
Embargoed for Release

December 16, 2013
9:00 am EST

CONTACT:

Barbara McMakin and Marian Emr
nindspressteam@ninds.nih.gov
(301) 496-5751

NIH and NFL tackle concussion research

NIH announces research projects funded largely by donation from the NFL

The National Institutes of Health has selected eight projects to receive support to answer some of the most fundamental problems on traumatic brain injury, including understanding long-term effects of repeated head injuries and improving diagnosis of concussions.

Funding is provided by the Sports and Health Research Program, a partnership among the NIH, the National Football League, and the Foundation for the National Institutes of Health (FNIH). In 2012, the NFL donated \$30 million to FNIH for research studies on injuries affecting athletes, with brain trauma being the primary area of focus.

Traumatic brain injury (TBI) is a major public health problem that affects all age groups and is the leading cause of death in young adults. Recently, concern has been raised about the potential long-term effects of repeated concussion, particularly in those most at risk: young athletes and those engaged in professions associated with frequent head injury, including men and women in the military. Current tests cannot reliably identify concussions, and there is no way to predict who will recover quickly, who will suffer long-term symptoms, and which few individuals will develop progressive brain degeneration, called chronic traumatic encephalopathy (CTE).

“We need to be able to predict which patterns of injury are rapidly reversible and which are not. This program will help researchers get closer to answering some of the important questions about concussion for our youth who play sports and their parents,” said Story Landis, Ph.D., director of the National Institute of Neurological Disorders and Stroke (NINDS), part of NIH.

Two (\$6 million each) are large, cooperative agreements focused on defining the scope of long-term changes that occur in the brain years after a head injury or after multiple concussions. The cooperative awards form a partnership between NINDS, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) and multiple academic medical centers.

NIH also will fund 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. If the

early results are encouraging, they may become the basis of more comprehensive projects. The NIH institutes responsible for managing these grants are NINDS, NICHD, and the National Institute on Deafness and Other Communication Disorders (NIDCD).

The eight projects were selected by the NIH following a rigorous scientific review process.

The cooperative awards bring together two teams of independent scientists to study and compare the brains of donors who were at high or low risk for developing long-term effects of TBI. Ten neuropathologists from eight universities will coordinate to describe the chronic effects of head injury in tissue from hundreds of individuals in order to develop standards for diagnosis.

The project includes four teams that will correlate brain scans with changes in brain tissue, using a variety of techniques. This may open the possibility of using these advanced brain imaging techniques to diagnose chronic effects of TBI in living individuals. The investigators in the two projects will also help NIH develop a registry dedicated to enrolling individuals with a history of TBI who are interested in donating brain and spinal cord tissue for study after their death. The new NIH Neurobiobank (<https://neurobiobank.nih.gov>) will coordinate the tissue collection, data gathering, and also distribute biospecimens, along with relevant information to enable other scientists to access this valuable tissue.

The two cooperative agreements are:

- CTE and Post-traumatic Neurodegeneration: Neuropathology and Ex Vivo Imaging
Principal Investigator: Ann C. McKee, M.D., Boston University School of Medicine and U.S. Department of Veterans Affairs

At present, the diagnosis of CTE is made by examining the brain after death; however, the range of specific features that identify this disorder has not been established. One goal of Dr. McKee's project is to define a clear set of criteria for the various stages of CTE and to distinguish it from Alzheimer's, amyotrophic lateral sclerosis, and other neurodegenerative disorders in post-mortem brain tissue. Once these characteristics have been defined in brain tissue, the imaging teams at Washington University in St. Louis and Massachusetts General Hospital in Boston will correlate them with brain scans to identify features that might eventually be used to diagnose CTE in individuals during their lifetimes.

