Feddermann Nina [<mailto:Nina.Feddermann@usz.ch>]  
Sent: Saturday, June 06, 2015 8:27 AM  
To: Wolf-Rodda, Julie (FNIH) [T]  
Cc: [Jiri.Dvorak@F-MARC.com](mailto:Jiri.Dvorak@F-MARC.com)<<mailto:Jiri.Dvorak@F-MARC.com>>  
Subject: RE: Thank you from FNIH!

Dear Julie,  
thanks for your mail and the information. We would appreciate to find opportunities for constructive collaboration and agree that it would be most efficient to discuss further steps on the phone.

As we have already discussed in Washington currently our primary research area is the diagnostic and therapeutic management of acute head trauma and post traumatic syndrome, which could be used as base for further research on discussed long term problems (as CTE). So we assume, that we could complement one another in a very positive way.

When would you be available? Could you please send 2-3 dates and time proposals (that would be suitable with European time zone)?

Wish you a nice weekend.  
Thanks & Kind regards from Zurich, Nina

Dr. med. Nina Feddermann-Demont

Department of Neurology  
University Hospital Zurich  
Frauenklinikstrasse 26  
CH- 8008 Zurich

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CH- 8008 Zurich

Phone: +41 44 255 4294  
Mobile: +41 78 65 (b) (6)  
[Nina.Feddermann@usz.ch](mailto:Nina.Feddermann@usz.ch)<<mailto:Nina.Feddermann@usz.ch>><<mailto:Nina.Feddermann@usz.ch>>

[unnamed]

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Von: Wolf-Rodda, Julie (FNIH) [T] [[jwolf-rodde@fnih.org](mailto:jwolf-rodde@fnih.org)<<mailto:jwolf-rodde@fnih.org>>]

Gesendet: Donnerstag, 4. Juni 2015 18:22

An: Feddermann Nina

Cc: 'Jiri.Dvorak@F-MARC.com'<<mailto:Jiri.Dvorak@F-MARC.com>>

Betreff: RE: Thank you from FNIH!

Dear Nina,

I hope this finds you well. Thanks again for joining us at the March 31 Sports and Health Research Program (SHRP) Stakeholder Board Meeting in Washington, DC. The National Institute of Neurological Disorders and Stroke (NINDS) has prepared the attached meeting summary, which is available now on the NINDS

website<[http://www.ninds.nih.gov/news\\_and\\_events/proceedings/shrp\\_mtg\\_summary\\_03312015.htm](http://www.ninds.nih.gov/news_and_events/proceedings/shrp_mtg_summary_03312015.htm)>. I hope you find it valuable.

As you heard at the meeting, SHRP has already funded a number of TBI research grants and NINDS will soon make a grant award for a longitudinal study of CTE. Additional private-sector support could strengthen the study in a number of ways and/or serve to fill other research gaps. I'd love to touch base with you to hear your thoughts on areas for collaboration and explore how we might work together to maximize the investments that are being made. I've taken the liberty of attaching our current overview of SHRP, including some possible next steps beginning on page 5. Would you have time for a call in the next few weeks to discuss this? I'll include Drs. Koroshetz and Bellgowan in the conversation as well. I look forward to talking with you soon.

Thanks again and best regards,

Julie

Julie Wolf-Rodda

Director of Development

Foundation for the National Institutes of Health

9650 Rockville Pike | Bethesda, MD 20814 | [www.fnih.org](http://www.fnih.org)<<http://www.fnih.org>>

Direct (301) 402-6027 | Fax (301) 480-2752



**From:** Finkelstein, Robert (NIH/NINDS) [E]  
**Sent:** 9 Sep 2015 13:03:36 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: CTE RFA

I think it will be fine. Hard to predict what they'll say.

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Wednesday, September 09, 2015 11:49 AM  
**To:** Finkelstein, Robert (NIH/NINDS) [E]  
**Subject:** Re: CTE RFA

Agree.  
Walter

**From:** Robert Finkelstein <FinkelsR@ninds.nih.gov>  
**Date:** Wednesday, September 9, 2015 at 11:47 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzw@ninds.nih.gov>, Patrick Bellgowan <patrick.frostbellgowan@nih.gov>  
**Cc:** Alan Willard <AlanW@ninds.nih.gov>  
**Subject:** RE: CTE RFA

I think we should ask the entire group (b) (5) That's what

(b) (5)

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Wednesday, September 09, 2015 11:42 AM  
**To:** Finkelstein, Robert (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Willard, Alan (NIH/NINDS) [E]  
**Subject:** Re: CTE RFA

Ok. (b) (5)  
(b) (5)

walter

**From:** Robert Finkelstein <FinkelsR@ninds.nih.gov>  
**Date:** Wednesday, September 9, 2015 at 11:35 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzw@ninds.nih.gov>, Patrick Bellgowan <patrick.frostbellgowan@nih.gov>  
**Cc:** Alan Willard <AlanW@ninds.nih.gov>  
**Subject:** RE: CTE RFA

General plan for the meeting is that (b) (5)

(b) (5)

(b) (5)

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Wednesday, September 09, 2015 11:32 AM  
**To:** Finkelstein, Robert (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Willard, Alan (NIH/NINDS) [E]  
**Subject:** Re: CTE RFA

(b) (5)

Walter

**From:** Robert Finkelstein <[FinkelsR@ninds.nih.gov](mailto:FinkelsR@ninds.nih.gov)>  
**Date:** Wednesday, September 9, 2015 at 11:26 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetz.w@ninds.nih.gov](mailto:koroshetz.w@ninds.nih.gov)>, Patrick Bellgowan <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Cc:** Alan Willard <[AlanW@ninds.nih.gov](mailto:AlanW@ninds.nih.gov)>  
**Subject:** RE: CTE RFA

(b)

Looks good to me. Just let me know beforehand (or at the table)

(b) (5)

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Wednesday, September 09, 2015 10:55 AM  
**To:** Finkelstein, Robert (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Willard, Alan (NIH/NINDS) [E]  
**Subject:** Re: CTE RFA

Can stay with the facts.

(b) (5)

Walter

**From:** Robert Finkelstein <[FinkelsR@ninds.nih.gov](mailto:FinkelsR@ninds.nih.gov)>  
**Date:** Wednesday, September 9, 2015 at 10:41 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetz.w@ninds.nih.gov](mailto:koroshetz.w@ninds.nih.gov)>, Patrick Bellgowan <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>

Cc: Alan Willard <AlanW@ninds.nih.gov>

Subject: RE: CTE RFA

(b) (5)

A large rectangular area of the document is redacted, indicated by a solid gray block.

**From:** Koroshetz, Walter (NIH/NINDS) [E]

**Sent:** Wednesday, September 09, 2015 10:33 AM

**To:** Bellgowan, Patrick (NIH/NINDS) [E]

**Cc:** Willard, Alan (NIH/NINDS) [E]; Finkelstein, Robert (NIH/NINDS) [E]

**Subject:** Re: CTE RFA

(b) (5)

A large rectangular area of the document is redacted, indicated by a solid gray block.

Walter

**From:** Stern, Robert A  
**Sent:** 9 Sep 2015 11:26:06 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: CTE U01

Hi Walter,

I hope the rest of your summer was great, though I would guess that you have been incredibly busy. I am writing to check in about the status of the U01 and the additional funding. I gather that your proposal to double the funding is being brought to Council tomorrow and Friday? Whichever way Council decides, is the plan to begin funding prior to the new fiscal year? Should I expect some news about how things are moving forward soon after Council? Any information you can provide would be much appreciated. My co-PIs and co-investigators are all eager for news and excited to get our project under way. Thanks much.

Regards,  
Bob

**From:** Koroshetz, Walter (NIH/NINDS) [E] [mailto:koroshetzw@ninds.nih.gov]  
**Sent:** Tuesday, July 28, 2015 12:12 PM  
**To:** Stern, Robert A <bobstern@bu.edu>  
**Subject:** Re: CTE U01

thanks would be interesting. Ncaa study pondering the follow up issue as well.  
W

Sent from my iPhone

On Jul 28, 2015, at 11:50 AM, Stern, Robert A <bobstern@bu.edu> wrote:

Phew! Our proposal does include the three-year follow-up for the control group, with the full in-person evaluation. The group that is not seen for the 3-year f/u is the former college football player group. That decision was based on two reasons: (1) the primary purpose of including them was for evaluation of risk determination (i.e., lower exposure to repetitive hits than the NFL group), so that could be determining through the cross-sectional baseline; and (2) budget issues...the cost of bringing them back in for the 3-yr f/u was too expensive, so I was planning on submitting a subsequent grant that would support them coming in. With that said, I would be delighted to include a telephone assessment of the former college players. We could also put in an annual telephone assessment (or web assessment, using some of the instruments currently being used in Mike Weiner's Brain Health Registry) for the entire cohort so we add to the longitudinal data. That would not take much additional work and could be done centrally.

Bob

**From:** Koroshetz, Walter (NIH/NINDS) [E] [mailto:koroshetzw@ninds.nih.gov]  
**Sent:** Tuesday, July 28, 2015 11:43 AM  
**To:** Stern, Robert A <bobstern@bu.edu>

**Cc:** Bellgowan, Patrick (NIH/NINDS) [E] <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Subject:** Re: CTE U01

We definitely need more money if going to fund two. What we do depends on how much more I can convince Council to put out. If zero then we are not going to be able to do two. Proposal will be to double the funding to do two.

Also think you should think about collecting some longitudinal data from your "control" group as a comparison- maybe put into the study a telephone assessment, computer assisted testing? ??

Walter

**From:** Bob Stern <[bobstern@bu.edu](mailto:bobstern@bu.edu)>  
**Date:** Tuesday, July 28, 2015 at 11:25 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Subject:** RE: CTE U01

Thanks. Much clearer. One important question that I know you cannot completely answer at this time but here it goes: Is the concept to split the available money in half (or some other fraction), similar to Ann and Wayne, such that our project's budget would be substantially reduced? Or, are there additional funds being made available to allow for an additional group/study but without substantial cuts?

Bob

**From:** Koroshetz, Walter (NIH/NINDS) [E] [<mailto:koroshetzw@ninds.nih.gov>]  
**Sent:** Tuesday, July 28, 2015 11:03 AM  
**To:** Stern, Robert A <[bobstern@bu.edu](mailto:bobstern@bu.edu)>  
**Subject:** Re: CTE U01

Sorry may not have been clear. Proposal would be to fund two groups, and integrate the two studies. Kind of like we did with Ann and Wayne. Might put in oversight group giving advice to investigators and to NINDS.

NIH can't talk about grants that are not funded so that's why can't get into it til know whether there will be another group.

Walter

**From:** Bob Stern <[bobstern@bu.edu](mailto:bobstern@bu.edu)>  
**Date:** Tuesday, July 28, 2015 at 10:02 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Cc:** Patrick Bellgowan <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Subject:** RE: CTE U01

Thanks very much, Walter. I really appreciate your response. It would be really helpful to have some type of glimpse into what is being planned (with full understanding that things are still being worked out) if for no other reason than to avoid my embarrassment and

awkwardness when someone tells me about other sites/investigators getting involved and I have no idea. Also, as you can imagine, with three other mPis, multiple subcontract PIs, and ~50 co-investigators, all anxiously awaiting some news (since they all know that Council approved it a couple months ago), I would love to be able to have a better sense of why there has been a delay. Again, I know nothing is written in stone at this point and there is need for lots of discussion and planning. I would just really appreciate an informal, confidential discussion about what some of the thoughts and options are. Please let me know if you would be okay with a phone call. Thanks again.

Bob

**From:** Koroshetz, Walter (NIH/NINDS) [E] [mailto:koroshetzw@ninds.nih.gov]  
**Sent:** Tuesday, July 28, 2015 9:21 AM  
**To:** Stern, Robert A <bobstern@bu.edu>  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E] <patrick.frostbellgowan@nih.gov>  
**Subject:** Re: CTE U01

We are committed to funding the project. Once we see how things settle out Pat and I will sit down with all the players and get into the weeds to make sure we reach our goal of nailing down the diagnostic criteria— clinical, imaging, other biomarkers. Similar to what we did with Ann and Wayne.

At that point we may ask you to make some changes to your original plan. Not worth talking about it now without knowing the scope of what we will fund.

Best

Walter

**From:** "bobstern@bu.edu" <bobstern@bu.edu>  
**Date:** Monday, July 27, 2015 at 1:45 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzw@ninds.nih.gov>  
**Cc:** Patrick Bellgowan <patrick.frostbellgowan@nih.gov>  
**Subject:** Re: CTE U01

Is the originally approved project funding at all in jeopardy or questionable at this time? Or is just the expansion questionable?

Bob

On Jul 27, 2015, at 1:41 PM, Koroshetz, Walter (NIH/NINDS) [E] <koroshetzw@ninds.nih.gov> wrote:

Thanks Bob. Not much to say at this point. Am planning to go to sept Council with a plan to expand the study but have no idea how it will turn out. Council is Sept 8,9. Will get on the phone soon afterwards.

Best,

Walter

**From:** "bobstern@bu.edu" <bobstern@bu.edu>

**Date:** Monday, July 27, 2015 at 12:26 PM

**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzw@ninds.nih.gov>, Patrick Bellgowan <patrick.frostbeligowan@nih.gov>

**Subject:** CTE U01

Hi Walter and Pat,

I apologize for yet another inquiry into the status of the U01 and timing of the NoGA. The last I had heard from Pat (10 days ago) was that it would take at least a few more weeks, so I was going to just wait until I hear something from you. However, I am writing now because since that time I have been hearing through the "grapevine" some unclear, unspecified talk about expanding the project to include other sites and investigators. Is there anything I should know as things move forward? Should we have a phone call to clarify what may or may not be going on. I look forward to hearing from you.

Regards,

Bob

Robert A. Stern, Ph.D.

Professor of Neurology, Neurosurgery, and Anatomy & Neurobiology

Director, Clinical Core, BU Alzheimer's Disease and CTE Center

Boston University School of Medicine

72 East Concord Street, Robinson 7800

Boston, MA 02118

tel: 617-638-5678

fax: 617-638-5679

email: [bobstern@bu.edu](mailto:bobstern@bu.edu)

[www.bu.edu/alzresearch](http://www.bu.edu/alzresearch)

**From:** Belligowan, Patrick (NIH/NINDS) [E]  
**Sent:** 9 Sep 2015 10:07:31 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Belligowan, Patrick (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Subject:** Re: CTE RFA

Thanks.

(b) (5)



Or

Maybe the specific question doesn't matter

Thanks

Pat

Patrick SF Belligowan, PhD  
Program Director  
NINDS / NIH  
301-496-1447  
[Pat.belligowan@nih.gov](mailto:Pat.belligowan@nih.gov)

On Sep 9, 2015, at 9:48 AM, "Koroshetz, Walter (NIH/NINDS) [E]"  
<[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)> wrote:

This looks perfect Pat.



Probably need to distribute written versions of the affidavit at beginning of closed session so folks have time to read it.

Hopefully one of the readers summarizes the gist of the affidavit.

Walter

**From:** Patrick Bellgowan <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>

**Date:** Tuesday, September 8, 2015 at 3:37 PM

**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>, Alan Willard <[AlanW@ninds.nih.gov](mailto:AlanW@ninds.nih.gov)>

**Subject:** CTE RFA

Hi Walter and Alan

Attached is a long-ish version of what I could present at Council. They will have the write-up so I could do a shorter summary version if that is more appropriate.

Thanks

Pat.

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>



**From:** Finkelstein, Robert (NIH/NINDS) [E]  
**Sent:** 8 Sep 2015 11:04:25 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Subject:** RE: new investigator talk at council  
**Attachments:** Finkelstein Javits talk.pptx

I'm working on the Javits slides now. Here's the current draft.

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Tuesday, September 08, 2015 10:27 AM  
**To:** Finkelstein, Robert (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Subject:** RE: new investigator talk at council

OK. Great that Anna presents the data. Send me the slides so I can take a look. Also the stuff on Javits.  
Thanks  
Walter

**From:** Finkelstein, Robert (NIH/NINDS) [E]  
**Sent:** Friday, September 04, 2015 3:02 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Subject:** new investigator talk at council

Anna and I have been working on this. Since she provided the data, I'm thinking that she should give the talk. We can always jump in if there are difficult questions. OK? I'll talk about the Javits and Closed Session procedures.

---

**Robert Finkelstein**  
Director, Division of Extramural Research  
NINDS  
6001 Executive Blvd., Rm 3307  
Bethesda, MD 20892-9531

For Fed Ex, change last line to:  
Rockville, MD 20852

Phone: (301) 496-9248  
FAX: (301) 402-4370



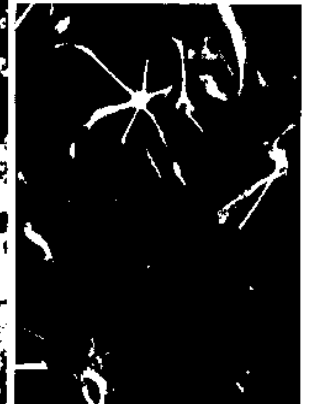
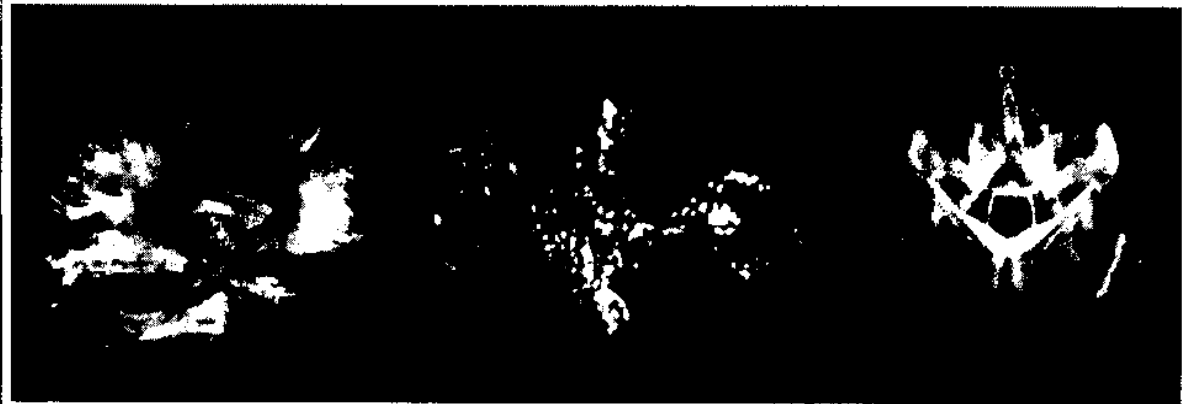
National Institute of  
Neurological Disorders  
and Stroke

# Future of Javits Investigator Award Program

**Robert Finkelstein, Ph.D.**

Director, Division of Extramural Research  
National Institute of Neurological Disorders  
and Stroke, NIH

September 10, 2015



# What is the Javits Award?

- ❖ Started by NINDS in 1984, in honor of Senator Jacob Javits (R-N.Y.)
- ❖ Provides longer term support (7 years) than a typical R01 award (4-5 years):

➤ **Four year award**



administrative review

➤ **Additional three years**

- ❖ Intended to be highly prestigious and to reduce grant-writing burden



# Javits Award criteria (published)

(<http://www.ninds.nih.gov/funding/javits.htm>)

- ❖ Record of substantial contributions at the “cutting edge” of neurological research
- ❖ Leader in the field (e.g., ideas, funding record, publications, awards)
- ❖ Expected to continue to be highly productive if funded for 7 years
- ❖ Record of service to NINDS and/or NIH



# Javits Nomination and Selection Process

- ❖ NINDS staff consider entire pool of eligible applications and propose candidates (Council members can also nominate)

➤ Investigators do not apply for Javits awards!



