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Tackling Concussions On and Off the Field

On July 5, 1924, the Yankees were in Washington's Griffith Stadium for a doubleheader with the Senators. During the fourth inning of the first game, Babe Ruth had a run-in with the right field wall knocking him unconscious. The trainer splashed cold water on Ruth's face to wake him up. Manager Miller Huggins wanted to take him out, but Ruth refused, finishing the game and playing the second game. *The New York Times* headline read the next day: Yanks Break Even and Fail to Advance; Ruth Knocked Senseless.

Being knocked unconscious didn't stop Babe Ruth from returning to play in that same game. That wouldn't be allowed today.

"Here we are 90 years later and are we that much better in assessing whether or not players should go back into the game?" says James M. Noble, MD, MS, a neurologist with NewYork-Presbyterian/Columbia University Medical Center. "The methods that we use right now to identify concussion are non-invasive, symptom-based, and we're often held, to some degree, to the will of the player who may be pushing to get back into the game. Today, Babe Ruth would not be allowed to return to play. But players have a vested interest to get back into the game. Our concern is that their own well-being may not be as much a priority."

"Concussion has become an important issue of discussion in athletics as an understanding of the long-term effects of mild brain injury has begun to emerge," says Roger Härtl, MD, Director of Spinal Surgery and Neurotrauma in the Department of Neurological Surgery at NewYork-Presbyterian/Weill Cornell Medical Center. "Research has shown that repeated concussion even without more severe injury may put some athletes at risk for cognitive and psychological problems down the road. Therefore, it is important for those involved in athletics to recognize concussion, rule out more severe injury, and safely navigate return-to-play decisions."

In college football players, concussions are reported in more than one in three football players, with many players suffering multiple occurrences. Consider a study a few years ago that used helmet accelerometers to measure the number of hard hits some collegiate football players took in a given season. "Quite remarkably, 75 percent of the players on the team took at least 214 hits to the helmet and 25 percent of the players took more than 600 hits in one season," says Dr. Noble. "So one of our major challenges is to figure out the true incidence of meaningful head injuries and their consequences down the line."

Less than a mile from NewYork-Presbyterian/Columbia is the Robert K. Kraft Field at Lawrence A. Wien Stadium, home to Columbia University's football team. In 2003, Dr. Noble met with a player who had been referred to him for headaches. "He told me about headaches that seemed to be second nature to him as part of playing football," recalls Dr. Noble. "He called them 'padding up' headaches, explaining that they would always occur on the first day that he would put on his pads for football. I asked him if anything else happened on the first day. 'You know, you're taking hits,' he said. Then I asked if this concerned him, and he replied that he didn't have to worry because his coaches were monitoring his brain function.

"I remembered that encounter for a number of years," continues Dr. Noble. "Once I started to get established in my field, I became more interested in this topic. I thought back to that player and decided to explore what he had said further. As it turned out, Columbia University had been

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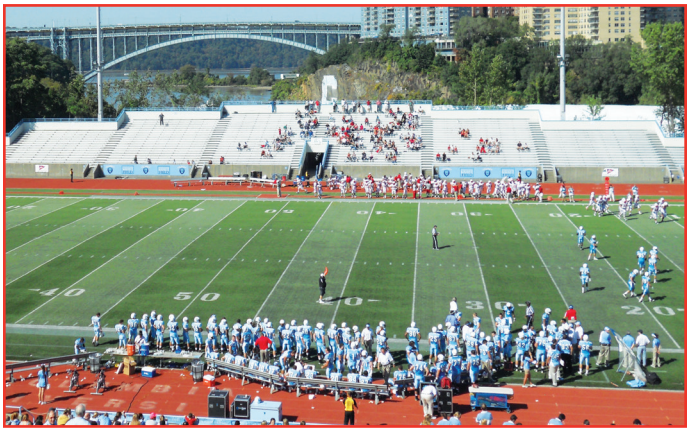
Tackling Concussions On and Off the Field *(continued from page 1)*

doing baseline and post-concussive neuropsychological testing on all of the football players since 2000 and there was a data set of psychometric testing that had not yet been examined. The program had been established for monitoring and management, but information had been fortuitously recorded so that research could be accomplished."



Data collected on past and present members of the Columbia Lions football team are contributing to research on concussion injuries in athletes.

At the October 2013 meeting of the American Neurological Association, Dr. Noble and his colleagues presented their first findings from a retrospective study of this data compiled on Columbia University football players between 2000 and 2011. "We basically took a first look at the data set to see how common concussions were," says Dr. Noble. "About 15 percent were getting concussions at some point during their collegiate football play. And about 35 percent of the players actually had known concussions prior to college. These numbers really caught our attention."

Each player had completed a baseline Concussion Resolution Index (CRI), which assesses reaction time, object recognition, and recall. CRI was repeated in those with suspected incident concussion. 647 CRIs were performed on 436 players, including 208 serial post-concussion evaluations on 70 athletes with at least one concussion. Following concussion, median duration prior to return-to-play was 10 days, with a range of five to 124 days. Players without prior concussion history had a slightly longer recovery.