- Neuropathology of CTE and Delayed Effects of TBI: Toward In Vivo Diagnostics
Principal Investigator: Wayne Gordon, Ph.D., Mount Sinai Hospital, New York City

The goal of Dr. Gordon's project is to identify and describe the chronic effects of mild, moderate and severe TBIs and compare these with the features of CTE. Dr. Gordon and his colleagues at the University of Washington in Seattle will comprehensively evaluate brain tissue obtained from an ongoing study of thousands of people, the Adult Changes in Thought (ACT) study, funded by the National Institute of Aging. They also will examine brain tissue from donors who suffered severe TBI and were cared for in the TBI Model Systems program funded by the Department of Education's National Institute on Disability and Rehabilitation Research. In Dr. Gordon's project, neuroimaging teams at Massachusetts General Hospital, Oregon Health Sciences University in Portland, and the University of Washington will use a variety of sophisticated brain scanning

techniques in patients with a range of head injuries, as well as on post-mortem tissue, to identify potential markers that may eventually be used to diagnose the degenerative effects of TBI in people.

“The investigators will collaborate to develop diagnostic criteria for identifying the chronic features of the entire scope of brain trauma ranging from mild TBI to full-blown CTE, and then work to extend these criteria to living humans using some of the most advanced neuroimaging tools available,” said Walter Koroshetz, M.D., deputy director of NINDS.

“Although the two cooperative agreements focus on different aspects of TBI, their combined results promise to answer critical questions about the chronic effects of single versus repetitive injuries on the brain, how repetitive TBI might lead to CTE, how commonly these changes occur in an adult population, and how CTE relates to neurodegenerative disorders like Alzheimer’s disease,” Dr. Landis said.

The pilot studies will focus on improving the diagnosis of concussion and identifying potential biomarkers that can be used to track a person’s recovery. The six pilot grants are:

- **Cortical GABA in Pediatric Sports Concussion**

Principal Investigator: Jeffrey G. Ojemann, M.D., Seattle Children’s Hospital

The brain contains numerous chemicals such as gamma-amino butyric acid (GABA), which is important for many brain functions, including cognition and movement, and may be altered by traumatic brain injury. Magnetic resonance (MR) spectroscopy is a scanning technique that can measure a variety of brain chemicals, including GABA. The goal of Dr. Ojemann’s project is to use MR spectroscopy to monitor GABA levels in adolescents who have sports-related concussions and compare those levels to uninjured controls. The researchers also will conduct preliminary comparisons of GABA levels with existing cognitive measures such as memory tests and structural brain imaging. Diagnostic tools that can reliably detect when the brain is injured and when it has recovered following a concussion are essential for determining when it is safe to resume normal activities.

- **Evaluation of Spot Light: A Concussion Injury Management App for Youth Sports**

Principal Investigators: Lara McKenzie, Ph.D., Center for Injury Research and Policy, The Research Institute at Nationwide Children’s Hospital, Columbus, Ohio and Dawn Comstock, Ph.D., Colorado School of Public Health, University of Colorado, Denver

Guidelines exist to help doctors diagnose and manage sports-related concussions, but guidelines are not fully supported by evidence-based research, are applied inconsistently, and those responsible for the care of injured athletes do not always fully communicate with each other. The goal of Drs. McKenzie and Comstock’s project is to test the effectiveness of Spot Light, an easy-to-use mobile application (or app), developed by Inlightened, LLC. This app was designed to help doctors, coaches, athletic trainers and parents of young football players track the progress of a young athlete from the time of a concussion injury until they are cleared to return to play. The researchers want to know if the app will result in more concussions being reported, a greater number of referrals to doctors and better adherence to return-to-play guidelines. The goal is to improve diagnosis of concussions that are occurring among young athletes, and ensure that they are receiving appropriate care and are fully recovered before getting back on the field.