- ❖ Candidates discussed in detail and final nominees selected (before Council)



- ❖ Council discusses and votes on each candidate



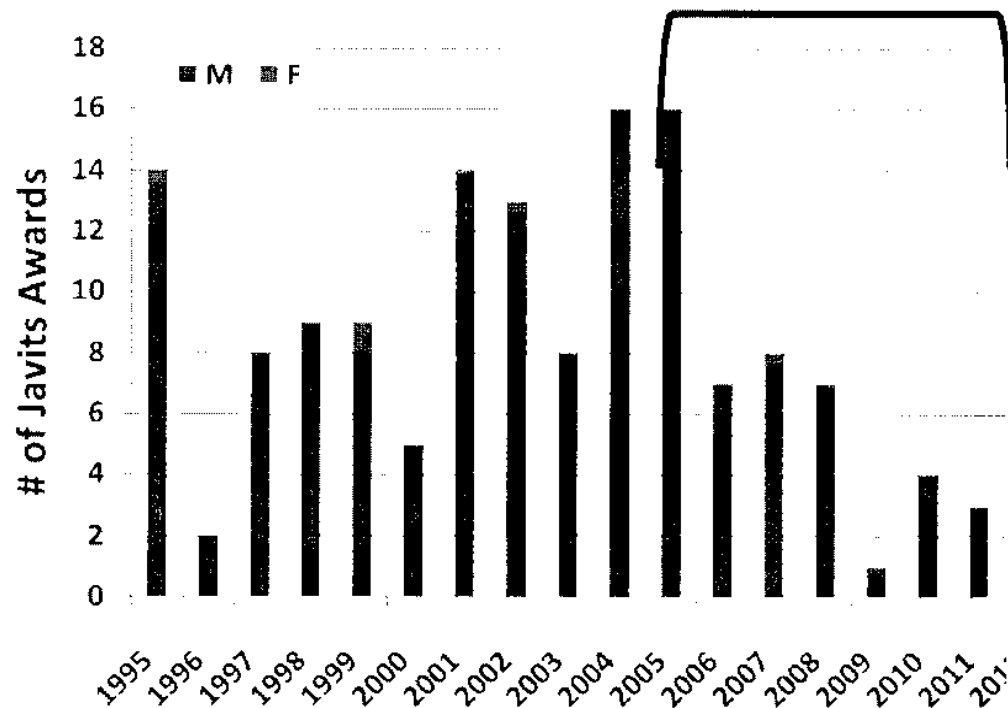
# Operational criteria (before 2012)

- ❖ R01 in question scored 5<sup>th</sup> percentile or better on first submission
- ❖ Renewal applications only
- ❖ PI has a long history of being funded without needing to revise/resubmit
- ❖ Expected to continue to be highly productive if funded for 7 years
- ❖ History of service to community (study section service, organizing meetings, etc.)
- ❖ Up to 13 Javits awards/year





# Gender disparity problem!



- Based on eligibility criteria, 2X disparity
- Discussed findings with Council (September 2011)

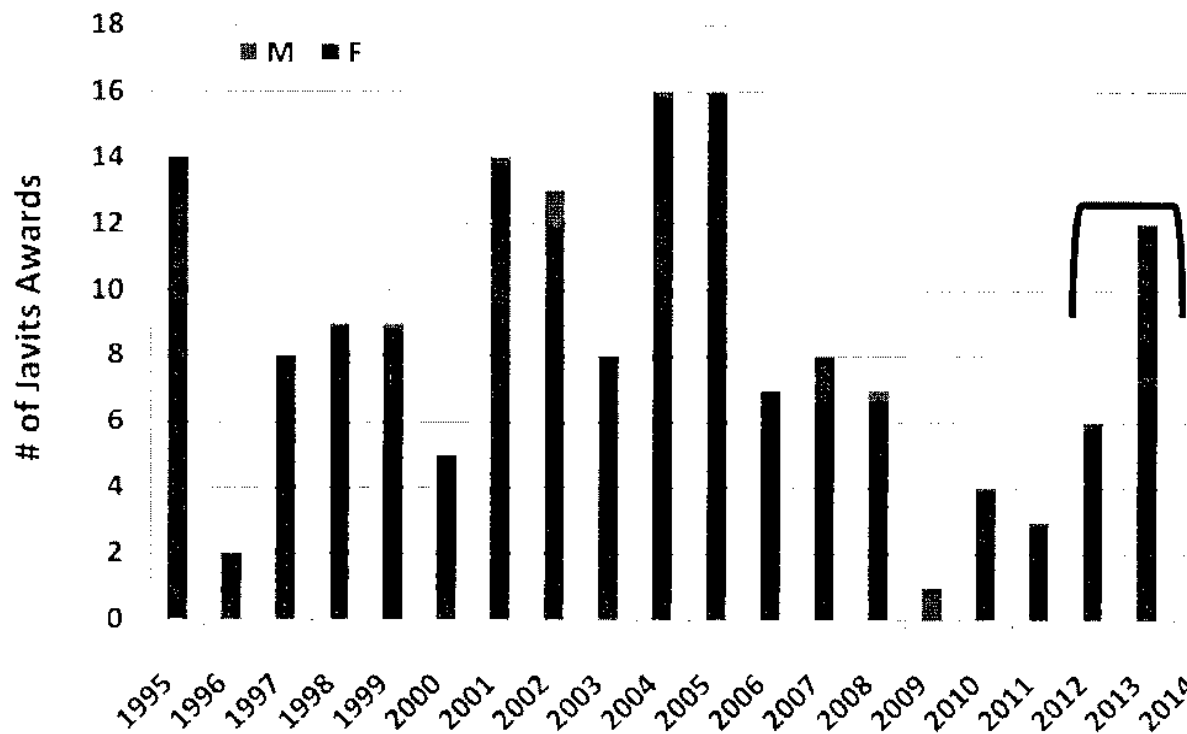


# Modified eligibility criteria (2012)

- ❖ R01 scored 8<sup>th</sup> percentile or better
- ❖ Revised applications permitted
- ❖ 10 years of continuous NINDS R01 funding
- ❖ Every application in this eligibility zone discussed



# It didn't help



- During FY12 and FY13, only 1 in 18 Javits awards to women!
- Discussed with Council in January 2014



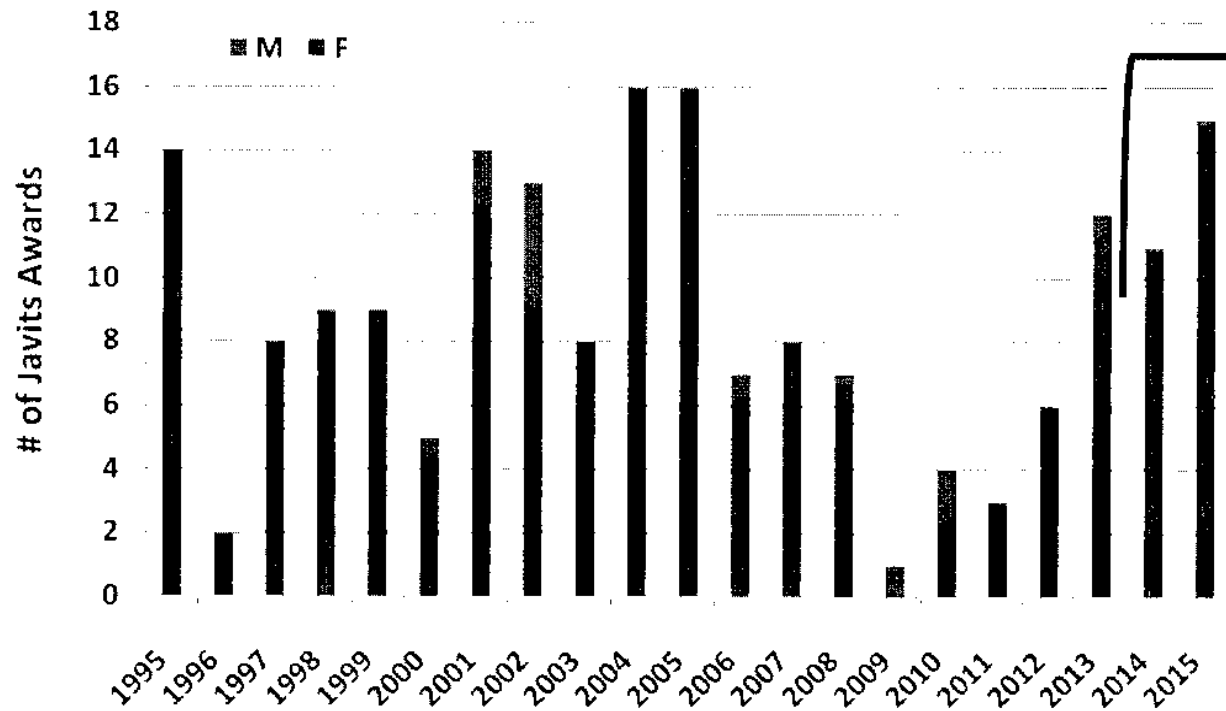


# Modified eligibility criteria (2014)

- ❖ Any R01 within the payline is eligible (new or renewal)
- ❖ 10 years of continuous NINDS R01 funding
- ❖ Focus is on quality and impact of the investigator, rather than on rigid eligibility criteria



# Recent History (2014 – present)



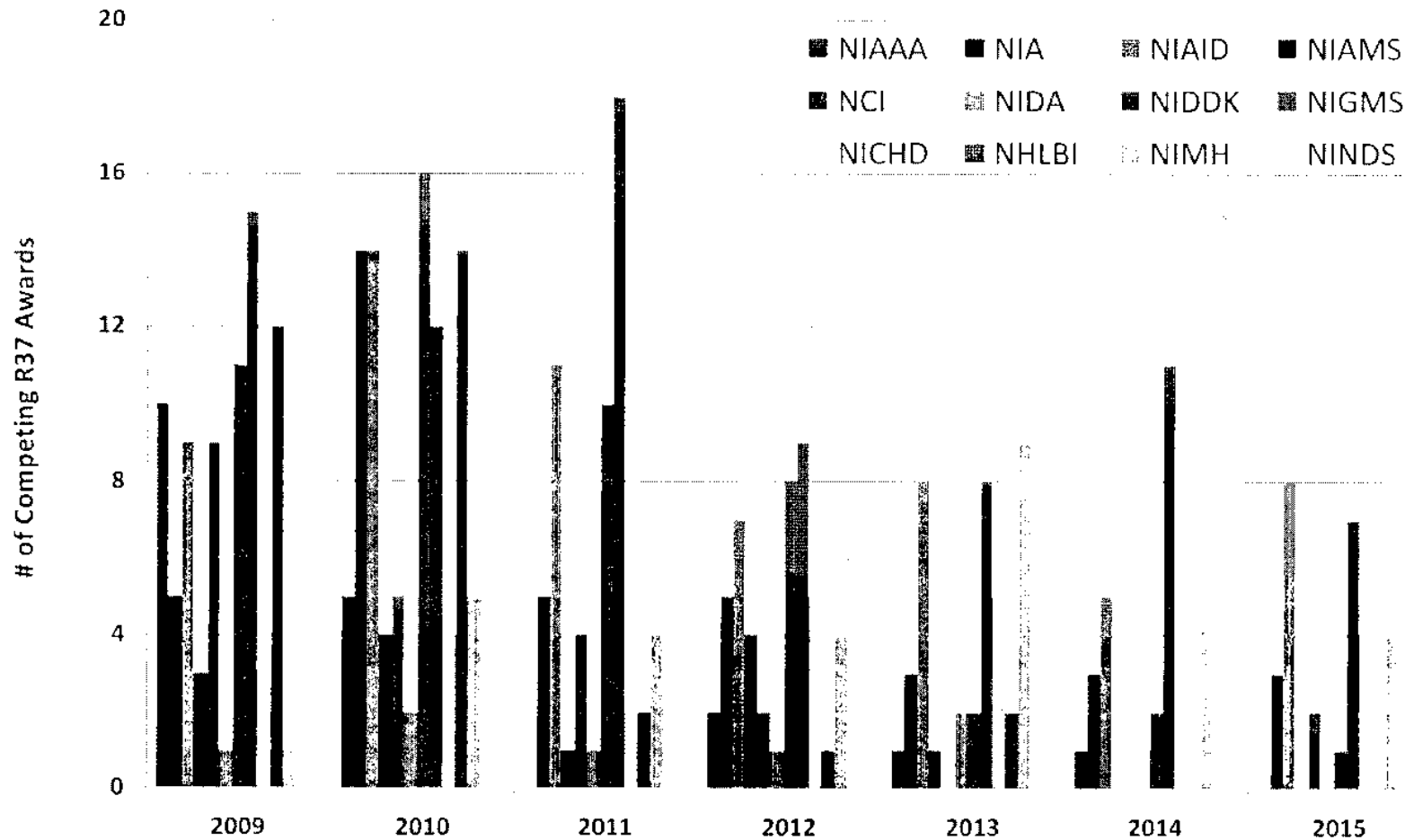
- During FY14 and FY15, 12 in 26 Javits awards to women
- Released R35 FOA in July 2015

# NINDS initiates Research Program Award (R35)

- ❖ “To provide longer-term support and increased flexibility to investigators with outstanding records of research achievement”
- ❖ Up to \$750,000 (direct costs)/year for 8 years
- ❖ Intended to support all NINDS-related research in the PI’s laboratory
- ❖ Goals
  - Create a more stable funding environment
  - Facilitate longer range, innovative research
  - Reduce time spent writing multiple grant applications
  - Enhance training environment



# R37 Award Programs Across NIH



# Proposal for Future of the Javits Award

- One award per council round
- Increase award length from 7 to 10 years (5 + 5)
- Publicize the award, enhance its prestige
- Maintain diversity!
- What should the criteria be?





**From:** Mink, Jonathan  
**Sent:** 3 Sep 2015 23:03:52 +0000  
**To:** Finkelstein, Robert (NIH/NINDS) [E]  
**Cc:** Byron's Gmail; RSacco@med.miami.edu; Baker, Kelly (NIH/NINDS) [E]; Wells, Nena (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]  
**Subject:** Re: Follow-up

That works for me.  
Jon

On Sep 3, 2015, at 3:28 PM, Finkelstein, Robert (NIH/NINDS) [E] <[FinkelsR@ninds.nih.gov](mailto:FinkelsR@ninds.nih.gov)> wrote:

Thanks. Let's pencil in tomorrow (Friday) at 5. Walter, Byron, Ralph, Pat and I can make it tomorrow, waiting to hear from Jon.

Toll free call in number: (712) 432- (b) (6)  
Participant Access Code: (b) (6)

Jon, if you can't make it then, we'll figure something out. Bob

**From:** Byron's Gmail [mailto:(b) (6)]  
**Sent:** Thursday, September 03, 2015 2:14 PM  
**To:** Finkelstein, Robert (NIH/NINDS) [E]  
**Cc:** [Jonathan.Mink@urmc.rochester.edu](mailto:Jonathan.Mink@urmc.rochester.edu); [RSacco@med.miami.edu](mailto:RSacco@med.miami.edu); Baker, Kelly (NIH/NINDS) [E]  
**Subject:** Re: Follow-up

Hi Bob. I am not available today, but I can do either of the other two call times.  
Byron

Sent from my iPhone

On Sep 3, 2015, at 10:51 AM, Finkelstein, Robert (NIH/NINDS) [E] <[FinkelsR@ninds.nih.gov](mailto:FinkelsR@ninds.nih.gov)> wrote:

Hello again,

This situation keeps evolving and Walter would like to attempt to set up a last-minute conference call to update you. Please let me know if you can do it at either 5 PM today (I realize this is unlikely), Sept. 4 at 5 PM, or Sept. 9 at 5 PM.

Thanks for your patience!  
Bob

---

On Sep 2, 2015, at 2:56 PM, Finkelstein, Robert (NIH/NINDS) [E]  
<[FinkelsR@ninds.nih.gov](mailto:FinkelsR@ninds.nih.gov)> wrote:

Dear Byron, Jonathan, and Ralph,

(b) (5)



Bob

---

**Robert Finkelstein**  
Director, Division of Extramural Research  
NINDS  
6001 Executive Blvd., Rm 3307  
Bethesda, MD 20892-9531

For Fed Ex, change last line to:

Rockville, MD 20852

Phone: (301) 496-9248

FAX: (301) 402-4370

<RFA NS 14-012.pdf>

**From:** Lyons, Ernest (NIH/NINDS) [E]  
**Sent:** 3 Sep 2015 17:03:23 -0400  
**To:** Willard, Alan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: conflict of interest guidelines for peer review

So this is more on the CTE review issue. I haven't seen the report, I just heard (from Walter) that CSR found it to be basically flawless. Is there a written report that could be shared? – just curious. -Ernie

**From:** Willard, Alan (NIH/NINDS) [E]  
**Sent:** Thursday, September 03, 2015 4:58 PM  
**To:** Lyons, Ernest (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: conflict of interest guidelines for peer review

None of us who have searched the literature have found any co-authored research articles. Manley may be confusing reviews or meeting reports with research publications.

Did CSR weigh in on that issue? I have not seen or heard their report.

Alan

**From:** Lyons, Ernest (NIH/NINDS) [E]  
**Sent:** Thursday, September 03, 2015 2:27 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Subject:** RE: conflict of interest guidelines for peer review

I think he is saying there were co-authored publications that should have been considered COI's. Agree, it would help to know what he is referring to specifically. I'm in the same boat – no idea what this is about but happy to weigh in anyway... ☺

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Thursday, September 03, 2015 1:43 PM  
**To:** Willard, Alan (NIH/NINDS) [E]; Lyons, Ernest (NIH/NINDS) [E]  
**Subject:** FW: conflict of interest guidelines for peer review

Doesn't say which people or which publications but we are sure that no conflicts on research papers? Or should I ask him to clarify?  
walter

**From:** Mitchel Berger <Mitchel.Berger@ucsf.edu>  
**Date:** Wednesday, September 2, 2015 at 10:01 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzw@ninds.nih.gov>  
**Cc:** Richard Ellenbogen <rge@neurosurgery.washington.edu>, Russell Lonser <Russell.Lonser@osumc.edu>  
**Subject:** RE: conflict of interest guidelines for peer review

According to what you sent me the 4 individuals should not have been allowed to review the application, i.e. section 2, since "within the past three years, the reviewer has been a collaborator..." These 4 people were in conflict based on this criteria and never should have been allowed to review this grant application. I think the Council should hear this explanation and be told whether they were allowed to

vote on the final score. If they voted on the final score then according to this document you list below, they were in conflict. Those publications were not "non research publications". Respectfully, mitch berger

---

**From:** Koroshetz, Walter (NIH/NINDS) [E] [[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)]  
**Sent:** Tuesday, September 01, 2015 6:08 PM  
**To:** Berger, Mitchel S.  
**Cc:** Ellenbogen, Richard ([rge@neurosurgery.washington.edu](mailto:rge@neurosurgery.washington.edu)); 'Lonser, Russell'  
**Subject:** conflict of interest guidelines for peer review

Dear Mitch,

As mentioned the conflict of interest guidelines for peer review can be found at  
<http://grants.nih.gov/grants/peer/Grant-Reviews-508.pdf>

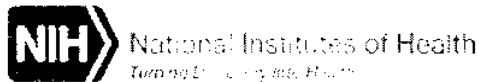
Long version at [http://grants.nih.gov/grants/peer/COI\\_Information.pdf](http://grants.nih.gov/grants/peer/COI_Information.pdf)

Note that it is not a conflict of interest if "The reviewer co-authored a review article, position paper, professional group or conference report with the PD/PI, one of multiple PDs/PIs, or an individual listed on the application as participating with either a major or minor role

Best wishes,

Walter

Walter Koroshetz, MD  
Director, National Institute of Neurological Disorders and Stroke



**From:** Finkelstein, Robert (NIH/NINDS) [E]  
**Sent:** 3 Sep 2015 11:22:31 -0400  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Important

Patrick, I agree 100% with what you've said below. (Note that I've removed your header). I think that

(b) (5)

Having said this, Walter knows far more about this than I do and it's clearly his call. I will do whatever you think is best. Need to know quickly whether we should arrange the pre-call (we have a few potential times).

Bob

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Friday, August 28, 2015 6:29 PM  
**To:** Finkelstein, Robert (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** More thoughts re: CTE U01s

Hi Walter, Alan, and Bob,

I just finished reading the affidavit from Dr. Stern. Dr. Stern seems to be arguing that a single symptom domain (cognitive) shouldn't be used to assess disability related to CTE. Though psychiatric symptoms associated with mild TBI and CTE are still a bit controversial, the controversy mostly revolves around whether the symptoms have a psychosomatic or neuropathological origin. Dr. Stern is simply expressing his opinion that CTE includes psychiatric symptoms which I find difficult to link to confirmation bias. In fact, I might suggest that this testimony could be used to argue against him having confirmation bias. (b) (5) has (b) (5) (a discussion point that is prominent in the summary statement). (b) (5) (b) (5) whereas Dr. Stern equally emphasizes cognition and psychiatric symptoms eliminating a bias against psychiatric symptoms being a key diagnostics and prognostic indicator.

The more I think about this, the more strongly I believe that NINDS should just stick to the plan of

(b) (5)

(b) (5)

(b) (5)

(b) (5)

After speaking with Alan it seems that including the report about the review of this RFA is a bit strange as no PIs asked it to be done.

Thanks for working this through with me,  
Pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
psfb@mail.nih.gov

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Finkelstein, Robert (NIH/NINDS) [E]  
**Sent:** Friday, August 28, 2015 2:39 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: CTE U01s

Pat, Alan is going to stop by to discuss this with you. FYI, if we do have a call, Kelly will be the person to set it up. Bob

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Friday, August 28, 2015 12:43 PM  
**To:** Finkelstein, Robert (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]; Owens, David (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** CTE U01s

Hi Alan, Dave and Bob,

After discussion with Walter, I think that I will be proposing to (b) (5)

(b) (5) to insure balanced scientific perspective and rigor to the process of developing diagnostic and prognostic criteria for the disease course of CTE. As was mentioned in the Pre-Council meeting (b) (5)

Plus, I think it

(b) (5)

(b) (5)



If this makes sense to you, I'll put together these documents in a folder and try to arrange a TC with these three Council Members.

Thanks  
Pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>



**From:** Folkerth, Rebecca Dunn, M.D.  
**Sent:** 2 Sep 2015 16:46:23 +0000  
**To:** 'Mckee, Ann C'; Cairns, Nigel; Dennis Dickson; Keene, Dirk (cdkeene@uw.edu); Irene Litvan; Perl, Daniel (daniel.perl@usuhs.edu); Stein, Thor; William Stewart; Tripodis, Yorghos; Jean Paul Vonsattel; John Crary; Bieniek, Kevin F.; Dams-o'connor, Kristen; Alvarez, Victor E; Gordon, Wayne; Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: Manuscript on First NINDS/NIBIB Consensus Meeting to Evaluate Neuropathological Criteria for the Diagnosis of CTE

So exciting! Thanks, Ann – I am really looking forward to seeing this. Rebecca

**From:** Mckee, Ann C [mailto:amckee@bu.edu]  
**Sent:** Wednesday, September 02, 2015 11:30 AM  
**To:** Cairns, Nigel; Dennis Dickson; Folkerth, Rebecca Dunn, M.D.; Keene, Dirk (cdkeene@uw.edu); Irene Litvan; Perl, Daniel (daniel.perl@usuhs.edu); Stein, Thor; William Stewart; Tripodis, Yorghos; Jean Paul Vonsattel; John Crary; Bieniek, Kevin F.; Dams-o'connor, Kristen; Alvarez, Victor E; Gordon, Wayne; Debra [E] Babcock; Patrick Bellgowan; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Manuscript on First NINDS/NIBIB Consensus Meeting to Evaluate Neuropathological Criteria for the Diagnosis of CTE

All,

I will be inviting you to a dropbox today containing the draft manuscript "The First NINDS/NIBIB Consensus Meeting to Evaluate Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy". Please click on the link to download the manuscript. I embedded the figures and the tables in the draft to make it easier to review as a single document, however, if you would prefer to receive the tables, figures and draft separately, please let me know.

I am hoping to hear back from all of you in 2 weeks, i.e. by September 16th, with your edits. The editor of Acta Neuropathologica, Werner Paulus, is eager to publish the consensus paper soon. Thank you all in advance for your help.

Ann

The information in this e-mail is intended only for the person to whom it is addressed. If you believe this e-mail was sent to you in error and the e-mail contains patient information, please contact the Partners Compliance HelpLine at <http://www.partners.org/complianceline>. If the e-mail was sent to you in error but does not contain patient information, please contact the sender and properly dispose of the e-mail.

**From:** Ann via Dropbox  
**Sent:** 2 Sep 2015 15:45:03 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Ann McKee shared "CTE U01 Consensus 9.2acm.docx" with you



From Ann:

"All,

This is the link to the draft manuscript "The First NINDS/NIBIB Consensus Meeting to Evaluate Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy". Please click on the link to download the manuscript.

THE PASSWORD IS (b) (6)

I embedded the figures and the tables in the draft to make it easier to review as a single document, however, if you would prefer to receive the tables, figures and draft separately, please let me know.

I am hoping to hear back from all of you in 2 weeks, i.e. by September 16th, with your edits. The editor of Acta Neuropathologica, Werner Paulus, is eager to publish the consensus paper soon. Thank you all in advance for your help.

Ann"

[Click here to view:](#)

(Ann shared these files using Dropbox. Enjoy!)

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** 2 Sep 2015 09:10:21 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Sony pictures/Concussion

Interesting developments, good to know in preparation for Council. Quote is from Jeff Miller.

Good luck!!

[http://www.nytimes.com/2015/09/02/sports/football/makers-of-sonys-concussion-film-tried-to-avoid-angering-nfl-emails-show.html?hp&action=click&pgtype=Homepage&module=first-column-region&region=top-news&WT.nav=top-news&\\_r=0](http://www.nytimes.com/2015/09/02/sports/football/makers-of-sonys-concussion-film-tried-to-avoid-angering-nfl-emails-show.html?hp&action=click&pgtype=Homepage&module=first-column-region&region=top-news&WT.nav=top-news&_r=0)

**From:** Ellenbogen, Richard  
**Sent:** 2 Sep 2015 03:00:39 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Berger, Mitchel S (Mitchel.Berger@ucsf.edu); Lonser, Russell  
**Subject:** Re: conflict of interest guidelines for peer review

Walter:

Thanks for that insight. However, I would respectfully ask that if there is a neurological surgeon on council any more that they also look at the study very carefully first before Council looks at it or you get a second review from an unbiased clinician doing TBI research. I am very disappointed that there was only one TBI clinician on the review study section after your very well run NIH conference in which 50 interested clinicians showed up. And, I am very concerned that we are about to spend a lot of money on a grant in which the PI clearly stated he knew the answers and has not maintained an open mind about the science. It is an affidavit. We are doomed to get a biased answer, just my opinion from a guy living in this TBI world every day. If I am to ask the NEI to give more money to the FNII, I need to reassure them that the review was fair and not biased which is how it appears by the stuff test. Thanks and respectfully, Rich

On Sep 1, 2015, at 9:08 PM, Koroshetz, Walter (NIH/NINDS) [E] wrote:

Dear Mitch,

As mentioned the conflict of interest guidelines for peer review can be found at <http://grants.nih.gov/grants/peer/Grant-Reviews-508.pdf>

Long version at <http://grants.nih.gov/grants/peer/COI-Information.pdf>

Note that it is not a conflict of interest if "The reviewer co-authored a review article, position paper, professional group or conference report with the PD PI, one of multiple PDs PIs, or an individual listed on the application as participating with either a major or minor role

Best wishes,

Walter

Walter Koroshetz, MD  
Director, National Institute of Neurological Disorders and Stroke

<image001.png>

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**From:** Finkelstein, Robert (NIH/NINDS) [E]  
**Sent:** 1 Sep 2015 15:43:17 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Willard, Alan (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]  
**Subject:** FW: Important Council matter

Thanks, this is much more comprehensible. Will try to get it out today.

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Monday, August 31, 2015 6:47 PM  
**To:** Finkelstein, Robert (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/OD) [E]  
**Subject:** RE: Important Council matter

OK---also made other changes to keep more objective and avoid misperception.

(b) (5)

Reworded to state that

(b) (5)

(b) (5)

Walter

**From:** Finkelstein, Robert (NIH/NINDS) [E]  
**Sent:** Monday, August 31, 2015 5:34 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/OD) [E]  
**Subject:** Important Council matter

We need to send the NFL-related stuff to the 3 Council members. Looking at the write-up (posted in below), I think you need to add a sentence or two towards the beginning (perhaps after the first sentence) explaining (b) (5)

(b) (5)

don't explain this up front.

(b) (5)



**From:** Willard, Alan (NIH/NINDS) [E]  
**Sent:** 1 Sep 2015 16:59:22 -0400  
**To:** Finkelstein, Robert (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/OD) [E]  
**Subject:** RE: Very strange

There are several people from MGH on the (b) (5) application, so I think (b) (5) in conflict!

**From:** Finkelstein, Robert (NIH/NINDS) [E]  
**Sent:** Tuesday, September 01, 2015 4:41 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/OD) [E]  
**Subject:** Very strange

This is very weird. We haven't sent anything to (b) (5) change that he's looking at the (b) (5) application...

**From:** Baker, Kelly (NIH/NINDS) [E]  
**Sent:** Tuesday, September 01, 2015 9:56 AM  
**To:** Finkelstein, Robert (NIH/NINDS) [E]  
**Subject:** You might find this interesting...

You haven't sent anything out about the (b) (5) FA/applications review yet to Council members, correct? Dr. Chiocca seems to be on top of it and has been searching for the information in the ECB already. I thought you might find this interesting... (but maybe you do not?!): ]

(b) (5)



**Kelly Baker**  
Committee Management Officer  
Division of Extramural Research  
NINDS/NIH  
6001 Executive Blvd., Suite 3309, MSC 9531  
Rockville, MD 20892-9531  
Phone: 301-496-6496  
Fax: 301-402-4370



**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** 1 Sep 2015 11:27:44 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Subject:** FYI concussion

In case you haven't seen it yet:

<https://www.washingtonpost.com/news/early-lead/wp/2015/08/31/will-smith-takes-on-the-nfl-in-concussion-trailer/>

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** 1 Sep 2015 09:09:05 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Finkelstein, Robert (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Subject:** RE: Important Council matter

A few nit-picky edits in red below. Feel free to take them or leave them!

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Monday, August 31, 2015 6:47 PM  
**To:** Finkelstein, Robert (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/OD) [E]  
**Subject:** RE: Important Council matter

OK—also made other changes to keep more objective and avoid misperception.

(b) (5)

Reworded to state that (b) (5)

(b) (5)

Walter

**From:** Finkelstein, Robert (NIH/NINDS) [E]  
**Sent:** Monday, August 31, 2015 5:34 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/OD) [E]  
**Subject:** Important Council matter

We need to send the NFL-related stuff to the 3 Council members. Looking at the write-up (pasted in below), I think you need to add a sentence or two towards the beginning (perhaps after the first sentence) explaining that (b) (5)

(b) (5)

This is alluded to further down, but will be confusing if you don't explain this up front.

(b) (5)



---

**From:** Frushour, Ken (NIH/NINDS) [E]  
**Sent:** Thursday, August 27, 2015 5:53 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: Extramural Balance ---currently (b) (5)

I'll make Council Slides with all this info..i just haven't had time to pull this all together

Sorry,  
Ken

**From:** Frushour, Ken (NIH/NINDS) [E]  
**Sent:** Thursday, August 27, 2015 5:43 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: Extramural Balance---currently (b) (5)

(b) (5)

Damn

Ken

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Thursday, August 27, 2015 5:27 PM  
**To:** Frushour, Ken (NIH/NINDS) [E]  
**Subject:** RE: Extramural Balance---currently (b) (5)

Thanks Ken.

(b) (5)

(b) (5)

walter

**From:** Frushour, Ken (NIH/NINDS) [E]

**Sent:** Thursday, August 27, 2015 5:06 PM

**To:** Koroshetz, Walter (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]; Finkelstein, Robert (NIH/NINDS) [E]; Owens, David (NIH/NINDS) [E]

**Cc:** Ly, Quynh (NIH/NINDS) [E]; Lam, Christine (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]; Taylor, Anna (NIH/NINDS) [E]

**Subject:** Extramural Balance---currently (b) (5)

**Importance:** High

Hi Guys,

Below is what we are currently planning for extramural budget closeout. You guys can see from below that we have included everything which has been discussed at all pre-Council meetings. There are still some estimates on this breakout:

(b) (5)

---

**From:** Lyons, Ernest (NIH/NINDS) [E]  
**Sent:** Thursday, August 27, 2015 4:19 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** FW: Help with a CTE Review end of April?

(b) (5)



(b) (5)


I'll go in and take a look at that one now for my own assessment. -Ernie

**From:** Rajaram, Shantadurga (NIH/NINDS) [E]  
**Sent:** Thursday, August 27, 2015 3:52 PM  
**To:** Lyons, Ernest (NIH/NINDS) [E]  
**Subject:** FW: Help with a CTE Review end of April?

Ernie,

All reviewers were given access to the list of key personnel at the time of recruitment.

(b) (5), (b) (6)



Shanta

**From:** (b) (5), (b) (6)  
**Sent:** Wednesday, March 11, 2015 2:45 PM  
**To:** Rajaram, Shantadurga (NIH/NINDS) [E]  
**Subject:** RE: Help with a CTE Review end of April?

Shanta,

I can do this.

I am on a committee with (b) (6) but there is no financial relationship.

(b) (5), (b) (6)



Available dates

4/20 8a-noon

4/23 noon-5p

4/24/ 9a-4p

4/28/9a-5p

4/29 11:30a-5p

4/30 2:30p-6p

5/1 11a-4p

**From:** Rajaram, Shantadurga (NIH/NINDS) [E] [mailto:rajarams@ninds.nih.gov]

**Sent:** Wednesday, March 11, 2015 11:23 AM

**To:** (b) (5), (b) (6)

**Subject:** Help with a CTE Review end of April?

**Importance:** High

Dear (b) (5), (b) (6)

I am writing from the scientific review branch of NINDS to ask for your help with the review of applications received in response to **RFA-NS-14-012 to Detect, Define and Measure the Progression of Chronic Traumatic Encephalopathy (CTE)**. *In 2013, you helped review the original program, this builds upon and your continued input would be very valuable to us.*

This initiative aims to support a multicenter and multidisciplinary longitudinal study of individuals with a "possible" diagnosis of CTE using brain **imaging and other fluid biomarkers**, along with appropriate control groups. The **goal** is to obtain and use **longitudinal data**, such as MRI and PET imaging, **cognitive and behavioral assessments**, and CSF or blood for **genomic and proteomic analysis**, to increase knowledge concerning the neurological mechanisms of CTE as it evolves over a 3 - 5 year period and enable the **development of consensus**, evidence-based **criteria** for clinical diagnosis.

(b) (5) **01** applications received in response to this initiative have been assigned to a special emphasis panel **ZNS1 SRB G(01)** and that would be the maximum number of your assignments (most likely fewer). We hope to accomplish this review via a 4 hour teleconference **between April 20<sup>th</sup> and May 1<sup>st</sup>.**

The list of involved key personnel on these applications is attached to this email. Please go over it carefully and identify any conflicts personal, professional or financial that may put you in conflict to review any of these applications.

If there are no significant conflicts, and you are able to help with this review, please let me know at your earliest possible convenience. In your response, please clearly indicate your availability for a 4 hour window on as many dates as possible between April 20<sup>th</sup> and May 1<sup>st</sup> 2015.

If simply impossible for you, I would also appreciate suggestions of other domestic and any international experts with similar expertise who might make thoughtful reviewers for this panel.

With sincere thanks and kind regards,  
Shanta

*Shanta Rajaram, Ph.D*

Scientific Review Branch  
NINDS  
6001 Executive Blvd., Ste 3208, MSC 9529  
Bethesda, MD 20892-9529  
(for courier delivery, use Rockville, MD 20852.)

Phone: 301-435-6033  
Fax: 301-402-0182  
Email: [rajarams@mail.nih.gov](mailto:rajarams@mail.nih.gov)

---

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Saturday, August 22, 2015 3:07 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Fwd: Council issue

Hi Walter

Please see Bob F's question below. I had assumed we were proposing to fund (b)(4); (b)(6) but defer to you.

Thanks  
Pat

Patrick SF Bellgowan, PhD  
Program Director  
NINDS / NIH  
301-496-1447  
[Pat.bellgowan@nih.gov](mailto:Pat.bellgowan@nih.gov)

Begin forwarded message:

**From:** "Finkelstein, Robert (NIH/NINDS) [E]" <[FinkelsR@ninds.nih.gov](mailto:FinkelsR@ninds.nih.gov)>  
**Date:** August 22, 2015 at 9:23:00 AM EDT  
**To:** "Bellgowan, Patrick (NIH/NINDS) [E]" <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Cc:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>, "Willard, Alan (NIH/NINDS) [E]" <[AlanW@ninds.nih.gov](mailto:AlanW@ninds.nih.gov)>, "Baker, Kelly (NIH/NINDS) [E]" <[bakerke@ninds.nih.gov](mailto:bakerke@ninds.nih.gov)>  
**Subject:** Re: Council issue

This is a good start Pat and I think there are some tweaks we can make to make it better (I'll send you my edits when I return on monday). The critical question though is whether we want to PROPOSE (b) (5) If you want to consider the latter course, you'd simply explain the pros and cons and ask them what they think. Perhaps you and Walter can make a decision about this and we can send out on monday. Bob

On Aug 21, 2015, at 2:55 PM, Bellgowan, Patrick (NIH/NINDS) [E] <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)> wrote:

Hi Bob

Attached is the statement/proposal to Council regarding the CTE U01. Walter and Alan have both read and commented on this version.

Thanks  
Pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS



301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Finkelstein, Robert (NIH/NINDS) [E]  
**Sent:** Thursday, August 20, 2015 5:29 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]; Baker, Kelly (NIH/NINDS) [E]  
**Subject:** Re: Council issue

Sounds good

On Aug 20, 2015, at 4:23 PM, Bellgowan, Patrick (NIH/NINDS) [E]  
<[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)> wrote:

What about Byron Ford, Jonathon Mink, Ralph Sacco?

I'll get you the paragraph tomorrow but I'd like to bounce it off Walter and Alan

Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Finkelstein, Robert (NIH/NINDS) [E]  
**Sent:** Thursday, August 20, 2015 9:38 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]  
**Cc:** Baker, Kelly (NIH/NINDS) [E]  
**Subject:** RE: Council issue

(b) (5)



Let us know ASAP which Council members you want me to send this too. Maybe we should send it to 3 since sometimes they don't all respond.

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Wednesday, August 19, 2015 3:31 PM  
**To:** Finkelstein, Robert (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]

**Cc:** Baker, Kelly (NIH/NINDS) [E]  
**Subject:** RE: Council issue

(b) (5)



Bob

**From:** Baker, Kelly (NIH/NINDS) [E]  
**Sent:** Tuesday, August 18, 2015 11:07 AM  
**To:** Finkelstein, Robert (NIH/NINDS) [E]  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** FNIH/NFL/NINDS Request from Council

Hi Bob,

Who are we going to send this information to? What is the RFA number and the applications that we are talking about? I don't have any of the details for this.

Thanks,  
Kelly : )

**Kelly Baker**  
Committee Management Officer  
Division of Extramural Research  
NINDS/NIH  
6001 Executive Blvd., Suite 3309, MSC 9531  
Rockville, MD 20892-9531  
Phone: 301-496-6496  
Fax: 301-402-4370



**From:** Miller, Bruce  
**Sent:** 21 Aug 2015 18:25:53 +0000  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Cc:** Miller, Bruce  
**Subject:** Re: 5:15 p.m. Conference Call RE (b) (4)

Thx

**Bruce L. Miller, MD**

A.W. and Mary Margaret Clausen Distinguished Professor of Neurology  
Director, Memory and Aging Center

**University of California, San Francisco**

675 Nelson Rising Lane, Suite 190 San Francisco, CA 94158

tel: 415.476.5591 | fax: 415.476.5573

[bmiller@memory.ucsf.edu](mailto:bmiller@memory.ucsf.edu)



Assistant: Leslie Goss – [lgoss@memory.ucsf.edu](mailto:lgoss@memory.ucsf.edu)

[memory.ucsf.edu](http://memory.ucsf.edu) | [facebook.com/ucsfinmemoryandaging](https://facebook.com/ucsfinmemoryandaging) | [twitter.com/UCSFmac](https://twitter.com/UCSFmac) | [youtube.com/ucsfinmemoryandaging](https://youtube.com/ucsfinmemoryandaging)

On Aug 21, 2015, at 11:23 AM, Bellgowan, Patrick (NIH/NINDS) [E]  
<[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)> wrote:

Hi Bruce

Call-in Number: 1-877-957-  
Passcode: (b) (6)

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Miller, Bruce [<mailto:Bruce.Miller@ucsf.edu>]  
**Sent:** Friday, August 21, 2015 2:14 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Guskiewicz, Kevin M; Bellgowan, Patrick (NIH/NINDS) [E]; Miller, Bruce; Mike McCrea

(mmccrea@mcw.edu)

Subject: Re: 8:15 p.m. - Conference Call RE

(b) (4)

(b) (4)

Can we get a call in conference number

**Bruce L. Miller, MD**

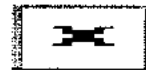
A.W. and Mary Margaret Clausen Distinguished Professor of Neurology  
Director, Memory and Aging Center

**University of California, San Francisco**

675 Nelson Rising Lane, Suite 190 | San Francisco, CA 94158

tel: 415.476.5591 | fax: 415.476.5573

[bmiller@memory.ucsf.edu](mailto:bmiller@memory.ucsf.edu)



Assistant: Leslie Goss -- [lgoss@memory.ucsf.edu](mailto:lgoss@memory.ucsf.edu)

[memory.ucsf.edu](http://memory.ucsf.edu) | [facebook.com/ucsfmemoryandaging](https://facebook.com/ucsfmemoryandaging) | [twitter.com/UCSFmac\\_yo](https://twitter.com/UCSFmac_yo)  
[youtube.com/ucsfmemoryandaging](https://youtube.com/ucsfmemoryandaging)

On Aug 21, 2015, at 8:42 AM, Koroshetz, Walter (NIH/NINDS) [E]

<[koroshetzwa@ninds.nih.gov](mailto:koroshetzwa@ninds.nih.gov)> wrote:

From: Koroshetz, Walter (NIH/NINDS) [E]

Sent: Thursday, August 20, 2015 9:20 AM

To: 'Guskiewicz, Kevin M'

Cc: Bellgowan, Patrick (NIH/NINDS) [E]; Walker, Paula  
(NIH/NINDS) [E]

Subject: RE (b) (4)

(b) (4)

Sure. I cc'ed Ms. Paula Walker who controls my schedule. And Pat  
Bellgowan.  
walter

From: Guskiewicz, Kevin M [<mailto:gus@email.unc.edu>]

Sent: Thursday, August 20, 2015 6:58 AM

To: Koroshetz, Walter (NIH/NINDS) [E]

Cc: Mike McCrea ([mmccrea@mcw.edu](mailto:mmccrea@mcw.edu)<<mailto:mmccrea@mcw.edu>>);

Miller, Bruce; Mike McCrea

([mmccrea@mcw.edu](mailto:mmccrea@mcw.edu)<<mailto:mmccrea@mcw.edu>>)

Subject: RE (b) (4)

(b) (4)

Walter,

Is there a chance that Bruce, Mike, and I could connect with you by phone in the next few days?

Kevin

From: Koroshetz, Walter (NIH/NINDS) [E]  
[mailto:koroshetzwa@ninds.nih.gov]

Sent: Wednesday, July 29, 2015 1:14 PM

To: Guskiewicz, Kevin M; Bellgowan, Patrick (NIH/NINDS) [E]

Cc: Mike McCrea (mmccrea@mcw.edu<mailto:mmccrea@mcw.edu>);

Miller, Bruce; Marshall, Steve; Bellgowan, Patrick (NIH/NINDS) [E];

Freire, Maria (FNIH) [E]

Subject: Re: (b) (4)

(b) (4)

Thanks Kevin. The documents were perfect. I sent them along to Dr. Betsy Nabel the CMO for NFL. I plan to make a proposal to our Sept Council, Sept 8/9.

Best,

Walter

From: Kevin Guskiewicz

<gus@email.unc.edu<mailto:gus@email.unc.edu>>

Date: Wednesday, July 29, 2015 at 1:04 PM

To: "Koroshetz, Walter (NIH/NINDS) [E]"

<koroshetzwa@ninds.nih.gov<mailto:koroshetzwa@ninds.nih.gov>>,

Patrick Bellgowan

<patrick.frostbellgowan@nih.gov<mailto:patrick.frostbellgowan@nih.gov>>

Cc: Michael McCrea

<mmccrea@mcw.edu<mailto:mmccrea@mcw.edu>>, Bruce Miller

<Bruce.Miller@uesf.edu<mailto:Bruce.Miller@uesf.edu>>, Steve

Marshall <smarshall@unc.edu<mailto:smarshall@unc.edu>>

Subject: RE: (b) (4)

(b) (4)

Hi Walter,

I am back from vacation, and happy to discuss the document we sent and next steps if it would be helpful. I want to be sure that what we have produced for you is what is needed at this point.

Thanks,

Kevin

From: Koroshetz, Walter (NIH/NINDS) [E]

[mailto:koroshetzwa@ninds.nih.gov]

Sent: Monday, July 20, 2015 5:18 PM  
To: Guskiewicz, Kevin M; Bellgowan, Patrick (NIH/NINDS) [E]  
Cc: Mike McCrea ([mmccrea@mcw.edu](mailto:mmccrea@mcw.edu); <mailto:mmccrea@mcw.edu>);  
Miller, Bruce; Marshall, Steve  
Subject: RE: (b) (4)  
(b) (4)

Thanks guys this is very helpful.  
Best wishes,  
Walter

From: Guskiewicz, Kevin M [<mailto:gus@email.unc.edu>]  
Sent: Monday, July 20, 2015 3:17 PM  
To: Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick  
(NIH/NINDS) [E]  
Cc: Mike McCrea ([mmccrea@mcw.edu](mailto:mmccrea@mcw.edu); <mailto:mmccrea@mcw.edu>);  
Miller, Bruce; Marshall, Steve; Guskiewicz, Kevin M  
Subject: (b) (4)  
(b) (4)

Dear Walter,  
Thanks again for your efforts to help fund our research. (b) (4)  
(b) (4)  
(b) (4)

As per your request from our phone conversation on July 10th, I have attached a cover letter and response to our summary statement. I have also copied Pat Bellgowan, who assisted us to better understand some of the reviewers' questions/concerns. Thanks Pat.