- Eye Movement Dynamics: A Rapid Objective Involuntary Measure of Concussion/Mild Traumatic Brain Injury

Principal Investigators: Nicholas Port, Ph.D. and Steven Hitzeman, O.D., Indiana University School of Optometry, Bloomington

People can choose where to look, but they do not have much control over some of the intricate eye muscle movements that are usually made without thinking. Studies have shown that eye movement problems are common in mild traumatic brain injury patients. Drs. Port and Hitzeman, in collaboration with team trainers and physicians at Indiana University and local high schools, plan to take advantage of the involuntary, reflex nature of eye movements. They will develop a portable eye tracking instrument that can be used to help diagnose concussions on the sidelines and to monitor injury progression in high school and college athletes. Drs. Port and Hitzeman will compare the eye tracking data to results from a commonly used cognitive test to determine if changes in eye movement can serve as a biomarker for sports-related mild traumatic brain injury. If successful, this study will help provide an objective and more reliable measure to detect traumatic brain injury than is currently available.

- Imaging and Biomarkers in Adolescents Cleared for Return to Play After Concussion

Principal Investigator: Harvey Levin, Ph.D., Baylor College of Medicine, Houston

Sports concussions may cause persistent long-term effects in young athletes -- in some cases, even after they have been allowed to return to play. Using a variety of neuroimaging techniques, Dr. Levin and his group will look at the effects of sports-related concussions on brain structure and function one month following injury in adolescents who have been cleared to play. In addition, this project will evaluate microRNAs (miRNAs) as potential biomarkers for concussions and recovery. These are small portions of RNA (a molecule that is similar to DNA, which contains our genetic code) that play a role in turning genes on or off. The researchers plan to measure levels of specific miRNAs and determine if they correspond with cognitive test results and neuroimaging data.

- Somatosensory Processing — Assessing Youth Sport-Related Concussion and Recovery

Principal Investigator: Stacy Jennifer Marcus Suskauer, M.D., Kennedy Krieger Institute, Baltimore

The somatosensory system provides information about our environment — for example, what an object feels like to the touch — and may be affected by brain injury. Dr. Suskauer and her colleagues will investigate whether somatosensory system information processing (SSIP) could be used as a biomarker for concussion and recovery in youth aged 13-17. For these experiments, the researchers will use a new portable device that delivers vibrations to fingertips. Perception of the vibrations reflects activity of sensory neurons in the brain, thereby providing a measure of SSIP. The researchers will also investigate whether changes in SSIP are related to differences in certain brain chemicals after head injury.

- Characterization of the Brain and Serum Metabolome in Mouse Models of Concussion

Principal Investigator: Michael J. Whalen, M.D., Massachusetts General Hospital, Boston

Metabolites are small molecules formed in the body as a result of the normal breakdown of proteins, drugs and other large molecules. The collection of all metabolites in the body is the metabolome. Studies have suggested that head injury may change levels of various brain byproducts, but this has

not been researched in a systematic way. Dr. Whalen and his group plan to use an experimental model of traumatic brain injury to conduct a detailed analysis of changes in the brain metabolome following concussion. The researchers will compare those differences with serum byproducts to determine if the changes can be revealed in blood samples. The results of this project may uncover metabolites that contribute to serious effects of traumatic brain injury and may help identify potential targets for detecting and treating concussions.

###

The NINDS (<http://www.ninds.nih.gov>) is the nation's leading funder of research on the brain and nervous system. The NINDS mission is to reduce the burden of neurological disease – a burden borne by every age group, by every segment of society, by people all over the world.

The NICHD (<http://www.nichd.nih.gov>) sponsors research on development, before and after birth; maternal, child, and family health; reproductive biology and population issues; and medical rehabilitation.

The NIDCD (<http://www.nidcd.nih.gov>) supports and conducts research and research training on the normal and disordered processes of hearing, balance, taste, smell, voice, speech, and language and provides health information, based upon scientific discovery, to the public.

About the National Institutes of Health (NIH): NIH, the nation's medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit <http://www.nih.gov>.

About the Foundation for the NIH (FNIH): Established by the United States Congress to support the mission of the NIH—improving health through scientific discovery in the search for cures—the Foundation for the NIH is a leader in identifying and addressing complex scientific and health issues. The foundation is a not-for-profit, 501(c)(3) charitable organization that raises private-sector funds for a broad portfolio of unique programs that complement and enhance NIH priorities and activities. For additional information about the Foundation for the NIH, please visit www.fnih.org.