Co-PI's Bruce Miller and Mike McCrea, as well as several members of our research team, assisted in responding to the summary statement.

Please confirm that you have received this, and let us know if you have additional questions or need anything more from us at this time. We look forward to hearing from you soon.

Many thanks,  
Kevin

-----  
Kevin Guskiewicz, PhD, ATC  
Kenan Distinguished Professor, Exercise and Sport Science  
Senior Associate Dean, Natural Sciences  
University of North Carolina at Chapel Hill

**From:** Miller, Jeff  
**Sent:** 20 Aug 2015 19:58:07 +0000  
**To:** Walker, Paula (NIH/NINDS) [E]  
**Cc:** Freire, Maria (FNIH) [T]; Gray, Felicia (FNIH) [T]; James, Stephanie (FNIH) [T]; Bellgowan, Patrick (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]  
**Subject:** Re: Follow up discussion  
**Attachments:** image001.png, image001.png

Can we hold noon to 1 or 1:30? Thanks

On Aug 19, 2015, at 3:54 PM, Walker, Paula (NIH/NINDS) [E] <walkerp@ninds.nih.gov> wrote:

Hello Everyone:

On August 27<sup>th</sup>, Dr. Koroshetz has a conflict from 11:00 a.m. 12:00 p.m. but is available for a call any time from 12:00 p.m.-4:00 p.m.

Please let know your availability for this time frame.

Thank you.

Paula Walker

**From:** Miller, Jeff [mailto:Jeff.Miller@AFL.com]  
**Sent:** Wednesday, August 19, 2015 3:35 PM  
**To:** Walker, Paula (NIH/NINDS) [E]  
**Cc:** Freire, Maria (FNIH) [T]; Gray, Felicia (FNIH) [T]  
**Subject:** Re: Follow up discussion

Can we hold the time on 8-27 for a call? We may need an in person meeting as well, but we'd like to hold the time for a call first.  
Thanks

On Aug 18, 2015, at 8:48 AM, Walker, Paula (NIH/NINDS) [E] <walkerp@ninds.nih.gov> wrote:

Hello Mr. Miller & Dr. Freire:

Per the email below, please let me know your availability for a conference call with Dr. Koroshetz for the dates below. The call will last for 1 to 2 hours.



- August 20 = 3:00 p.m.-5:00 p.m.
- August 21 = 2:00 p.m.-5:00 p.m.
- August 27 = 11:00 a.m.-1:00 p.m.

Thank you.

Paula Walker

**From:** Jeff Miller <Jeff.Miller@NFL.com>  
**Date:** Monday, August 17, 2015 at 2:57 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetaw@ninds.nih.gov>  
**Cc:** "Freire, Maria (FNIH) [T]" <freiremc@od.nih.gov>  
**Subject:** Follow up discussion

Dr. Koroshetz,

I hope you're well. After a conversation with Dr. Friere and some understanding of the request for further NFL investment, I am hoping that we can schedule a time to meet with you in the next few days. Should an in-person meeting be difficult to schedule, we would like to find time for a teleconference as your calendar allows.

Please let us know some potential times you may be available in the next week or two.

Thank you for your consideration,  
Jeff

<image001.png>

#SB50  
[SuperBowl.com](http://SuperBowl.com)  
**Jeff Miller**  
*Senior Vice President*  
**NATIONAL FOOTBALL LEAGUE**  
P: 212-450-2072 | E: [jeffmiller@nfl.com](mailto:jeffmiller@nfl.com)

<image001.png>

---

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Thursday, August 20, 2015 6:26 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: FNIH

SO I was planning on taking the following route for my write-up to send to Council:

(b) (5)

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Thursday, August 20, 2015 6:20 PM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: FNIH

I can fill you in,  
by Council.  
walter

(b) (5)

But know that we are bound

**From:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Sent:** Wednesday, August 19, 2015 12:25 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** FNIH

Hi Walter,

(b) (5)

Thanks  
pat

Patrick SF Bellgowan, PhD  
Program Director, Repair and Plasticity  
NIH/NINDS  
301-496-1447  
[psfb@mail.nih.gov](mailto:psfb@mail.nih.gov)

<http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** 14 Aug 2015 17:16:55 -0400  
**To:** Finkelstein, Robert (NIH/NINDS) [E]; Frushour, Ken (NIH/NINDS) [E]; Koretsky, Alan (NIH/NINDS) [E]; Lewis, Caroline (NIH/NINDS) [E]; Nath, Avindra (NIH/NINDS) [E]; Owens, David (NIH/NINDS) [E]; McNeil, D Elizabeth (NIH/NINDS) [E]; Willard, Alan (NIH/NINDS) [E]; Sofranko, Mary Ann (NIH/NINDS) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Agenda & Materials: Monday Senior Staff Meeting  
**Attachments:** Summary Statement; outside the scope of the request - Wall Street Journal July 17 2015.pdf, Aug 17 Senior Staff.docx

Hi everyone,

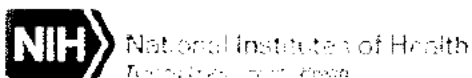
Please find attached and below the agenda and materials for our Senior Staff meeting on Monday morning from 9:00-10:00am in 31/8A28. Call in information is below.

Call: 1-877-95-(b) (6), scode (b) (6)

Have a great weekend!  
Meghan

--

**Meghan Mott, Ph.D.**  
*AAAS Science & Technology Policy Fellow*  
*Special Assistant to the Director*  
Office of the Director  
National Institute of Neurological Disorders and Stroke  
31 Center Drive, Room 8A52  
Bethesda MD 20892-2540  
Email: [mgmott@mail.nih.gov](mailto:mgmott@mail.nih.gov)  
Office Phone: (301) 594-4470  
Cell: (301) 221-(b) (6)



**From:** outside the scope of the request -  
**Sent:** Friday, August 07, 2015 4:39 PM  
**To:** Owens, David (NIH/NINDS) [E]; Owens, David (NIH/NINDS) [E]  
**Cc:** Lavaute, Timothy (NIH/NINDS) [E]  
**Subject:** Re: Summary Statement; outside the scope of

Dr. David Owens  
Division of Extramural Research *NIH/NINDS*  
Dear David

outside the scope of the request - unrelated to the nfl, the Stern grant, SHRP, or CTE





## **Senior Staff Team Meeting**

**August 17, 2015**

### **Agenda**

- 1) Council Agenda – Walter
- 2) CTE grant – Walter
- 3) Supplement Request – Dave Owens
- 4) Changing the Council Closed Session Process – Bob Finkelstein
- 5) Proposing Eliminating the Javits Award to Council – Bob Finkelstein

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** 10 Aug 2015 18:45:28 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Emails 8/10

Hi Walter,

Hope you are enjoying vacation!!

Here are your emails from today:

| Sender                             | Date/time              | Subject                                                                                  | Follow up                                                                                                                                                                                                                                                                                                                   |
|------------------------------------|------------------------|------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Janne Axelsen                      | Mon 8/10/2015 10:02 AM | Invitation for The Brain Prize Dinner during the annual Society for Neuroscience Meeting | The Brain Prize Dinner during the annual Society for Neuroscience Meeting – Oct 19 cocktails start at 7:30, dinner at 8:30 (Note, that is the evening of the diversity neuroscience reception. However, it ends at 8:00pm, so I think you could make the Brain Prize dinner. Do you want to go??? Need to RSVP with Janne)  |
| Sally Rockey                       | Mon 8/10/2015 11:40 AM | Seeking end of year support                                                              | National Academies study on “Strengthening the Disaster Preparedness of Academic Biomedical Research Communities.” We still need to raise ~\$700,000 in order to move forward with the study. If <b>your IC has end-of-year funding to contribute, please let me know by August 12<sup>th</sup></b> (and cc Liza Bundesen). |
| Nora Volkow/Kathy Hudson/Tom Insel | Re: PMI query          | Mon 8/10/2015 4:39 PM                                                                    | ACD wg would recommend launching the cohort before the mechanisms are worked out for including folks from these groups. (Nora and Tom both replied)                                                                                                                                                                         |
| Paul Scott                         | Mon 8/10/2015 1:29 PM  | upcoming Human Fetal Tissue Data Call for DIR                                            | the IC Directors will soon get a request for information about the use of human fetal tissue in intramural laboratories. The intent of this request is to gather information to gain a better understanding of the use of this tissue in the intramural program as                                                          |



|                   |                        |                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                         |
|-------------------|------------------------|-----------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                   |                        |                                                                       | well as respond to IHHS questions.                                                                                                                                                                                                                                                                                                                                                                      |
| Kelly Baker       | Mon 8/10/2015 4:29 PM  | Agenda for the August 18th DER Pre Council Meeting                    | Attached is the agenda for the August 18 <sup>th</sup> Pre Council meeting at 9:00 a.m., NSC/2172. It may still be modified slightly before the meeting.                                                                                                                                                                                                                                                |
| Christine Lam     | Fri 8/7/2015 4:05 PM   | FW: NINDS Support for the FIC Fellows Program                         | Just want to make sure you are ok with funding these two fellows through Fogarty's R25:<br>(b) (4)                                                                                                                                                                                                                                                                                                      |
| Carsten Bonnemann | Mon 8/10/2015 10:40 AM | Re: give a call if have a chance                                      | He is back in the office now, available to talk re: Ms. Tipton.                                                                                                                                                                                                                                                                                                                                         |
| Paula Walker      | Mon 8/10/2015 11:29 AM | Revised Schedule for August 24th Meeting w/Dr. Clinton Wright         |                                                                                                                                                                                                                                                                                                                                                                                                         |
| Claudia Moy       | Mon 8/10/2015 12:36 PM | FW: Visit by Dr. Collins to China in September - Need input by Aug 17 | Dr. Collins will be making a trip to Dalian, China, to attend the World Economic Forum's Annual Meeting of New Champions. Again, as part of this background briefing material he has asked us to provide him with key highlight of your IC's activities with Chinese counterparts, both in the intramural and extramural programs. Please send your input to me by <b><u>COB MONDAY, AUGUST 17.</u></b> |
| Ned Talley        | Mon 8/10/2015 1:32 PM  | FW: BRAIN PPP X02 pre-application                                     | Attached are the FOAs for the BRAIN PPP. We'd like to forward them for review by the Guide first thing next week because of the tight schedule (timeline is at the bottom of the email), and we've proposed sending them to the BRAIN IC Directors after feedback from the CT on Wednesday.                                                                                                             |

|               |                                                                                                    |                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|---------------|----------------------------------------------------------------------------------------------------|------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Janet Wright  | Mon 8/10/2015 9:55 AM                                                                              | NINDS + Million Hearts: key actions by quarter | <p>Sept 9 QLC will focus on the following and we will be back in touch in late August with more detail:</p> <ul style="list-style-type: none"> <li>• Where we are now: Q3 accomplishments (in the format attached); data on heart attack and stroke, ABCS, other</li> <li>• What we can (still) do: examples and tips from agencies about actions feasible to implement in next 16 months</li> <li>• Brief look ahead at 2016: beginning to tell the story of your impact on the people you serve.</li> </ul> |
| Richard Hodes | Tue 6/23/2015 11:49 AM                                                                             | AD funding                                     | We should get together to discuss funding for AD and ADRD in FY16 and FY17. Do you have any time between 1:00 and 3:00 this afternoon? An alternative for me would be 5:30 tomorrow, following Blueprint IC meeting.                                                                                                                                                                                                                                                                                          |
| Neil Shapiro  | Tue 6/23/2015 11:42 AM                                                                             | RE: BRAIN                                      | I'd be happy to go over the House mark for NINDS with your staff and see how it would affect your requests for Alzheimer-related programs.                                                                                                                                                                                                                                                                                                                                                                    |
| Holli Jaffee  | Tue 6/23/2015 6:12 AM                                                                              | RE: (b) (6)                                    | (b) (5)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Neil Shapiro  | RE: Request for Slides: Basic/Translational/Clinical Research Presentations at 6/25/15 ICD Meeting | Tue 6/23/2015 11:17 AM                         | Slides from Neil for the ICD meeting.                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Stephen Korn  | your AUPN talk                                                                                     | Tue 6/23/2015                                  | Your AUPN talk has many slides                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

|                                    |                        |                                                                    |                                                                                                                                                                                                                                          |
|------------------------------------|------------------------|--------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                    |                        | 9:22 AM                                                            | that are duplicates of mine (and my talk). Possible for you to focus on scientific opportunities and needs, leave the funding slides to me? Attached are my slides.<br><i>(I forwarded this to Amy to and OSL is working on them...)</i> |
| Caroline Lewis/Rita Devine         | FW: (b) (6)            | Tue 6/23/2015 4:21 PM                                              | (b) (5)                                                                                                                                                                                                                                  |
| Joanne Katz                        | Tue 6/23/2015 3:39 AM  | WCNR 2016 Invited Speaker Invitation Letter -Walter Koroshetz.docx | Speaker invitation to WCNR 2016 – May 10-13 (this is already on your calendar)                                                                                                                                                           |
| Maria Freire                       | Tue 6/23/2015 8:24 AM  | RE: NFL- FNIH                                                      | Any luck with Betsy? M.                                                                                                                                                                                                                  |
| Betsy Nabel                        | Tue 6/23/2015 1:24 PM  | RE: concussion                                                     | Apparently a Dr. Stern, who may also be with this group, has filed independent testimony in the NFL/Players Association settlement. I hope this group is able to approach their research in an unbiased manner.                          |
| Joanne Pomponio                    | Tue 6/23/2015 11:06 AM | RE: Telework Renewals                                              | Please complete the following trainings: <b>NIH Telework 101 for Employees</b> and <b>NIH Telework 101 for Managers</b> . Please see the attached instructions for accessing the training.                                               |
| The TMJ Association (Terry Cowley) | Tue 6/23/2015 1:24 PM  | Re: Request for Meeting July 1st                                   | attached an electronic copy of the CPRA white paper for your review.                                                                                                                                                                     |
| Leighton Chan                      | Tue 6/23/2015 1:14 PM  | FW: The Konkussion Retreat                                         | Do you know about the Konkussion Retreat in Toronto Sept 25, 2015? Any CNRM representation?                                                                                                                                              |
| Tom Insel/Clare Stroud             | Tue 6/23/2015 2:27 PM  | Re: Informal Meeting Recap - Neuroscience                          | Minutes from IOM meeting. Tom: "Also would be good to capture the Forum's                                                                                                                                                                |

|                               |                        |                                                                                                  |                                                                                                                                                                                                                                                                                               |
|-------------------------------|------------------------|--------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                               |                        | Forum Meeting<br>(June 4-5, 2015)                                                                | endorsement for a coordinating presence (uber-BRAIN) for public and private projects in BRAIN. We will be discussing this later this week with SfN and others, but having IOM Forum verbal (not financial) support may prove helpful."                                                        |
| Khaled Moussawi               | Tue 6/23/2015 6:34 AM  | Re: Neurology Grand Rounds at the Massachusetts General Hospital                                 | Would any of the following dates work for you?<br>-Oct 8 2015<br>-June 30 2016<br>-July 7 2016<br>-July 14 2016<br><i>(I forwarded this to Paula to see if any of those dates work...)</i>                                                                                                    |
| Peter Bridgman                | Tue 6/23/2015 12:24 PM | RE: Stroke intervention initiative?                                                              | I would like to see NINDS, the National Stroke Association, and the American Heart Association/American stroke Association set up a consensus conference to give us some guidelines.                                                                                                          |
| Frances Jensen                | Tue 6/23/2015 10:29 AM | Re: October 30th                                                                                 | (b) (6)                                                                                                                                                                                                                                                                                       |
| Tom Insel/Ned Talley          | Tue 6/23/2015 10:06 AM | Re: Opportunity for BRAIN publicity                                                              | Marian is asking for intramural labs to interview for BRAIN documentary. Dietmar has an award, others are doing highly relevant work. Do you have preferences?                                                                                                                                |
| Natacha Pires                 | Tue 6/23/2015 2:28 PM  | Congratulations; an invitation to join Dysautonomia International's annual conference in July... | <b>I'm writing to extend an invitation to you / your staff to join us next month for Dysautonomia International's third annual Conference &amp; Lobby Day (July 17-20, 2015, at the Hyatt Dulles at Dulles International Airport, Herndon, VA). (You will be in Portland at OHSU then...)</b> |
| Ann Corley<br>{PAINS project} | Tue 6/23/2015 11:04 AM | prep for next week's PAINS meeting in DC                                                         | final agenda, with highlights noted below, including who introduces who. <b>If you are</b>                                                                                                                                                                                                    |

|  |  |  |                                                                                                              |
|--|--|--|--------------------------------------------------------------------------------------------------------------|
|  |  |  | planning to have a slide deck, I would greatly appreciate it if you can send me a copy before Monday morning |
|--|--|--|--------------------------------------------------------------------------------------------------------------|

**From:** Theriault, Elizabeth  
**Sent:** 6 Aug 2015 20:05:52 +0000  
**To:** mark.daley@uwo.ca  
**Cc:** Ravi Menon;Pratik Mukherjee;Anthony Phillips;Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** invitation  
**Attachments:** Draft ToRs WGs InTBIR\_05 08 2015.docx, Draft Agenda TBI Research Meeting Brussels BLUE draft\_20150727d\_clean.docx

Hi Mark

On the recommendation of Dr. Ravi Menon, we would like to invite you to become a member of the Neuroimaging Working Group of the International Initiative for Traumatic Brain Injury Research (InTBIR: <http://intbir.nih.gov>).

InTBIR is a cooperative effort of the European Commission (EC), CIHR and the NIH to coordinate and leverage clinical research activities on TBI research, and was established in 2012. InTBIR's goal is to improve and lessen the global burden of TBI by 2020 through the discovery of causal relationships between treatments and clinically meaningful outcomes. InTBIR seeks to encourage well-designed, hypothesis-driven studies that include the collection of high quality data followed by rigorous statistical analysis.

At our annual meeting, held last year in San Francisco, InTBIR's International Scientific Advisory Board (of which Ravi is a member) and the collective funding agencies made a number of recommendations. In particular, one of these recommendations was the formation of several subcommittees to enhance the mission of InTBIR including WGs for biomarkers, neuroimaging, data sharing and informatics. The Terms of Reference and deliverables for these Working Groups have been drafted and are under review (please see attached draft), but basically the desire is to get them started asap. The data analysis and informatics group has been active for a year already, while the biomarkers and neuroimaging groups are just now forming. Each WG will have members from Canada, the US and the EU.

In preparation for the next InTBIR Meeting, which will be held in Brussels October 13-14, 2015, the Neuroimaging WG, co-led by Dr. Pratik Mukerjee copied above, a couple of teleconferences are being planned. The Working Groups will then meet face to face in Brussels and will have the opportunity to further discuss and present their deliberations. Please see the attached draft Agenda for this meeting. On behalf of Dr. Anthony Phillips, Scientific Director of CIHR's Institute of Neurosciences, Mental Health and Addiction, we would like to invite you to be part of the InTBIR Neuroimaging WG. We hope you will be both interested and available. Please note, for the meeting in Brussels, INMHA will cover your economy airfare, hotel costs and provide a per diem to attend this meeting.

Looking forward to your reply.

Best regards,  
Elizabeth

-----  
Elizabeth Theriault, PhD  
Assistant Scientific Director / Directrice scientifique adjointe

Institute of Neurosciences, Mental Health and Addiction / Institut de neurosciences, de la santé  
mentale et des toxicomanies  
Canadian Institutes of Health Research / Instituts de recherche en santé du Canada  
University of British Columbia  
Djavad Mowafaghian Centre for Brain Health  
Room 3404 - 2215 Westbrook Mall  
Vancouver, B.C. V6T 1Z3  
Phone/Tél.: 604 827-4744  
Fax: 604 822-0361  
E-mail/courriel: [Elizabeth.Theriault@ubc.ca](mailto:Elizabeth.Theriault@ubc.ca)

**Remit & mode of operation InTBIR working groups, context for InTBIR meeting October 13-14, 2015 in Brussels**

**3 working groups on InTBIR relevant focal issues**

**1) Data management, data analysis, clinical endpoints (established already):**

Co-leaders: Steve Wisniewski & Lindsay Wilson

Exemplary issues: CDEs, data management, data sharing, statistical analysis planning, clinical endpoints, regulatory expectations.

**2) Neuroimaging**

Co-leaders: Pratik Mukherjee & Pim Pullens

Exemplary issues: protocols fMRI, calibrating MRI scanners, software.

**3) Fluid Biomarkers**

Co-leaders: Ramon Diaz-Arrastia & Roberto Latini

Exemplary issues: protocols, regulatory standards, variability of results.

**Mission, scope and mode of action:**

- Each WG is focused on pivotal issues of TBI research where cooperation in the InTBIR context can help
- Outcome: suggestions to InTBIR community (PIs and funders) in the form of a thematic "roadmap" as to how to address key issues of common interest in TBI research, as well as proposed guidelines/policies<sup>1</sup> to be implemented within the InTBIR consortium.
- Mode of operation, context 2015 for the InTBIR meeting:

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<sup>1</sup> See as an example the IRDiRC policies and guidelines document available at [http://www.irdirc.org/wp-content/uploads/2013/06/IRDiRC\\_policies\\_24MayApr2013.pdf](http://www.irdirc.org/wp-content/uploads/2013/06/IRDiRC_policies_24MayApr2013.pdf)



- 2 Chairpersons for each working group, one serving as primary contact
- InTBIR funders provide Chairpersons in August 2015 with WG background info and 6-8 names of appropriate/interested PIs from US/EU/CA InTBIR projects
- Chairpersons contact 'their' WG members, provide info and convene preparatory teleconferences around August/Sept 2015, InTBIR members are informed and participate in teleconferences as observers
- Each WG prepares a draft roadmap relevant to the WG's theme highlighting key issues and opportunities in the respective focal area, draft road maps circulated between WGs and InTBIR funders (to avoid overlap and check for congruency), to be presented during Oct meeting day 1 plenary session, input on key issues gathered from plenary (gaps, prioritisation, practical issues, interested players, etc.)
- Each WG meets in separate breakout groups day 2 afternoon after plenary part of Oct meeting, tasks: refine roadmap including new input, elaborate goals and modes of further work, define output goals and milestones for 2016, elaborate specific work targets and modes of further work, establish logistics like mailing lists, logistics support needed, practical issues, meeting/teleconference dates etc., prepare 2 pager summary note for InTBIR records; InTBIR members are invited to participate in breakout groups as observers.
- WGs continue to work through teleconferences/or face2face on occasions of other meetings between annual InTBIR meetings, small minutes to be produced (support from InTBIR members as relevant) and to be circulated with InTBIR funders, Chairpersons in regular contact with InTBIR funders (InTBIR funders nominate contact persons)
- InTBIR funders identify for each WG (an) expertise-wise appropriate and interested contact person(s) from amongst the InTBIR funders, as well as (an) appropriate ISAB member(s) to serve as competent interface with the respective working group

## International Brain Injury Research Meeting

Coventry Building, Brussels, Belgium

14-16-2015

### 08:15 Welcome

*Ruxandra Draghia-Akli, Director, Health Directorate,  
European Commission, DG Research and Innovation*  
*Walter Koroshetz, Director, NIH/NINDS*  
*Anthony Phillips, Scientific Director CIHR-INMHA*  
*Peter Chiarelli, Chief Executive officer OneMind4Research*

### 08:30 InTBIR Annual Meeting: Opening Statements

- Concept of the meeting, ways to work together - Ruxandra Draghia-Akli
- InTBIR new Member: One Mind - Peter Chiarelli
- ISAB recommendations from 2014 meeting - Sam Weiss

### 09:00 Session I: Progress of the InTBIR Projects

- TRACK-TBI – Geoff Manley
- Managing severe TBI without ICP monitoring - guidelines development and testing – Randy Chesnut
- ADAPT – Mike Bell
- CENTER TBI – Andrew Maas
- CReACTIVE – Guido Bertolini
- mTBI in youth ice hockey players – Kathryn Schneider
- Improving the diagnosis and treatment of mTBI in children and youth – Isabelle Gagnon
- Neurocare – Michelle Keightley
- Post-Concussive Syndrome in youth – Karen Barlow
- SP study – Roger Zemek
- TBI Prognosis Study – Alexis Turgeon

### 11:00 Coffee Break

### 11:15 Session II – Working Groups: Priority Goals and Plans

- Data management, Data analysis & Clinical Endpoints - Steve Wisniewski & Lindsay Wilson
- Regulatory view points (FDA, Health Canada, EMA)

### 13:15 Lunch

### 14:00 Session II – continued

- Neuroimaging - Pratik Mukherjee & Pim Pullens
- Fluid Biomarkers - Ramon Diaz-Arrastia & Roberto Latini

### 16:00 Coffee Break

### 16:15 Session III – Safe Common Clinical Data Sharing

- Level(s) of aggregation/anonymization/access – Guido Bertolini
- Methodology panel discussion: Menon, Manley, Hill, Hicks, McAuliffe, Bertolini, Hutchison

### 17:30 Day 1 Meeting Adjourns

Cocktail: One Mind joining InTBIR

### 9:30 Session IV – InTBIR Satellite Projects and, External Cooperation (Invited speakers from outside InTBIR, moderated discussion)

#### Collaboration in data management and analysis

- HBP – Opportunities for Collaborations - Sean Hill

#### Better integration of patient views and priorities

- Patient organization - InTBIR project partner?
- Patients Like Me – Jamie Heywood or Michael Evers

#### Collaboration in clinical endpoint selection

- Presentation on ongoing TED initiative on clinical endpoints (Geoff Manley)

#### Collaboration with other funding agencies

- Presentation of the DoD-funded CARE and CENC projects (Colonel Rasmussen/??/?)

#### Collaboration/alignment/integration of projects/initiatives outside InTBIR

- FIFA studies, NCAA (USA) and CTE (EU, USA)
- Hockey
- ?

### 12:00 Where do we go from here - Final plenary - (moderation by ?)

- Short feedback from the 3 Working Groups
- Observations by the ISAB
- Views and conclusions by InTBIR funders

### 13:00 Lunch

### 14:00 Parallel Meetings:

- InTBIR Members Forum (closed session)
- ISAB Meeting (closed session)
- Followed by a joint meeting of InTBIR funders and ISAB – Progress in InTBIR (closed session)
- 3 Working groups follow-up meetings (closed session)
  - Data management, Data analysis & Clinical Endpoints
  - Neuroimaging
  - Fluid Biomarkers
- Informal Pls Networking (open for invited speakers from outside InTBIR)

### 17:00 Day 2 Meeting Adjourns

**From:** Warren, Margo (NIH/NINDS) [E]  
**Sent:** 6 Aug 2015 11:04:39 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Thomas, Christopher (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: Upcoming BU NFL Player TBI Study

Thanks for the guidance. I will let BU know they can proceed without us. Do you want to take press calls if we get any on this, or will you be away next week?

Margo

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Thursday, August 06, 2015 10:29 AM  
**To:** Thomas, Christopher (NIH/NINDS) [E]; Warren, Margo (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: Upcoming BU NFL Player TBI Study

Dear Chris,

This is pretty small study, small differences, arbitrary cut off at 12 years of age, not clear what their study to study variance is, so could be noise. No control group.  
not sure it's the level for an NINDS quote or press release.  
walter

**From:** Thomas, Christopher (NIH/NINDS) [E]  
**Sent:** Thursday, August 06, 2015 10:10 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Warren, Margo (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Upcoming BU NFL Player TBI Study

Hi Walter,

Attached is a brain imaging study of NFL players conducted by researchers at BU. According to the BU communications office, it should be published early next week. They will send us a copy of their press release soon.

When you get a chance can you please take look at the study? BU might be willing to take a quote from an NIH representative. The study was funded by multiple institutes (NINDS, NIBIB, NCATS, NIA). Would you like NINDS to be represented with a quote in the BU release?

Thanks,

Chris

---

**From:** Stern, Robert A <[bobstern@bu.edu](mailto:bobstern@bu.edu)>  
**Sent:** Tuesday, July 28, 2015 12:26 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Re: CTE U01

Harmonizing/integrating across all the exciting current studies will be really critical. Re: NCAA study, that's why I included Brian Hainline and Tom McAllister in our Advisory Board, not to mention Mike Weiner, Art Toga, and Bruce Miller, to harmonize with other major studies.

Bob

On Jul 28, 2015, at 12:12 PM, Koroshetz, Walter (NIH/NINDS) [E] <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)> wrote:

thanks would be interesting. Ncaa study pondering the follow up issue as well.  
W

Sent from my iPhone

On Jul 28, 2015, at 11:50 AM, Stern, Robert A <[bobstern@bu.edu](mailto:bobstern@bu.edu)> wrote:

Phew! Our proposal does include the three-year follow-up for the control group, with the full in-person evaluation. The group that is not seen for the 3-year f/u is the former college football player group. That decision was based on two reasons: (1) the primary purpose of including them was for evaluation of risk determination (i.e., lower exposure to repetitive hits than the NFL group), so that could be determining through the cross-sectional baseline; and (2) budget issues...the cost of bringing them back in for the 3-yr f/u was too expensive, so I was planning on submitting a subsequent grant that would support them coming in. With that said, I would be delighted to include a telephone assessment of the former college players. We could also put in an annual telephone assessment (or web assessment, using some of the instruments currently being used in Mike Weiner's Brain Health Registry) for the entire cohort so we add to the longitudinal data. That would not take much additional work and could be done centrally.

Bob

**From:** Koroshetz, Walter (NIH/NINDS) [E] [<mailto:koroshetzw@ninds.nih.gov>]  
**Sent:** Tuesday, July 28, 2015 11:43 AM  
**To:** Stern, Robert A <[bobstern@bu.edu](mailto:bobstern@bu.edu)>  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E] <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Subject:** Re: CTE U01

We definitely need more money if going to fund two. What we do depends on how much more I can convince Council to put out. If zero then we are not going to be able to do two. Proposal will be to double the funding to do two.

Also think you should think about collecting some longitudinal data from your "control" group as a comparison- maybe put into the study a telephone assessment, computer assisted testing? ??

Walter

**From:** Bob Stern <[bobstern@bu.edu](mailto:bobstern@bu.edu)>  
**Date:** Tuesday, July 28, 2015 at 11:25 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Subject:** RE: CTE U01

Thanks. Much clearer. One important question that I know you cannot completely answer at this time but here it goes: Is the concept to split the available money in half (or some other fraction), similar to Ann and Wayne, such that our project's budget would be substantially reduced? Or, are there additional funds being made available to allow for an additional group/study but without substantial cuts?

Bob

**From:** Koroshetz, Walter (NIH/NINDS) [E] [<mailto:koroshetzw@ninds.nih.gov>]  
**Sent:** Tuesday, July 28, 2015 11:03 AM  
**To:** Stern, Robert A <[bobstern@bu.edu](mailto:bobstern@bu.edu)>  
**Subject:** Re: CTE U01

Sorry may not have been clear. Proposal would be to fund two groups, and integrate the two studies. Kind of like we did with Ann and Wayne. Might put in oversight group giving advice to investigators and to NINDS.

NIH can't talk about grants that are not funded so that's why can't get into it til know whether there will be another group.

Walter

**From:** Bob Stern <[bobstern@bu.edu](mailto:bobstern@bu.edu)>  
**Date:** Tuesday, July 28, 2015 at 10:02 AM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Cc:** Patrick Bellgowan <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Subject:** RE: CTE U01

Thanks very much, Walter. I really appreciate your response. It would be really helpful to have some type of glimpse into what is being planned (with full understanding that things are still being worked out) if for no other reason than to avoid my embarrassment and awkwardness when someone tells me about other sites/investigators getting involved and I have no idea. Also, as you can imagine, with three other mPIs, multiple subcontract PIs, and ~50 co-investigators, all anxiously awaiting some news (since they all know that Council approved it a couple months ago), I would love to be able to have a better sense of why there has been a delay. Again, I know nothing is written in stone at this point and there is need for lots of discussion and planning. I would just really appreciate an informal, confidential discussion about what some of the thoughts and options are. Please let me know if you would be okay with a phone call. Thanks again.

Bob

**From:** Koroshetz, Walter (NIH/NINDS) [E] [<mailto:koroshetzw@ninds.nih.gov>]  
**Sent:** Tuesday, July 28, 2015 9:21 AM  
**To:** Stern, Robert A <[bobstern@bu.edu](mailto:bobstern@bu.edu)>

**Cc:** Bellgowan, Patrick (NIH/NINDS) [E] <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Subject:** Re: CTE U01

We are committed to funding the project. Once we see how things settle out Pat and I will sit down with all the players and get into the weeds to make sure we reach our goal of nailing down the diagnostic criteria-- clinical, imaging, other biomarkers. Similar to what we did with Ann and Wayne.

At that point we may ask you to make some changes to your original plan. Not worth talking about it now without knowing the scope of what we will fund.

Best

Walter

**From:** "bobstern@bu.edu" <[bobstern@bu.edu](mailto:bobstern@bu.edu)>  
**Date:** Monday, July 27, 2015 at 1:45 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Cc:** Patrick Bellgowan <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Subject:** Re: CTE U01

Is the originally approved project funding at all in jeopardy or questionable at this time? Or is just the expansion questionable?

Bob

On Jul 27, 2015, at 1:41 PM, Koroshetz, Walter (NIH/NINDS) [E] <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)> wrote:

Thanks Bob. Not much to say at this point. Am planning to go to sept Council with a plan to expand the study but have no idea how it will turn out.  
Council is Sept 8,9. Will get on the phone soon afterwards.

Best,

Walter

**From:** "bobstern@bu.edu" <[bobstern@bu.edu](mailto:bobstern@bu.edu)>  
**Date:** Monday, July 27, 2015 at 12:26 PM  
**To:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>, Patrick Bellgowan <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>  
**Subject:** CTE U01

Hi Walter and Pat,  
I apologize for yet another inquiry into the status of the U01 and timing of the NoGA. The last I had heard from Pat (10 days ago) was that it would take at least a few more weeks, so I was going to just wait until I hear something from you. However, I am writing now because since that time I have been hearing through the "grapevine" some unclear, unspecified talk about expanding the project to include other sites and investigators. Is there anything I should know as things move forward?

Should we have a phone call to clarify what may or may not be going on.  
I look forward to hearing from you.

Regards,

Bob

Robert A. Stern, Ph.D.  
Professor of Neurology, Neurosurgery, and Anatomy & Neurobiology  
Director, Clinical Core, BU Alzheimer's Disease and CTE Center  
Boston University School of Medicine

72 East Concord Street, Robinson 7800  
Boston, MA 02118

tel: 617-638-5678  
fax: 617-638-5679  
email: [bobstern@bu.edu](mailto:bobstern@bu.edu)

[www.bu.edu/alzresearch](http://www.bu.edu/alzresearch)

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** 9 Jul 2015 13:35:54 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** FW: Interview Request\_YoungStroke for WHUR Radio

Walter,

It took some digging, but I think this radio show is pretty legit and reaches a diverse local DC audience.

Darryl's show is featured on **WHUR 96.3 Radio station** – from Howard University, so it is local and the broadcast reaches from north of Baltimore to Richmond, VA. WHUR is a previous award recipient for *Best Urban Station of the Year*.

(more info: <http://www.whur.com/about-whur/>)

Darryl likes to tie in nutrition and exercise with most of his podcasts. He's interested in disease causes & prevention.

For example, he has interviewed stroke docs before for DC Stroke Awareness day. In July 2012, he interviewed Amie Hsia (Med Director at MedStar Stroke Center) as his special guest.  
[http://www.darrylhaleybnb.com/fitnessfriday\\_audiolibrary.php](http://www.darrylhaleybnb.com/fitnessfriday_audiolibrary.php) -- click #2 at the bottom of the page to see list of interviews with Amy (Part 2 and Part 3 are relevant).

Up to you, but I do think this would be worth doing. I think you would want to talk about stroke over all and give a plug for stroke in young adults as well. Does seem like a good opportunity.

Thanks,  
Meghan

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** Wednesday, July 08, 2015 2:19 PM  
**To:** Mott, Meghan (NIH/OD) [E]  
**Subject:** RE: Interview Request\_YoungStroke for WHUR Radio

Thanks, Meghan. Assuming that Walter wants to do the interview, I'll follow up with Amy and get information about the request, and also get the clearances going.  
Marian

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** Wednesday, July 08, 2015 2:03 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** Interview Request\_YoungStroke for WHUR Radio



## Cornell, Susan (NIH/OD) [E]

---

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Friday, July 10, 2015 8:20 AM  
**To:** Elizabeth Nabel  
**Cc:** Freire, Maria (FNIH) [T]  
**Subject:** CTE study

Dear Betsy,  
Spoke with Maria (now in Peru). Any time for a chat this afternoon, evening or weekend?  
My cell is 617 256 (b) (6) home is 240 499 (b) (6) Cell service spotty at home.  
Also see below info on COI rules for review panels.  
Best wishes,

Walter

--

Walter J. Koroshetz, M.D.

Acting Director

National Institute of Neurological Disorders and Stroke

National Institutes of Health

Rm 8A52, Bldg 31, 31 Center Drive

Bethesda, Md, 20892

Tel 301 496 3167

Fax 301 496 0296



Dear Betsy: here is some relevant policy information about COI in peer review taken from the NIH Grants Policy :

Note question 4, which covers all 4 of the review articles co-authored by individual study section members and Drs. McKee or Cantu. Worth reiterating that no study section members have ever co-authored a paper with Dr. Stern.

#### **4. Which relationships do NOT constitute a conflict?**

- Provision of resources or services that are freely available to the entire scientific community
- Co-authorship of a review article, position paper, professional group or conference report
- Data donations to a central repository or consortium
- Institutional membership in a multicenter network unrelated to the application under review

Bottom line from info I have at this point: "Based on co-authorships and NIH definition of COI, there are zero conflicts of interest between the members of the peer review panel and the investigators on the MPI grant from Stern, Cummings, Reiman and Shenton".

Marian -- FYI

**From:** amy.edmunds@youngstroke.org [mailto:amy.edmunds@youngstroke.org]  
**Sent:** Wednesday, July 08, 2015 11:13 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Interview Request\_YoungStroke for WHUR Radio

Good morning, Walter -

May you have availability anytime during the week of September 20 to tape a radio interview with Darryl Haley? He is a former NFL player who now hosts the FITNESS FRIDAY event on the national mall. This interview would provide a prime opportunity to raise awareness about the issue of stroke among young adults as well as to highlight innovations in stroke care supported by NINDS.

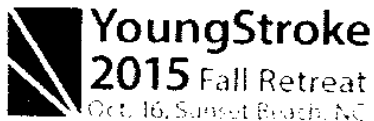
At your convenience, Darryl would come to your office for the taping. Please advise of your interest and availability.

Thanks for your consideration,  
Amy



**Amy L. Edmunds**

Founder & CEO, YoungStroke, Inc.  
843.655.2835 Skype: youngstroke  
[amy.edmunds@youngstroke.org](mailto:amy.edmunds@youngstroke.org)



**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 8 Jul 2015 18:20:29 +0000  
**To:** Walker, Paula (NIH/NINDS) [E]  
**Subject:** FW: Interview Request\_YoungStroke for WHUR Radio

Here is the background.  
Marian

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** Wednesday, July 08, 2015 2:03 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** PRIORITY ACTION: Interview Request\_YoungStroke for WHUR Radio

Marian -- FYI

**From:** amy.edmunds@youngstroke.org [<mailto:amy.edmunds@youngstroke.org>]  
**Sent:** Wednesday, July 08, 2015 11:13 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Interview Request\_YoungStroke for WHUR Radio

Good morning, Walter -

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At your convenience, Darryl would come to your office for the taping. Please advise of your interest and availability.

Thanks for your consideration,  
Amy



**Amy L. Edmunds**  
Founder & CEO, YoungStroke, Inc.

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 8 Jul 2015 18:24:08 +0000  
**To:** 'amy.edmunds@youngstroke.org'  
**Bcc:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** FW: Interview Request\_YoungStroke for WHUR Radio

Hi, Amy. What a nice opportunity! Thanks for including NINDS.  
Is Darryl working on a program that Young Stroke is producing? If not, could you write to him and send him my contact information so that my team can make the necessary arrangements for the interview. To help simplify the process, I can tell you that Dr. Koroshetz would be happy to do the interview and that he is currently available on September 23<sup>rd</sup> anytime between 10 am and 3 pm.

Cheers,  
Marian

*Marian Emr  
Director, Office of Communications and Public Liaison/NINDS  
NIH Building 31, Room 8A07  
Phone: (301) 496-5924  
[marian.emr@nih.gov](mailto:marian.emr@nih.gov)*

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** Wednesday, July 08, 2015 2:03 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** Interview Request\_YoungStroke for WHUR Radio

Marian -- FYI

**From:** amy.edmunds@youngstroke.org [<mailto:amy.edmunds@youngstroke.org>]  
**Sent:** Wednesday, July 08, 2015 11:13 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Interview Request\_YoungStroke for WHUR Radio

Good morning, Walter -

May you have availability anytime during the week of September 20 to tape a radio interview with Darryl Haley? He is a former NFL player who now hosts the FITNESS FRIDAY event on the national mall. This interview would provide a prime opportunity to raise awareness about the issue of stroke among young adults as well as to highlight innovations in stroke care supported by NINDS.

At your convenience, Darryl would come to your office for the taping. Please advise of your interest and availability.

Thanks for your consideration,  
Amy

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 8 Jul 2015 18:25:51 +0000  
**To:** Warren, Margo (NIH/NINDS) [E]  
**Bcc:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** FW: Interview Request\_YoungStroke for WHUR Radio

Please send this one through clearance. I've written to Amy to get additional information and will coordinate with Walter et al. ....but I need help with clearance.

Thanks.  
Marian

**From:** amy.edmunds@youngstroke.org [mailto:[amy.edmunds@youngstroke.org](mailto:amy.edmunds@youngstroke.org)]  
**Sent:** Wednesday, July 08, 2015 11:13 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Interview Request\_YoungStroke for WHUR Radio

Good morning, Walter -

May you have availability anytime during the week of September 20 to tape a radio interview with Darryl Haley? He is a former NFL player who now hosts the FITNESS FRIDAY event on the national mall. This interview would provide a prime opportunity to raise awareness about the issue of stroke among young adults as well as to highlight innovations in stroke care supported by NINDS.

At your convenience, Darryl would come to your office for the taping. Please advise of your interest and availability.

Thanks for your consideration,  
Amy



**Amy L. Edmunds**

Founder & CEO, YoungStroke, Inc.  
843.655.2835 Skype: youngstroke  
[amy.edmunds@youngstroke.org](mailto:amy.edmunds@youngstroke.org)



---

**From:** Muroff, Julie (NIH/OD) [E]  
**Sent:** Tuesday, June 30, 2015 3:33 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** (b) (5)

Hello, Dr. Koroshetz-

(b) (5)

(b) (5)

Please let me know how

best to proceed with scheduling. Thank you, Julie

Julie A. Muroff, J.D., LL.M.

Senior Attorney

His Office of the General Counsel, PHD, NIH Branch

31 Center Drive, Bldg. 31, Rm. 2B-47

Bethesda, MD 20892

301-451-4710 (direct)

301-462-1934 (fax)

Julie.Muroff@nih.gov

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such information.*

## Cornell, Susan (NIH/OD) [E]

---

**From:** Gray, Felicia (FNIH) [T]  
**Sent:** Monday, June 29, 2015 9:42 AM  
**To:** Wolf-Rodda, Julie (FNIH) [T]; Freire, Maria (FNIH) [T]; James, Stephanie (FNIH) [T]; Miller, Jeff (Jeff.Miller@NFL.com) (Jeff.Miller@NFL.com); Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: Call this week

Here is the dial in information for today's call at 10:30am:

Dial in: 866-316 (b) (6)  
Passcode: (b) (6)  
Moderator: (b) (6) (JWR will be the moderator)

Mr. Miller, please feel free to forward dial-in information to other participants.

Thank you,  
Felicia

-----Original Message-----

**From:** Freire, Maria (FNIH) [T]  
**Sent:** Monday, June 29, 2015 9:34 AM  
**To:** Miller, Jeff  
**Cc:** Felicia Gray; Wolf-Rodda, Julie (FNIH) [T]; Koroshetz, Walter (NIH/NINDS) [E]; James, Stephanie (FNIH) [T]  
**Subject:** Re: Call this week

Yes, we will. You will get it shortly.

Original Message  
**From:** Miller, Jeff  
**Sent:** Monday, June 29, 2015 9:31 AM  
**To:** Freire, Maria (FNIH) [T]  
**Subject:** RE: Call this week

Maria,  
Thanks again for the time last week.  
One logistical question for the call this morning: is someone sending around a call in number? thanks

-----Original Message-----  
**From:** Freire, Maria (FNIH) [T] [mailto:freirem@od.nih.gov]  
**Sent:** Saturday, June 27, 2015 9:38 PM  
**To:** Miller, Jeff  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** Re: Call this week

Good evening. As you know from Russ' e-mail, Walter can do a call at 10:30 on Monday.  
Maria



Original Message

From: Miller, Jeff

Sent: Saturday, June 27, 2015 12:32 PM

To: Freire, Maria (FNIH) [T]

Subject: Call this week

Good afternoon -

Thank you again for the time yesterday afternoon. Following up on the call, we'd like to accept the offer to have members of our head neck and spine committee speak with Dr. Koroshetz. Monday afternoon works best and keeps, I believe, with your hope to schedule this discussion quickly.

Please let me know.

Jeff

## Cornell, Susan (NIH/OD) [E]

---

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Friday, June 26, 2015 8:17 AM  
**To:** Freire, Maria (FNIH) [T]  
**Subject:** Re: NFL- FNIH

Sure. Just emphasize that this is a cooperative agreement with NIH oversight and it is multi center with four principle investigators, so not a one man show.

Former NFL players will be a major focus and enrolled in Cleveland, NYC, Phoenix as well as Boston. NFL help in recruiting subjects would be appreciated.

Betsy had concerns about review. I have asked our program directors to look into this quickly. They tell me that following standard operating procedures, there were certain people on the panel that were recused from discussing this grant due to conflicts. Program did think there was a high level of integrity in the review process.

The real take home point is that this study will in all likelihood set the standard for diagnosis of CTE in living people with NFL level exposures. And of course NIH is going to fund it with or without NFL support. So in fact it is high risk for NFL to drop out.

Trying to think of compromise and.... one thought is expansion of the study with say double the number of sites, subjects, and PIs so that the Boston site which the NFL fears doesn't dominate? They also cut their follow up of the control collegiate group due to budget constraints which I don't like and would like to fund if had the money.

The other point to make is that the study generates a lot of objective data that will go into FITBIR for data sharing. The imaging, blood, CSF samples and imaging will be available for others to verify the findings. In my mind it's the tau PET imaging that breaks the field open if it works in CTE. That is objective data not so easily subject to bias.

Walter

Sent from my iPhone

> On Jun 26, 2015, at 7:45 AM, Freire, Maria (FNIH) [T] <freiremc@od.nih.gov> wrote:

>

> Walter, Stephanie and I think it might be good to find out what they want and offer a follow up with you. Does that work? M.

>

> Original Message

> From: Koroshetz, Walter (NIH/NINDS) [E]

> Sent: Thursday, June 25, 2015 8:59 PM

> To: Freire, Maria (FNIH) [T]

> Subject: RE: NFL- FNIH

>

>

> Dear Maria,

> Very complicated business. I would recommend that we offer to set up a call with the NFL designates and the four Principal Investigators of the research grant. I spoke with the contact PI on the grant and he was fine with going ahead with that. This would put research plan on the table to inform the NFL's team.

>

> Besides Stern who is the main PI, the other PIs are Martha Shenton at the Brigham, Jeffrey Cummings at Cleveland Clinic, Eric Reiman at Banner Health research Phoenix. In addition to Boston, Phoenix and Cleveland subjects will also be seen at NYU. Imaging goes to Washington U in St Louis. Spinal fluid analyzed at U of Washington. Blood analyzed at VA Puget Sound and U of Washington. So it is truly multicenter and not a one man show.

>

> I am back but go to another BRIAN meeting in Chicago tomorrow. I could call in from Chicago tomorrow at 3 PM if you wish.

>

> Thoughts?

>

> Walter

>

> -----Original Message-----

> From: Freire, Maria (FNIH) [T]

> Sent: Tuesday, June 23, 2015 8:24 AM

> To: Koroshetz, Walter (NIH/NINDS) [E]

> Subject: RE: NFL- FNIH

>

> Hi, Walter. Any luck with Betsy? M.

>

> -----Original Message-----

> From: Koroshetz, Walter (NIH/NINDS) [E]

> Sent: Friday, June 19, 2015 10:47 AM

> To: Freire, Maria (FNIH) [T]

> Subject: Re: NFL- FNIH

>

> yes, will see if Betsy can help.

> Walter

>

> Sent from my iPhone

>

>> On Jun 19, 2015, at 9:48 PM, Freire, Maria (FNIH) [T] <freiremc@od.nih.gov> wrote:

>>

>> It may be wise, since you have already spoken to Betsy, to go back to her to help clear the waters. Please note, we do not have the funds at FNIH, we were preparing to request year 1 funds from NFL, per your budget, when this came up. This is SOP. In our opinion it is unwise to make the funding commitment until this is resolved.

>>

>> Original Message

>> From: Bellgowan, Patrick (NIH/NINDS) [E]

>> Sent: Friday, June 19, 2015 9:25 AM

>> To: James, Stephanie (FNIH) [T]; Koroshetz, Walter (NIH/NINDS) [E]

>> Cc: Wolf-Rodda, Julie (FNIH) [T]; Freire, Maria (FNIH) [T]

>> Subject: RE: NFL- FNIH

>>

>> Walter,

>>

>> We are planning on finalizing the Milestones next week. I presume we should continue to get the NOA out assume the NFL will provide the funds.

>>

>> Pat

>>

>>

>> \_\_\_\_\_

>> From: James, Stephanie (FNIH) [T]  
 >> Sent: Friday, June 19, 2015 8:55 AM  
 >> To: Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS)  
 >> [E]  
 >> Cc: Wolf-Rodda, Julie (FNIH) [T]; Freire, Maria (FNIH) [T]  
 >> Subject: RE: NFL- FNIH

>>

>> Hi, Walter. We think FNIH just needs to point out that while, under the terms of our agreement, NFL cannot influence NINDS's decision on the award, there is a chance they might say they don't want their funding used under these circumstances. I don't know how they heard about the prospective grantee before we did, but if there is any way to ease their concerns now, before they have more time to stew, I suspect it would be advisable.

>>

>> FNIH is ready to help in any way we can.

>>

>> Best, Stephanie

>>

>> Stephanie James, Ph.D.  
 >> Director, Science Division

>> \_\_\_\_\_

>>

>> Foundation for the National Institutes of Health

>>

>>

>>

>> -----Original Message-----

>> From: Koroshetz, Walter (NIH/NINDS) [E]  
 >> Sent: Thursday, June 18, 2015 10:24 PM  
 >> To: James, Stephanie (FNIH) [T]; Bellgowan, Patrick (NIH/NINDS) [E]  
 >> Cc: Wolf-Rodda, Julie (FNIH) [T]  
 >> Subject: Re: NFL- FNIH

>>

>> Legally can't talk til NGA goes out.

>> Walter

>>

>>

>> Walter J. Koroshetz, M.D.  
 >> Acting Director  
 >> National Institute of Neurological Disorders and Stroke National  
 >> Institutes of Health Rm 8A52, Bldg 31, 31 Center Drive Bethesda, Md,  
 >> 20892 Tel 301 496 3167 Fax 301 496 0296

>>

>>

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>>

>>

>>

>>

>>> On 6/17/15, 1:58 PM, "James, Stephanie (FNIH) [T]" <sjames@fnihi.org> wrote:

>>>

>>> These are all good points, Pat, and I was thinking the same thing

>>> given the long list of collaborators you mentioned on the call yesterday.

>>> Sounds like we need to organize a call with NFL to explain this directly.  
>>> At what point in the process would NINDS be comfortable with such a call?  
>>>  
>>> Stephanie James, Ph.D.  
>>> Director, Science Division  
>>> \_\_\_\_\_  
>>>  
>>> Foundation for the National Institutes of Health  
>>>  
>>>  
>>>  
>>>  
>>> -----Original Message-----  
>>> From: Bellgowan, Patrick (NIH/NINDS) [E]  
>>> Sent: Wednesday, June 17, 2015 2:52 PM  
>>> To: James, Stephanie (FNIH) [T]; Koroshetz, Walter (NIH/NINDS) [E]  
>>> Cc: Wolf-Rodda, Julie (FNIH) [T]  
>>> Subject: RE: NFL- FNIH  
>>>  
>>> I think the large group of multi-site collaborators, the diverse  
>>> steering committee and overall NIH peer-review process can help to  
>>> address their concerns. The U01 mechanism at NIH is a cooperative  
>>> program where NIH program officials have substantial programmatic  
>>> input. Plus, their advisory board includes COL Hack, Thomas  
>>> McAllister, Art Toga, Brian Hainline (NCAA) and Michael Haynes (NFL  
>>> advisor) which is a list of persons with varying perspectives and interests in this topic.  
>>>  
>>> The Key Personnel include investigators from the following:  
>>>  
>>> Boston University School of Medicine and School of Public Health €  
>>> Brigham and Women's Hospital, Harvard Medical School € Cleveland  
>>> Clinic Lou Ruvo Center for Brain Health € Mayo Clinic Arizona and  
>>> Banner Alzheimer's Institute € NYU Langone Medical Center and New  
>>> York University School of Medicine € VA Puget Sound and University  
>>> of Washington € Molecular NeuroImaging € Neuroinformatics Research  
>>> Group and Central Neuroimaging Data Archive (CNDA) at Washington  
>>> University School of Medicine  
>>>  
>>>  
>>>  
>>>  
>>> Patrick SF Bellgowan, PhD  
>>> Program Director, Repair and Plasticity NIH/NINDS  
>>> 301-496-1447  
>>> psfb@mail.nih.gov  
>>>  
>>> <http://www.ninds.nih.gov/disorders/tbi/tbi.htm>  
>>>  
>>>  
>>> -----Original Message-----  
>>> From: James, Stephanie (FNIH) [T]  
>>> Sent: Wednesday, June 17, 2015 2:00 PM

>>> To: Bellgowan, Patrick (NIH/NINDS) [E]  
>>> Cc: Wolf-Rodda, Julie (FNIH) [T]  
>>> Subject: FW: NFL- FNIH  
>>>  
>>> Pat, I don't know when Walter will see this email below so thought  
>>> you had better be copied on it as well. Feel free to call if you  
>>> want to talk about this.  
>>>  
>>> Stephanie James, Ph.D.  
>>> Director, Science Division  
>>> \_\_\_\_\_  
>>>  
>>> Foundation for the National Institutes of Health  
>>>  
>>>  
>>>  
>>>  
>>> -----Original Message-----  
>>> From: Freire, Maria (FNIH) [T]  
>>> Sent: Wednesday, June 17, 2015 1:35 PM  
>>> To: Koroshetz, Walter (NIH/NINDS) [E]  
>>> Cc: James, Stephanie (FNIH) [T]; Wolf-Rodda, Julie (FNIH) [T]  
>>> Subject: FW: NFL- FNIH  
>>>  
>>> Hi, Walter. I hope you are well and enjoying your new role -  
>>> congratulations again!  
>>>  
>>> I am jumping the gun here because Stephanie and Julie are out at  
>>> meetings but I wanted to alert you to Elliot's note below. Could we  
>>> circle back on this once I speak to my folks, please?  
>>>  
>>> Best, M.  
>>>  
>>> -----Original Message-----  
>>> From: Elliot Pellman, M.D. [mailto:EPellman@ProHEALTHcare.com]  
>>> Sent: Wednesday, June 17, 2015 1:03 PM  
>>> To: Freire, Maria (FNIH) [T]  
>>> Subject: NFL- FNIH  
>>>  
>>> Maria, hope all is well. I am currently traveling (now in Florence,  
>>> Italy) hence the reason I'm emailing you instead of calling. I  
>>> received some information that Walter and the NINDS is close to  
>>> signing off on awarding Boston University the monies for the third  
>>> and final stage of the NFL grant for the longitudinal study. There  
>>> are many of us who have significant concerns re BU and their ability  
>>> to be unbiased and collaborative. Betsy Nabel (now NFL Chief Medical  
>>> Officer), Richard Ellenbogen, Russell Lonser and others are included  
>>> in that concerned group. I return to NY on June and was wondering if  
>>> Betsy, Jeff Miller and I (possibly Rich Ellenbogen as well) could  
>>> schedule a teleconference with you to discuss. Meanwhile I'm hoping  
>>> that you could communicate our concerns and slow down the process  
>>> until we all have a chance to speak to figure this out.

>>>

>>> Thank you.

>>>

>>> Elliot

>>> .....

>>> Elliot J Pellman MD

>>>

>>>

>>>

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>>

## Cornell, Susan (NIH/OD) [E]

---

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Thursday, June 25, 2015 9:09 PM  
**To:** Freire, Maria (FNIH) [T]  
**Subject:** FW: concussion

What I sent to Betsy.  
w

---

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Thursday, June 25, 2015 9:08 PM  
**To:** 'Nabel, Elizabeth G.,M.D.'  
**Subject:** RE: concussion

Dear Betsey,

NINDS can certainly try to enforce strict objectivity in the study and work the group dynamic as there are four Principal investigators. One is Martha Shenton at the Brigham, the others include a very experienced sports concussion investigator, Jeffrey Cummings at Cleveland Clinic, and Eric Reiman at Banner Health Phoenix/Mayo Phoenix. NYU is also a clinical site, with Laura Balcer as site PI. So it is a multi-site study,

I would suggest a meeting—either face to face or teleconference with all the PIs informing you and your medical team about the study, discuss scientific concerns. Go from there?

Thoughts?

Walter

---

**From:** Nabel, Elizabeth G.,M.D. [<mailto:ENABEL@PARTNERS.ORG>]  
**Sent:** Tuesday, June 23, 2015 1:24 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: concussion

Thanks Walter.

Apparently a Dr. Stern, who may also be with this group, has filed independent testimony in the NFL/Players Association settlement. I hope this group is able to approach their research in an unbiased manner.

Safe travels and talk with you soon,  
Betsy

---

**From:** Koroshetz, Walter (NIH/NINDS) [E] [<mailto:koroshetzw@ninds.nih.gov>]  
**Sent:** Monday, June 22, 2015 5:56 PM  
**To:** Nabel, Elizabeth G.,M.D.  
**Subject:** Re: concussion

Thanks Betsy. Am in China at BRAIN initiative meeting. Will talk to review folks when I get get back.



Best wishes,  
Walter

Sent from my iPhone

On Jun 23, 2015, at 3:39 AM, Nabel, Elizabeth G.,M.D. <[ENABEL@PARTNERS.ORG](mailto:ENABEL@PARTNERS.ORG)> wrote:

Hi Walter,

Great to hear from you – I was away as well, in Ireland.

I've attached a pdf that I received through the NFL that may have come from one of the grant applicants. I am taking a neutral stance here, but I believe the concern is that members of the study section had published within the past two years with Dr. McKee or Dr. Cantu, who the grant applicant believes will receive the NOGA.

Obviously my goal is to make sure the science goes forward.

Safe travels and take care,  
Betsy

---

**From:** Koroshetz, Walter (NIH/NINDS) [E] [<mailto:koroshetzw@ninds.nih.gov>]  
**Sent:** Thursday, June 18, 2015 11:15 PM  
**To:** Nabel, Elizabeth G.,M.D.  
**Subject:** Re: concussion

Dear Betsy,

Got message from fNIH that NFL questioning NIH funding decision of the longitudinal study and asking fNIH to slow down the process. So legally I don't think NIH can talk about a study til NGA is out. And as you know we can't allow outside parties to influence NIH funding decisions, which we made clear to NFL going in.

I am certain that the study will be high level science and unbiased. It is a cooperative agreement so NINDS sets milestones and are involved in oversight.

I understand very well the emotion around this and the complicated history. We would be happy to sit down with you, go through the study in detail and get your input once public.

Sorry to get you into the middle of this but you're the perfect position to ensure that the science advances.

Will be happy to allay concerns with NFL folks when we can publicly discuss.

Sound OK?

Again, apologize for the upset.

Best wishes,

Walter

N.B. Am in China at BRAIN initiative meetings. Back next Wednesday.

Walter J. Koroshetz,M.D.  
Acting Director  
National Institute of Neurological Disorders and Stroke  
National Institutes of Health  
Rm 8A52, Bldg 31, 31 Center Drive  
Bethesda, Md, 20892  
Tel 301 496 3167  
Fax 301 496 0296

<image001.png>

**From:** <Koroshetz>, Walter Koroshetz <koroshetzw@ninds.nih.gov>

**Date:** Wednesday, June 17, 2015 at 10:30 PM

**To:** "Nabel, Elizabeth G.,M.D." <ENABEL@PARTNERS.ORG>

**Subject:** FW: concussion

Dear Betsy

Good talking today.

Points we discussed:

- 1) Yes the longitudinal trial that will launch soon is very multi center. Will get you details as soon as NGA is out. Also may know that at BWH Martha Shenton is tied in to most of our activities.
- 2) I attached the concepts floated to NFL in 2012.
- 3) The widest gap is lack of info to inform parents about risk/benefit of kids playing contact sports. Modifying the NCAA study for high schools and leveraging the ABCD study to a cohort enriched in those with concussion are attractive to think about now. Some Pis have done studies in high school but tend to be small. Like we have with the other NFL projects would think about a workshop to get at details of what are the most important questions, what is feasible to collect (ie. Grades) who the partners could be, etc. There are two groups interested in starting studies. I attached their proposals which have come in.
- 4) My opinion is that we need the answers coming out of path/neuroimaging/clinical data from the two NFL funded studies to inform what to look for in a study of asymptomatic players. Without some bio marker, diagnostic, or even a clear definition of the clinical syndrome might be hard to learn anything and would be expensive. That being said the emergence of tau PET imaging could put the pressure on for serial scanning even before we know what it means. In addition there may be reason to fund a study to follow an asymptomatic cohort like the NCAA athletes with concussion and their age matched controls so we don't lose them, as it will be important to know over time if they ever have any long term effects.
- 5) The AAN meeting on sports concussion (agenda attached) is probably going to be mixed in terms of quality of science. Target is practitioners. I don't know every but some are quite good. If go might want to sit down with Steve Broglio who is a leader of the NCAA study, Dawn Comstock who has concentrated on studies in high school students. Sam Gandy and Steve DeKosky are high level. Barry Jordan has specialized in taking care of boxers and for decades so has interesting though mostly non published insights. The organizers are long term investigators in sports concussion.

Will follow up.

Best,

Walter

Walter J. Koroshetz, M.D.  
Acting Director  
National Institute of Neurological Disorders and Stroke  
National Institutes of Health  
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Bethesda, Md, 20892  
Tel 301 496 3167  
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<7CE89468-17C0-4BD3-9774-F13519A4382F[18].png>

<Draft NIH NFL NFLPA partnership concept.doc>

<Attachment.pdf>

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## Cornell, Susan (NIH/OD) [E]

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**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Thursday, June 18, 2015 10:34 PM  
**To:** Freire, Maria (FNIH) [T]  
**Subject:** Re: NFL- FNIH

Yes we knew this was coming. Lot of history here. But our process was not tainted and all above board. The grant will go to a multisite group around the country. NINDS will manage it. The data will be believable and unbiased. Trouble is of course is that the group is led by the people who first broke the science open and NFL owners and leadership think of them as the creators of the problem. I think we need to go to Betsy Nabel first and get her on board (Betsy is their chief medical officer). We spoke this week.

Walter

Walter J. Koroshetz, M.D.  
Acting Director  
National Institute of Neurological Disorders and Stroke National Institutes of Health Rm 8A52, Bldg 31, 31 Center Drive  
Bethesda, Md, 20892 Tel 301 496 3167 Fax 301 496 0296

On 6/17/15, 12:34 PM, "Freire, Maria (FNIH) [T]" <freiremc@od.nih.gov> wrote:

>Hi, Walter. I hope you are well and enjoying your new role -  
>congratulations again!  
>  
>I am jumping the gun here because Stephanie and Julie are out at  
>meetings but I wanted to alert you to Elliot's note below. Could we  
>circle back on this once I speak to my folks, please?  
>  
>Best, M.  
>  
>-----Original Message-----  
>From: Elliot Pellman, M.D. [mailto:EPellman@ProHEALTHcare.com]  
>Sent: Wednesday, June 17, 2015 1:03 PM  
>To: Freire, Maria (FNIH) [T]  
>Subject: NFL- FNIH  
>  
>Maria, hope all is well. I am currently traveling (now in Florence,  
>Italy) hence the reason I'm emailing you instead of calling. I received  
>some information that Walter and the NINDS is close to signing off on

>awarding Boston University the monies for the third and final stage of  
>the NFL grant for the longitudinal study. There are many of us who have  
>significant concerns re BU and their ability to be unbiased and  
>collaborative. Betsy Nabel (now NFL Chief Medical Officer), Richard  
>Ellenbogen, Russell Lonser and others are included in that concerned  
>group. I return to NY on June and was wondering if Betsy, Jeff Miller  
>and I (possibly Rich Ellenbogen as well) could schedule a  
>teleconference with you to discuss. Meanwhile I'm hoping that you could  
>communicate our concerns and slow down the process until we all have a  
>chance to speak to figure this out.

>

>Thank you.

>

>Elliot

>.....

>Elliot J Pellman MD

>

>

>

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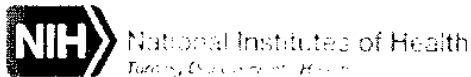
**From:** Hainline, Brian  
**Sent:** 17 Jun 2015 13:47:27 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: Youth Concussion Surveillance and Registry

That is fine. Thanks Walter.

**From:** Koroshetz, Walter (NIH/NINDS) [E] [mailto:koroshetzw@ninds.nih.gov]  
**Sent:** Tuesday, June 16, 2015 8:07 PM  
**To:** Hainline, Brian  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Re: Youth Concussion Surveillance and Registry

Dear Brian,  
Would it be a bad thing if we shared the proposals with our contacts (Betsy Nabel) giving advice to NFL on future research projects?  
Walter

Walter J. Koroshetz, M.D.  
Acting Director  
National Institute of Neurological Disorders and Stroke  
National Institutes of Health  
Rm 5A52, Bldg 31, 31 Center Drive  
Bethesda, Md, 20892  
Tel 301 496 3167  
Fax 301 496 0296



**From:** <Hainline>, Brian Hainline <bhainline@ncaa.org>  
**Date:** Thursday, June 11, 2015 at 10:38 AM  
**To:** Walter Koroshetz <koroshetzw@ninds.nih.gov>  
**Cc:** Dallas Hack <dallas.c.hack.mil@mail.mil>  
**Subject:** Youth Concussion Surveillance and Registry

Hi Walter,

When we met, we discussed the possibility of developing youth concussion projects that would help to give wings to both sides of the NCAA-DoD CARE Consortium (the other wing is building the project out longitudinally). I have attached a proposal which resulted from a think tank at the NCAA. Please advise if you believe there is a pathway in the NIH to explore.

Thanks.

Brian



Brian Hamline, MD  
NCAA Chief Medical Officer  
w: 317-917-6994, e: (b) (6) @ncaa.org  
Post Office Box 6222, Indianapolis, IN 46206-6222

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**From:** Babcock, Debra (NIH/NINDS) [E]  
**Sent:** Monday, June 15, 2015 11:56 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** RE: Enhancing enrollment in the LE-TBI study: (b) (4)

Hi Walter,

This is essentially the request he sent Patrick and I. Originally, I believe (b) (5) but he has since brought the budget down at our request.

We have 2 concerns with this request. (b) (5)

(b) (5)

(b) (5)

Thanks,

Deb

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Monday, June 15, 2015 8:21 AM  
**To:** Bellgowan, Patrick (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]  
**Subject:** Re: Enhancing enrollment in the LE-TBI study: the need for supplemental funds

(b) (5)

walter

Walter J. Koroshetz, M.D.

Acting Director

National Institute of Neurological Disorders and Stroke

National Institutes of Health

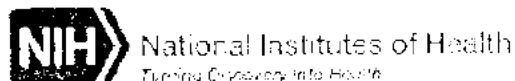
Rm 8A52, Bldg 31, 31 Center Drive

Bethesda, Md, 20892



Tel 301 496 3167

Fax 301 496 0296



**From:** <Gordon>, Wayne Gordon <[wayne.gordon@mountsinai.org](mailto:wayne.gordon@mountsinai.org)>

**Date:** Monday, June 15, 2015 at 7:28 AM

**To:** Walter Koroshetz <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>

**Cc:** "Bellgowan, Patrick (NIH/NINDS) [E]" <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>, Debra Babcock <[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)>, "Dams-o'connor, Kristen" <[kristen.dams-o'connor@mountsinai.org](mailto:kristen.dams-o'connor@mountsinai.org)>, "Paul Crane ([pcrane@u.washington.edu](mailto:pcrane@u.washington.edu))" <[pcrane@u.washington.edu](mailto:pcrane@u.washington.edu)>, "[cdkeene@uw.edu](mailto:cdkeene@uw.edu)" <[cdkeene@uw.edu](mailto:cdkeene@uw.edu)>, "Bruce Fischl ([fischl@nmr.mgh.harvard.edu](mailto:fischl@nmr.mgh.harvard.edu))" <[fischl@nmr.mgh.harvard.edu](mailto:fischl@nmr.mgh.harvard.edu)>, "Brian Edlow ([BEDLOW@partners.org](mailto:BEDLOW@partners.org))" <[BEDLOW@partners.org](mailto:BEDLOW@partners.org)>, "Rebecca Folkerth ([rfolkerth@gmail.com](mailto:rfolkerth@gmail.com))" <[rfolkerth@gmail.com](mailto:rfolkerth@gmail.com)>, Daniel Perl <[daniel.perl@usuhs.edu](mailto:daniel.perl@usuhs.edu)>

**Subject:** Enhancing enrollment in the LE-TBI study (b) (4)

Walter:

Thank you again for taking the time to talk with me last Tuesday. The information below briefly describes the basis for

(b) (4)

Your consideration of this request

Wayne

(b) (4)



**From:** Donnelly, Meredith (FNIH) [T]  
**Sent:** 11 Jun 2015 14:00:46 -0400  
**To:** 'McQuiston, Beth'; Wolf-Rodda, Julie (FNIH) [T]; James, Stephanie (FNIH) [T]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Walker, Paula (NIH/NINDS) [E]; Bullion, Renee (FNIH) [T]; Francis, Tiffany (FNIH) [T]; Sanghrajka, Anisa (FNIH) [T]  
**Subject:** Abbott, NINDS & FNIH discuss SHRP

**From:** Donnelly, Meredith (FNIH) [T]  
**Sent:** 11 Jun 2015 13:59:31 -0400  
**To:** Wolf-Rodda, Julie (FNIH) [T]; James, Stephanie (FNIH) [T]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Walker, Paula (NIH/NINDS) [E]; Bullion, Renee (FNIH) [T]; Francis, Tiffany (FNIH) [T]; Sanghrajka, Anisa (FNIH) [T]  
**Subject:** Abbott, NINDS & FNIH discuss SHRP

Hi,

The new time is June 15 = 2:30 p.m.-3:30 p.m. ET

We will send out a revised scheduler shortly.

Best,

**Meredith Donnelly**  
Development Officer  
FNIH  
9650 Rockville Pike | Bethesda, MD 20814 | [www.fnih.org](http://www.fnih.org)  
Direct (301) 443-1744 | Mobile (240) 281-(b) (6) | Fax (301) 480-2752



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Combined Federal Campaign (CFC) #29165

## Porter, Kevin (NIH/OD) [E]

---

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Tuesday, April 07, 2015 9:59 AM  
**To:** Collins, Francis (NIH/OD) [E]  
**Cc:** Pelis, Kim (NIH/OD) [E]; George, Jill (NIH/OD) [E]; Kuska, Robert (NIH/NIDCR) [E]; Bijal Trivedi (bijal\_trivedi@mac.com); Kolberg, Rebecca (NIH/OD) [E]; Burklow, John (NIH/OD) [E]  
**Subject:** RE: Tau PET scans for CTE  
**Categories:** Important

Thanks—think it's a landmark paper demonstrating power of tau-radioligand to detect tau aggregates in CTE. Caveat is that there are others in development. How well each matches up against the pathology in CTE still remains to be determined.

- 1) tau PET scanning should revolutionize how we diagnose and provide powerful biomarker for disease modifying therapy development. Though Abeta may be the gun in AD, tau seems to be the bullet. Tau also the central culprit in neuronal death in CTE, the tau form of FTD, and progressive supranuclear palsy. Oddly tau KO's are normal. So a great therapeutic target from that standpoint.
- 2) CTE diagnosis is now only possible at autopsy. Tau PET is the answer we need to be able to make dx in living persons, this would allow unbiased study of large numbers which is now impossible. To that end we have grants in review this month to use tau-PET to identify the disorder in those suspected cases and define the clinical syndrome at the different stages of the disease. <http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-14-012.html>

From the RFA which is supported in large part by the fNIH sports health research program with NFL backing.

"Areas of interest include but are not limited to:

- **Advanced imaging studies, including high field MRI scans, tau-radioligand and/or other PET studies aimed at defining the regional distribution and other characteristic features of CTE in high-risk, symptomatic individuals with "possible" or "probable" CTE.**
- A qualitative and quantitative assessment of the progression of the neurodegeneration over a 3 - 5 year period in symptomatic individuals considered to be at high risk for CTE.
- Evaluation of the utility of various neuroimaging approaches and other surrogate markers for establishing a clinical diagnosis of CTE and tracking its progression over a 3 - 5 year period.
- Hypotheses-driven studies to advance knowledge about the underlying pathophysiological mechanisms of CTE and its progression.
- Investigation of the temporal correspondence between the neurodegenerative changes and the clinical signs and symptoms of CTE
- Clinical studies that include data that could lead to the identification of risk factors for CTE. "

- 3) The distribution of the PET signal with this ligand is a bit odd when compared to the pathology based on immunostaining. They get all the right places but the ratios are not quite what expected. The blazing hot signal in the brainstem is difficult to reconcile with the pathology. It's also where they see binding in controls so I suspect

something related to non-tau binding. On path the real hot spots are in cortex, they do see signal in the cortex. We also fund a major neuropath project on CTE through fNIH SHRP and we just had our joint meeting and issued a consensus path diagnosis. <http://www.ninds.nih.gov/research/tbi/ReportFirstNIHConsensusConference.htm>. The pathologic signature is in cortex so wouldn't buy into the theory in this paper of mechanical disortortion of brainstem just yet.

So in summary—tau PET imaging is what the field has been waiting for to go after CTE. This study is the first to convincingly demonstrate abnormal signal with the F18-FDDNP PET ligand. There are other tau ligands in early stage evaluation and investigators will have opportunity to compare their relative value for diagnosing and studying CTE.

Happy to help with the piece.

Walter

---

**From:** Collins, Francis (NIH/OD) [E]  
**Sent:** Tuesday, April 07, 2015 7:51 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Pelis, Kim (NIH/OD) [E]; George, Jill (NIH/OD) [E]; Kuska, Robert (NIH/NIDCR) [E]; Bijal Trivedi ([bijal\\_trivedi@mac.com](mailto:bijal_trivedi@mac.com)); Kolberg, Rebecca (NIH/OD) [E]; Burklow, John (NIH/OD) [E]  
**Subject:** Tau PET scans for CTE

Hi Walter,

I noted this PNAS publication with interest, and I'm thinking of blogging about it next week. Any comments on the study?

Francis

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 31 Mar 2015 15:39:40 +0000  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: Science Interview Request

of course!

**Marian Emr**

Director, Office of Communications and Public Liaison/NINDS  
31 Center Drive MSC 2540  
Building 31, Room 8A07  
Bethesda, MD 20892-2540  
Phone: (301) 496-5924  
Fax: (301) 402-2186  
me201@nih.gov



National Institutes of Health  
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**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** Tuesday, March 31, 2015 11:39 AM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** RE: Science Interview Request

Working on it now! ☺

Thanks,  
Barbara

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** Tuesday, March 31, 2015 11:39 AM  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: Science Interview Request

...and of course, you'll have clearance by then, right?  
Marian

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** Tuesday, March 31, 2015 11:35 AM  
**To:** Walker, Paula (NIH/NINDS) [E]  
**Cc:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** FW: Science Interview Request

Hi Paula,

Emily Underwood is available at 12:30pm tomorrow to interview Dr. Koroshetz. I will tell her to call 301-496-3167 at that time.

Thank you,  
Barbara

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 31 Mar 2015 15:11:39 +0000  
**To:** Mott, Meghan (NIH/OD) [E]  
**Cc:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** FW: CTE workshop

The updated CTE workshop summary is now live at  
<http://www.ninds.nih.gov/research/tbi/ReportFirstNIHConsensusConference.htm>.  
Marian



**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** Tuesday, March 31, 2015 10:28 AM  
**To:** Walker, Paula (NIH/NINDS) [E]  
**Cc:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: Science Interview Request

Thanks, Paula. Barbara is working with the reporter. She will contact you as soon as she gets confirmation for a April 1, 12:30 interview.  
Marian

**From:** Walker, Paula (NIH/NINDS) [E]  
**Sent:** Tuesday, March 31, 2015 10:09 AM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** PRIORITY ACTION: Science Interview Request

Hi Marian:

Walter now has a congressional visit in D.C. tomorrow morning, so he is no longer available from 9:00 a.m.-10:00 a.m. ONLY 12:30 p.m.-1:00 p.m.

Thank you.

Paula Walker

**From:** Walker, Paula (NIH/NINDS) [E]  
**Sent:** Tuesday, March 31, 2015 9:55 AM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** Science Interview Request

Hi Marian:

Walter is available tomorrow for a half hour phone interview with Emily Underwood from 9:00 a.m.-10:00 a.m. and 12:30 p.m.-1:00 p.m.

Can you send Emily these times?

Thank you.

Paula Walker

**From:** Mott, Meghan (NIH/OD) [E]  
**Sent:** Tuesday, March 31, 2015 9:36 AM  
**To:** Emr, Marian (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Walker, Paula (NIH/NINDS) [E]  
**Subject:** RE: CTE workshop summary and Science interview request

Hi Marian,

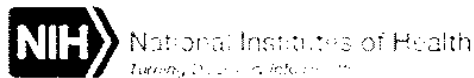
I asked Amy to upload the newest version of the CTE workshop write-up to the website yesterday. We hope to see it up sometime today! Also, we are downtown all day today for a meeting of the Sports Health Research Program Stakeholders. Walter said he could do ~1/2 hour interview tomorrow via phone with Emily, he has a few times available during the day. Paula, would you mind helping to arrange it?

Thanks,  
Meghan

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** Tuesday, March 31, 2015 9:07 AM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/OD) [E]  
**Subject:** CTE workshop summary and Science interview request

Walter: I don't think that anyone gave the order to the web team to make my changes (and the additional ones you wanted to make) to the CTE summary on the web. Did you want to do that? Also, Emily Underwood wants to interview you for a Science article about the Boston meeting. Do you have time today or tomorrow?  
Marian

**Marian Emr**  
Director, Office of Communications and Public Liaison/NINDS  
31 Center Drive MSC 2540  
Building 31, Room 8A07  
Bethesda, MD 20892-2540  
Phone: (301) 496-5924  
Fax: (301) 402-2186  
[me2001a@nih.gov](mailto:me2001a@nih.gov)



**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Saturday, March 28, 2015 4:51 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Cc:** Mott, Meghan (NIH/OD) [E]; Adams, Amy (NIH) [C]  
**Subject:** FOLLOW UP: CTE workshop summary  
**Importance:** High

Thanks Marian. I don't see it on the website. I made a few changes also if not too late. Have to get it up Monday though as the meeting is Tuesday. We can always buff it later.  
Walter

**From:** <Emr>, Marian Emr <[emrm@ninds.nih.gov](mailto:emrm@ninds.nih.gov)>  
**Date:** Saturday, March 28, 2015 at 11:19 AM  
**To:** walter j koroshetz <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>



**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 30 Mar 2015 12:51:12 +0000  
**To:** Michel, Mary Ellen (NIH/NICHHD) [E]  
**Subject:** RE: concussion conference

Thanks. Theory confirmed for the quick release of the statement.  
Marian

**From:** Michel, Mary Ellen (NIH/NICHHD) [E]  
**Sent:** Monday, March 30, 2015 8:44 AM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** FYI: concussion conference

Sent from my iPhone

Begin forwarded message:

**From:** "Koroshetz, Walter (NIH/NINDS) [E]" <[koroshetzwa@ninds.nih.gov](mailto:koroshetzwa@ninds.nih.gov)>  
**Date:** March 29, 2015 at 6:50:44 PM EDT  
**To:** Rich Ellenbogen <[rge@u.washington.edu](mailto:rge@u.washington.edu)>, Russell Lonser <[RR.Lonser@osame.edu](mailto:RR.Lonser@osame.edu)>, Jeff Miller <[Jeff.Miller@NFL.com](mailto:Jeff.Miller@NFL.com)>, Hunt Batjer <[Hunt.Batjer@UTSouthwestern.edu](mailto:Hunt.Batjer@UTSouthwestern.edu)>, "sbrowd@seattlechildrens.org" <[sbrowd@seattlechildrens.org](mailto:sbrowd@seattlechildrens.org)>, "nina.feddermann@usz.ch" <[nina.feddermann@usz.ch](mailto:nina.feddermann@usz.ch)>, "Freund, Michelle (NIH/NIMH) [E]" <[freundm@mail.nih.gov](mailto:freundm@mail.nih.gov)>, "jgrand@nhl.com" <[jgrand@nhl.com](mailto:jgrand@nhl.com)>, (b) (6) <[edkeene@uw.edu](mailto:edkeene@uw.edu)>, "edkeene@uw.edu" <[edkeene@uw.edu](mailto:edkeene@uw.edu)>, kristen.dams-oconnor@missm.edu <[kristen.dams-oconnor@missm.edu](mailto:kristen.dams-oconnor@missm.edu)>, "wayne.gordon@missm.edu" <[wayne.gordon@missm.edu](mailto:wayne.gordon@missm.edu)>, "kingla@ohsu.edu" <[kingla@ohsu.edu](mailto:kingla@ohsu.edu)>, "hleyin@bcm.edu" <[hleyin@bcm.edu](mailto:hleyin@bcm.edu)>, "lara.mckenzie@nationwidechildrens.org" <[lara.mckenzie@nationwidechildrens.org](mailto:lara.mckenzie@nationwidechildrens.org)>, "beth.mcquiston@abbot.com" <[beth.mcquiston@abbot.com](mailto:beth.mcquiston@abbot.com)>, "mwhalen@partners.org" <[mwhalen@partners.org](mailto:mwhalen@partners.org)>, "suskauer@kennedykrieger.org" <[suskauer@kennedykrieger.org](mailto:suskauer@kennedykrieger.org)>, "nport@indiana.edu" <[nport@indiana.edu](mailto:nport@indiana.edu)>, "kristina.shoun@usoc.org" <[kristina.shoun@usoc.org](mailto:kristina.shoun@usoc.org)>, "beth.mcquiston@abbot.com" <[beth.mcquiston@abbot.com](mailto:beth.mcquiston@abbot.com)>  
**Cc:** "Donnelly, Meredith (FNIH) [T]" <[mdonnelly@fnih.org](mailto:mdonnelly@fnih.org)>, "Cernich, Alison (NIH/NICHHD) [E]" <[alison.cernich@nih.gov](mailto:alison.cernich@nih.gov)>, "Bullion, Renee (FNIH) [T]" <[rbullion@fnih.org](mailto:rbullion@fnih.org)>, "Babcock, Debra (NIH/NINDS) [E]" <[dbabcock@ninds.nih.gov](mailto:dbabcock@ninds.nih.gov)>, "Bellgowan, Patrick (NIH/NINDS) [E]" <[patrick.frostbellgowan@nih.gov](mailto:patrick.frostbellgowan@nih.gov)>, "James, Stephanie (FNIH) [T]" <[sjames@fnih.org](mailto:sjames@fnih.org)>, "Michel, Mary Ellen (NIH/NICHHD) [E]" <[michelmf@mail.nih.gov](mailto:michelmf@mail.nih.gov)>, "Tarver, Erika (FNIH) [T]" <[etarver@fnih.org](mailto:etarver@fnih.org)>, "Platt, Christopher (NIH/NIDCD) [E]" <[platte@nidcd.nih.gov](mailto:platte@nidcd.nih.gov)>, "McAuliffe, Matthew

(NIH/CIT) [E]" <mcmatt@exchange.nih.gov>

**Subject: concussion conference**

Dear colleagues,

I very much look forward to seeing you at the Sports Health Research Program meeting Tuesday in D.C. Lots of interesting research in progress to be presented. Thanks to the SHRP partners, investigators and research subjects.

One of the first milestones for the neuropathology/neuroimaging program was to come to a consensus on the pathologic diagnosis of chronic traumatic encephalopathy.

The report of the First NIH Consensus conference is now posted

<http://www.ninds.nih.gov/research/tbi/ReportFirstNIHConsensusConference.htm>

This report provides guidelines for neuropathologists as they examine cases. It's a necessary first step to discover how commonly the condition occurs and which risk factors are associated.

See you Tuesday.

Best wishes,

Walter

Walter J. Koroshetz, M.D.

Acting Director, National Institute of Neurological Disorders and Stroke



**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 26 Mar 2015 17:11:50 +0000  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: CTE report

It is what it is... there is no defense, particularly without peer review.  
Marian

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** Thursday, March 26, 2015 1:10 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** RE: CTE report

Thanks for sharing this copy with me - I'm excited to read it.

I wasn't sure if this was a case that required some "defense" on our part (just thinking about any potential effects of an article on the Science website and wondering what other reporters Anne McKee has been talking to).

Barbara

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** Thursday, March 26, 2015 1:04 PM  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: CTE report

I don't know.... it's pretty powerful stuff so I'm not sure that I want to light a fire under it. Also not sure why they aren't trying for publication in a journal. Peer review would do us a lot of good. See what you think. Also, feel free to redline it but don't, under any circumstances, circulate the draft copy.  
Marian

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** Thursday, March 26, 2015 12:47 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** RE: CTE report

Ok, thanks I'll let her know. Do you want us to do anything with it?

Barbara

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** Thursday, March 26, 2015 12:44 PM  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: CTE report

You can let Emily know that a short summary of the workshop will be published on the website by the end of the week. (FYI: I'm looking at it now.) WK promised he would let us respond. May be too busy to remember, though.  
Marian

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** Wednesday, March 25, 2015 9:34 AM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** ACTION: CTE report

FYI, Emily Underwood just sent the following email to Dr. Koroshetz re: CTE, even though I told her I'm looking into the issue. I was hoping she would let us take care of this, instead of contacting him directly.

Thanks,  
Barbara

**From:** Emily Underwood [<mailto:eunderwo@aaaas.org>]  
**Sent:** Wednesday, March 25, 2015 9:28 AM  
**To:** McMakin, Barbara (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** CTE report

Hello Dr. Koroschetz and Barbara,

I'm curious if you know whether the new CTE report will be presented at the April 15-16 TBI meeting coming up in DC; that seems a natural place to report the findings.

Best,

Emily Underwood

Staff Reporter  
Science Magazine  
1200 New York Ave NW  
Washington DC 20005  
202-326-6627

**From:** McMakin, Barbara (NIH/NINDS) [E] [<mailto:mcmakinbi@ninds.nih.gov>]  
**Sent:** Tuesday, March 24, 2015 1:45 PM  
**To:** Emily Underwood  
**Subject:** RE: CTE report

Apparently the report is still being revised and there is no publication date yet. I'll let you know once that changes.

Thanks!  
Barbara

**From:** Emily Underwood [<mailto:eunderwo@aaaas.org>]  
**Sent:** Tuesday, March 24, 2015 1:38 PM  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: CTE report

Thanks Barbara – this is being headed up by Walter Koroschetz, yes? I can also contact him directly if that's easier on your end...



**From:** McMakin, Barbara (NIH/NINDS) [E] [<mailto:mcmakinbi@ninds.nih.gov>]  
**Sent:** Tuesday, March 24, 2015 1:32 PM  
**To:** Emily Underwood  
**Subject:** CTE report

Hi Emily,

I'm looking into the CTE report and also wanted to pass along my contact info.

I'll let you know if I hear anything.

Best,  
Barbara

***Barbara L. McMakin***  
Science Writer  
Office of Communications and Public Liaison  
National Institute of Neurological Disorders & Stroke  
National Institutes of Health  
Building 31, Room 8A07  
31 Center Drive MSC 2540  
Bethesda, MD 20892-2540  
Main Office Line (301) 496-5754  
Direct Line (301) 435-7747  
Email: [mcmakinbi@ninds.nih.gov](mailto:mcmakinbi@ninds.nih.gov)

**From:** Perl, Daniel  
**Sent:** 19 Mar 2015 15:57:43 -0400  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Dickson, Dennis W., M.D.; amckee@bu.edu; jgv2001@cumc.columbia.edu; cairns@wustl.edu; ilitvan@ucsd.edu; tdstein@bu.edu; William.Stewart@glasgow.ac.uk; Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]  
**Subject:** Re: report of the CTE path conference

Walter,

I added a few corrections and comments with Track Changes. Good summary.

Dan

On Thu, Mar 19, 2015 at 1:56 PM, Koroshetz, Walter (NIH/NINDS) [E] <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)> wrote:

Thanks Dennis. These all made sense to me. Much better.

walter

**From:** Dickson, Dennis W., M.D. [<mailto:dickson.dennis@mayo.edu>]  
**Sent:** Thursday, March 19, 2015 1:53 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; 'amckee@bu.edu'; 'jgv2001@cumc.columbia.edu'; 'cairns@wustl.edu'; Daniel Perl ([daniel.perl@usuhs.edu](mailto:daniel.perl@usuhs.edu)); 'ilitvan@ucsd.edu'; 'tdstein@bu.edu'; 'William.Stewart@glasgow.ac.uk'  
**Cc:** Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]  
**Subject:** RE: report of the CTE path conference

I made some edits with Track Changes.

Dennis

**From:** Koroshetz, Walter (NIH/NINDS) [E] [<mailto:koroshetzw@ninds.nih.gov>]  
**Sent:** Thursday, March 19, 2015 12:28 PM  
**To:** 'amckee@bu.edu'; 'jgv2001@cumc.columbia.edu'; Dickson, Dennis W., M.D.; 'cairns@wustl.edu'; Daniel Perl ([daniel.perl@usuhs.edu](mailto:daniel.perl@usuhs.edu)); 'ilitvan@ucsd.edu'; 'tdstein@bu.edu'; 'William.Stewart@glasgow.ac.uk'  
**Cc:** Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Mott, Meghan

(NIH/OD) [E]

**Subject:** report of the CTE path conference

Dear colleagues,

Sorry to be so late with the report summary.

Please take a look send suggestions for edits. Idea is that we would post on NINDS website anything we talk about at the upcoming meeting with foundation for nih and their partners.

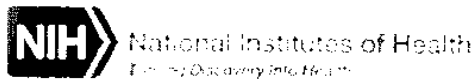
Please find my mistakes---errors of omission or commission.

Thanks

Best wishes,

Walter

Walter Koroshetz, MD  
Acting Director, National Institute of Neurological Disorders and Stroke



--  
Daniel P. Perl, MD  
Professor of Pathology (Neuropathology)  
Uniformed Services University of the Health Sciences  
F Edward Hebert School of Medicine  
*"America's Medical School"*  
4301 Jones Bridge Road, Room B-3138  
Bethesda, MD 20814

Director, Neuropathology Core

Center for Neurosciences and Regenerative Medicine (CNRM)

tel. 301 295-5534

e-mail: [daniel.perl@usuhs.edu](mailto:daniel.perl@usuhs.edu)

**From:** Dickson, Dennis W., M.D.  
**Sent:** 19 Mar 2015 17:53:01 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; 'amckee@bu.edu'; 'jgv2001@cumc.columbia.edu'; 'cairns@wustl.edu'; Daniel Perl (daniel.perl@usuhs.edu); 'ilitvan@ucsd.edu'; 'tdstein@bu.edu'; 'William.Stewart@glasgow.ac.uk'  
**Cc:** Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]  
**Subject:** RE: report of the CTE path conference  
**Attachments:** Defining the pathologic signature of Chronic Traumatic Encephalopathy.docx

I made some edits with Track Changes.

Dennis

**From:** Koroshetz, Walter (NIH/NINDS) [E] [mailto:koroshetzw@ninds.nih.gov]  
**Sent:** Thursday, March 19, 2015 12:28 PM  
**To:** 'amckee@bu.edu'; 'jgv2001@cumc.columbia.edu'; Dickson, Dennis W., M.D.; 'cairns@wustl.edu'; Daniel Perl (daniel.perl@usuhs.edu); 'ilitvan@ucsd.edu'; 'tdstein@bu.edu'; 'William.Stewart@glasgow.ac.uk'  
**Cc:** Babcock, Debra (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Mott, Meghan (NIH/OD) [E]  
**Subject:** report of the CTE path conference

Dear colleagues,

Sorry to be so late with the report summary.

**Please take a look send suggestions for edits.** Idea is that we would post on NINDS website anything we talk about at the upcoming meeting with foundation for nih and their partners.

Please find my mistakes—errors of omission or commission.

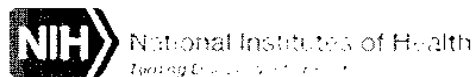
Thanks

Best wishes,

Walter

Walter Koroshetz, MD

Acting Director, National Institute of Neurological Disorders and Stroke





**From:** Guttmacher, Alan (NIH/NICHD) [E]  
**Sent:** 4 Mar 2015 15:06:18 -0500  
**To:** Cernich, Alison (NIH/NICHD) [E]; Koroshetz, Walter (NIH/NINDS) [E]  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E]; Michel, Mary Ellen (NIH/NICHD) [E]; Maholmes, Valerie (NIH/NICHD) [E]  
**Subject:** RE: NCAA concussion meeting

Thanks for the summary, Alison. Re your second bullet, there would seem to be the potential there for something meaningful if they worked together. (And, of course, as always the case, the primary reply to funding frustration is send us good proposals, since the majority of what we fund is investigator initiated...

Alan

**From:** Cernich, Alison (NIH/NICHD) [E]  
**Sent:** Tuesday, March 03, 2015 4:46 PM  
**To:** Koroshetz, Walter (NIH/NINDS) [E]; Guttmacher, Alan (NIH/NICHD) [E]  
**Cc:** Bellgowan, Patrick (NIH/NINDS) [E]; Michel, Mary Ellen (NIH/NICHD) [E]; Maholmes, Valerie (NIH/NICHD) [E]  
**Subject:** NCAA concussion meeting

All,

Just finishing the NCAA meeting. Detailed notes are attached. Summary points are below:

- There are existing systems in NCAA, high school, and some medical systems that might be a base for a proposal in youth concussion. High school seems to be feasible given the availability of High School RIO and their infrastructure and the potential presence of reliable data collection through certified athletic trainers.
  - The clinic based groups at CHOP, NYU, National Children's Medical (DC), UCLA, and Houston Methodist have existing programs and may need to work together to propose a larger clinic based model for pediatric practice for reporting or a research proposal.
  - Are there existing models from High School RIO or Datalys's NATION project that could be proposed to NCAA/DoD for a possible funding.
  - CDC will conduct a telephonic surveillance initiative in response to the IOM Youth Concussion Report that will be nationally representative and will include land-line and cell phone based calls.
- 
- NIH specific: Questions related to level of funding commitment we have for pediatric TBI and pediatric concussion; major frustration from this audience was focus on CTE rather than the developmental trajectory and how the injury impacts pediatric population and their development and educational readiness. There was discussion around the low level of funding for this issue from NIH and small number of projects that have a pediatric focus. Request for follow-up meeting on this issue sponsored by NIH in 6 months. Deferred question.

Best,  
Alison

Alison Cernich, Ph.D., ABPP-Cn  
Director  
National Center for Medical Rehabilitation Research  
National Institute of Child Health and Human Development  
National Institutes of Health  
6100 Executive Boulevard  
Rockville, MD 20852  
301-296-0295  
[Alison.Cernich@nih.gov](mailto:Alison.Cernich@nih.gov)



**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 17 Feb 2015 21:12:48 +0000  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** RE: Request for interview - CTE "consensus" meeting - February 25-27

Excellent. Maybe I should stop reading my email now so I can get some other work done!  
Marian

**From:** McMakin, Barbara (NIH/NINDS) [E]  
**Sent:** Tuesday, February 17, 2015 4:11 PM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** RE: Request for interview - CTE "consensus" meeting - February 25-27

BHS just cleared this interview request.

Thanks,  
Barbara

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** Tuesday, February 17, 2015 3:40 PM  
**To:** McMakin, Barbara (NIH/NINDS) [E]  
**Subject:** Request for interview - CTE "consensus" meeting - February 25-27

Could you please clear this interview? The reporter's name is Helen Shen; she's a free-lance science writer. Her office number is 650-396-7358; her cell is 650-906-(b) (6) (specific time). I gave Walter her contact info so he may simply call her without telling me.

Thanks,  
Marian

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Tuesday, February 17, 2015 3:05 PM  
**To:** Emr, Marian (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]  
**Subject:** Re: CTE "consensus" meeting - February 25-27?  
**Importance:** High

The Neuropath based CTE grantees have as first milestone coming together to establish pathologic criteria for CTE and different stages of CTE. This will be a "deep in the woods" meeting of a bunch of neuropathologists looking at slides. . . Would not be something open to public. We do hope that they come to consensus and publish their criteria.

Walter

**From:** <Emr>, Marian Emr <emrm@ninds.nih.gov>  
**Date:** Tuesday, February 17, 2015 2:59 PM  
**To:** walter.j.koroshetz <koroshetz.w@ninds.nih.gov>, "Bellgowan, Patrick (NIH/NINDS) [E]" <patrick.frostbellgowan@nih.gov>  
**Subject:** CTE "consensus" meeting - February 25-27?

**From:** Emr, Marian (NIH/NINDS) [E]  
**Sent:** 18 Feb 2015 14:26:05 +0000  
**To:** Koroshetz, Walter (NIH/NINDS) [E]  
**Subject:** RE: introduction: CTE story

OK. Thanks. I'll let you know if we get other inquiries.  
Marian

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Wednesday, February 18, 2015 9:25 AM  
**To:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** Re: introduction: CTE story

Nothing really. It's a working meeting of the dozen neuropathologists from the two grants to work out a standardized, classification system that they can use going forward.  
walter

**From:** <Emr>, Marian Emr <[emrm@ninds.nih.gov](mailto:emrm@ninds.nih.gov)>  
**Date:** Wednesday, February 18, 2015 6:57 AM  
**To:** walter j koroshetz <[koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)>  
**Subject:** RE: introduction: CTE story

Good morning, Walter, and thanks for talking with Helen. I anticipated you would and got HHS clearance yesterday afternoon. Attached is the final copy of the NFL grant release for your files and future use. Do you have additional information about the Boston meeting that you can share?  
Marian

**From:** Koroshetz, Walter (NIH/NINDS) [E]  
**Sent:** Tuesday, February 17, 2015 7:05 PM  
**To:** 'Helen Shen'  
**Cc:** Emr, Marian (NIH/NINDS) [E]  
**Subject:** RE: introduction: CTE story

Dear Helen  
Good talking with you today.

The link that explains the study in living individuals that is now in for peer review is at:  
<http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-14-012.html>

The report from the workshop in this topic that we held prior to soliciting grant proposals is at:  
[http://www.ninds.nih.gov/news\\_and\\_events/proceedings/TBI-related\\_neurodegeneration\\_workshop\\_report.htm](http://www.ninds.nih.gov/news_and_events/proceedings/TBI-related_neurodegeneration_workshop_report.htm)

We did hold a workshop on the pathology of CTE prior to issuing the call for grants and the write up of the meeting is at:  
[http://www.ninds.nih.gov/news\\_and\\_events/proceedings/201212\\_CTE\\_workshop\\_report.htm](http://www.ninds.nih.gov/news_and_events/proceedings/201212_CTE_workshop_report.htm)

- ? The link that explains the Neuropathology project is at [Cooperative Agreements: Collaborative Research on Chronic Traumatic Encephalopathy and Delayed Effects of Traumatic Brain Injury: Neuropathology and Neuroimaging Correlation \(U01\)](#)

Forgot to mention that to test whether the tau PET will work in CTE it is necessary to see if the PET ligand binds to brain where the CTE changes are. So we need brain tissue with defined stages of CTE to see how much binding signal we can expect when go to living person.

I attached the press release that came out when the grants were announced which includes the names of all the involved hospitals.

The abstract of the McKee project is:

**Project Number:** SU01NS086659-02

**Contact PI / Project Leader:** [MCKEE, ANN C.](#)

**Title:** CTE AND POSTTRAUMATIC NEURODEGENERATION: NEUROPATHOLOGY AND EX VIVO IMAGING

**Awardee Organization:** BOSTON UNIVERSITY MEDICAL CAMPUS

**Abstract Text:**

DESCRIPTION (provided by applicant): Traumatic brain injury (TBI) is associated clinically with progressive cognitive decline and dementia and pathologically with axonal injury and the deposition of multiple aggregated proteins. Repetitive mild TBI can trigger chronic traumatic encephalopathy (CTE), a unique tauopathy, and single TBI can provoke an Alzheimer's-like neurodegeneration. Unfortunately, the only way to diagnose these posttraumatic neurodegenerations, including CTE, is by post-mortem brain examination. In order to conduct prospective research into the incidence, prevalence, risk factors, clinical course, and ultimately, treatment for posttraumatic neurodegeneration, consensus criteria for diagnosis as well as objective biomarkers for disease must first be established. This initiative will assemble a multicenter team of expert neuroscientists to evaluate the late effects of TBI, including single and repetitive TBI of varying severity, and CTE, using histological examination of postmortem bio specimens and neuroimaging tools as a foundation to develop in vivo diagnostics. As a first aim, this proposal will bring together a team of 5 accomplished neuropathologists in neurodegenerative disease to establish consensus criteria for the post-mortem diagnosis of CTE. This team will also define the stages of CTE pathology, the features that differentiate CTE from other neurodegenerations and the

effects of substance abuse, and the characteristics of posttraumatic neurodegeneration after single TBI. As a second aim, this proposal will establish a national bio specimen and data bank for TBI (Understanding Neurological Injury and Traumatic Encephalopathy (UNITE) bio bank) by developing a nationwide brain donor registry and hotline to acquire high quality bio specimens and data. The UNITE bank will use strictly standardized protocols and a web-based interface to ensure that tissue and data are readily available to qualified investigators. Comprehensive retrospective clinical data including clinical symptoms, brain trauma and substance abuse history, and medical records (including common data elements) will be entered into a secure database. Behavioral/ mood dysfunction, cognitive changes, substance abuse and traumatic exposure will be correlated with quantitative assessment of the multifocal tauopathy, Ass deposition and axonal injury. As a third aim, neuroimaging signatures of the neuropathology will be determined in post-mortem tissue using high spatial resolution diffusion tensor imaging (DTI) and autoradiography using a highly selective PET ligand for tau. Quantitative assessment of axonal injury, tau, and Ass will be correlated with ex vivo DTI abnormalities and tau ligand autoradiography. Pilot neuroimaging studies of individuals at high risk for the development of CTE will also be conducted in the final 2 years of the proposal. This proposal will determine the clinical and neuroimaging correlates of CTE and posttraumatic neurodegeneration and create the groundwork for establishing their incidence and prevalence. This study will have a tremendous impact on public health of millions of Americans and greatly increase our understanding of the latent effects of brain trauma.

The abstract of the Wayne Gordon grant is:

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|------------------------|------------------------------------------------------------------------------|-------------------------------------|-----------------------------------------|
| <b>Project Number:</b> | 5U01NS086625-02                                                              | <b>Contact PI / Project Leader:</b> | <u>GORDON, WAYNE A</u>                  |
| <b>Title:</b>          | NEUROPATHOLOGY OF CTE AND DELAYED EFFECTS OF TBI: TOWARD IN-VIVO DIAGNOSTICS | <b>Awardee Organization:</b>        | ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI |
| <b>Abstract Text:</b>  |                                                                              |                                     |                                         |

DESCRIPTION (provided by applicant): The proposed project, "Neuropathology of CTE and Late Effects of TBI: Toward In-Vivo Diagnostics" is a multi-center and multi-disciplinary study designed to dramatically increase our understanding of chronic traumatic encephalopathy (CTE) and other late effects of traumatic brain injury (TBI). TBI is a major public health concern in the US, as the current prevalence of TBI in the US is unprecedented. Some TBI survivors experience particularly poor outcomes as they age; these include accelerated cognitive and health decline, dementia, and in some cases, CTE. CTE is thought to be a tauopathy but has been described only in convenience samples of people with repetitive head trauma. CTE is incompletely described in individuals with mild, moderate and severe TBI. The population incidence and prevalence, risk factors, and causal role of multifocal tauopathy on associated symptoms are unknown. Overlapping clinical features, postmortem pathologies and patterns of involvement exist in TBI, CTE, and Alzheimer's disease pose challenges to accurate diagnosis. Premortem diagnosis of CTE is currently impossible. The neuropathological consequences of single mild or moderate-severe TBI and its relationship with CTE and known dementias are unclear. The proposed project will leverage extensive resources from an ongoing population-based prospective cohort study of brain aging (Adult Changes in Thought; ACT, n=2,305) which includes excellent medical, behavioral, and genetic characterization of a cohort (20% of whom have a history of mild-moderate TBI) in addition to state-of-the-art neuropathology workup upon death. Neuropathological study of TBI effects can begin immediately in the existing ACT autopsy sample (n=489, 20% with TBI exposure). Additional cohorts of TBI-exposed individuals will come from the Brain Injury Research Center at Mount Sinai (n=150 individuals with moderate-severe TBI), the University of Texas Southwestern (n=50 retired boxers with repetitive TBI exposure), and the National Football League (n=76 retired players with repetitive TBI exposure). All participants in the proposed study (ACT and other sites) will undergo uniform harmonized neurobehavioral assessment (chosen to maximize correspondence with existing large-scale TBI and dementia studies), MRI scan, and genomic analysis. Those individuals who expire during the course of the study will undergo ex-vivo neuroimaging and

extensive neuropathological exam using state-of-the-art techniques (such as Histelide) designed to quantify tau and A $\beta$  in whole brain specimens. Only by examining postmortem pathology in a sample of individuals with varying levels of TBI exposure who are well characterized during life (as proposed herein) can postmortem pathology facilitate identification of in-vivo biomarkers that can act as diagnostic tools. This project represents the most systematic and scientifically rigorous effort to date to develop a more complete understanding of the long-term clinical and neuropathological sequelae of single and multiple TBI.

**From:** (b) (6) on Behalf Of Helen Shen  
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**Subject:** introduction: CTE story

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**From:** Collins, Francis (NIH/OD) [E]  
**Sent:** Sunday, February 01, 2015 4:53 PM  
**To:** Tabak, Lawrence (NIH/OD) [E] <Lawrence.Tabak@nih.gov>  
**Cc:** NIH Director's Executive Committee <OD-SmallStaff@mail.nih.gov>  
**Subject:** RE: NFL Will Name Elizabeth Nabel as Its Chief Medical Officer

OMG!

**From:** Tabak, Lawrence (NIH/OD) [E]  
**Sent:** Sunday, February 01, 2015 4:51 PM  
**To:** Collins, Francis (NIH/OD) [E]  
**Cc:** NIH Director's Executive Committee  
**Subject:** NFL Will Name Elizabeth Nabel as Its Chief Medical Officer

Interesting – a cardiologist for the NFL CMO.

## NFL Will Name Elizabeth Nabel as Its Chief Medical Officer

by Scott Soshnick  
2:20 PM EST  
February 1, 2015

(Bloomberg) -- The National Football League will name Elizabeth G. Nabel, president of Brigham and Women's Hospital in Boston, as its chief medical officer, two people with direct knowledge of the hire said.

The people requested anonymity because the league, which is staging its championship game today in Phoenix, hasn't announced the move.

NFL spokesman Brian McCarthy and hospital spokeswoman Michelle Cerulli declined to comment.

Commissioner Roger Goodell during his Jan. 30 state of the league address said the most-watched U.S. sports league would create the chief medical officer position as part of the NFL's commitment to making the game safer.

Goodell said since 2012 concussions in regular-season games have dropped to 111 from 173.

Awareness of the dangers of concussions has grown in the past decade as doctors tied neurological damage, dementia and early death in athletes to repetitive head injuries. In July, a U.S. district judge gave preliminary approval to a head injury settlement in which the NFL would pay at least \$675 million to retired players who suffer from a list of qualified injuries including Alzheimer's, Parkinson's disease and amyotrophic lateral sclerosis, or ALS.

"There's more to do on player health and safety," Goodell said. "Carefully reviewing and approving our concussion protocols will be a focus of our medical committees this offseason."

"This individual, who we expect to have in place very soon, will oversee our medical-related policies, ensure that we update them regularly, and work closely with our medical committees, our advisers, and the Players' Association," Goodell said.

## Hospital Meeting

Nabel, according to the hospital website, has served as president of Harvard-affiliated Brigham and Women's Hospital since 2010. A cardiologist and distinguished biomedical researcher, Nabel is Professor of Medicine at Harvard Medical School.

Nabel is scheduled to meet with Brigham and Women's Hospital officials tomorrow, according to one of the people.

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