"One item of particular interest about this data set was that the return-to-play strategy was based on several factors, including symptom recovery and passing the automated psychometric testing," says Dr. Noble. "While there is no one, single best test for identifying a concussion, psychometric testing is a fairly decent objective measure. Interestingly, the thresholds considered normal for returning to play for these collegiate-level players might not be considered normal in an average person."

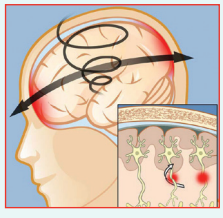
Basically results within about one standard deviation were considered normal. But Dr. Noble raises the question: "Should we be considering any deviation normal? I wanted to know how severe the injuries were that were occurring, as well as how often they were occurring. The question of how could we predict who would recover, and when, really troubled us. Based on neuropsychological testing, balance testing, or simply symptom recording, it seems as though most players who sustain a concussion would be better and back to normal within a week's time provided that they returned to play gradually and in a safe manner. However, about 10 to 15 percent of these players don't get better; in fact, they take a long time to recover. Additionally, among those students who do recover, data from functional MRI studies suggest that there are meaningful changes in the brain – even in the absence of a concussion or concussion symptoms being reported. That has raised a lot more concern in our community."

Dr. James M. Noble

As a prelude to developing a larger study, Dr. Noble and his colleagues undertook a review of the epidemiology of sport-related concussion (SRC) and the studies describing concussion incidence in various sports. "In high risk contact sports – football, soccer, hockey, lacrosse, and basketball – athletes experience concussion unintentionally during the course of play," says Dr. Noble. "Among these, football concussion has been a focus of study among the other contact sports because it has a high concussion incidence, the largest number of players, and some studies have shown long-term neurophysiologic and neurodegenerative outcomes. Mechanisms of injury differ significantly by sport and can be potential targets for concussion risk mitigation. Despite the apparent high incidence of SRC, however, risk factors determining initial concussion, recovery periods, recurrence, and long-term outcomes remain poorly understood and warrant further study."

From their data on injuries in former Columbia football players, the researchers are now seeking research funding to develop a larger study of Columbia alumni varsity athletes, including other sports. The same tests they studied in football players are also available on virtually every varsity athlete at Columbia since 2002. Such a

Teaming Up with NFL in Concussion Studies

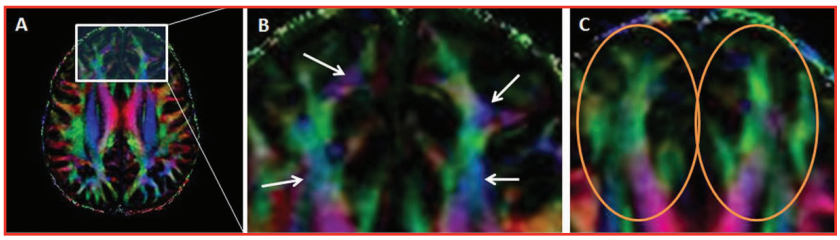


The National Football League, in a new initiative with General Electric – the GE-NFL Head Health Challenge – is supporting research to better understand early-stage traumatic brain injuries and improve brain protection. NewYork-Presbyterian/Weill Cornell is among 16 organizations selected from more than 400 applications to be awarded a grant to support research in this area. Weill Cornell investigators, led by Paul D. Mozley, MD, Chief of the Division of Nuclear Medicine, and his team are using nuclear medicine and advanced MRI techniques to diagnose dangerous head injuries in athletes immediately after they take place, even before damage to the brain is visible. The potential breakthrough technique may overcome one of the fundamental barriers to diagnosing concussions. The Weill Cornell team will be comparing scans from former professional boxers with known, long-term head injuries against those of NFL players in whom a concussion is suspected.

Tackling Concussions On and Off the Field *(continued from page 2)*

comprehensive study could include neuropsychological testing – around the time of injury and up to several years after the fact – as well as multimodal imaging and investigations of candidate genes that look promising for predicting risk for long-term outcomes associated with concussion, including chronic traumatic encephalopathy.

"We want to identify a host of measures that will be readily generalizable across different patient populations," says Dr. Noble. "Ultimately, we want to prevent injuries from happening in the first place, but our current concern is to more accurately diagnose concussion, particularly subtle injury and recovery, and safely return athletes back to play."



Diffusion tensor imaging of a patient with concussion. Image B is a blowup of frontal region seen in image A. Note heterogeneous color suggesting discontinuity of tracts (arrows). Fibers should normally all run anterior-posterior (green fibers) as seen in the area circled in a control patient.

Concussions Up Close and Personal

As neurosurgeon to the New York Football Giants, Dr. Härtl holds a special position on the team roster, helping to keep players safe from serious brain injury. In this role, Dr. Härtl has identified his share of concussions, but agrees with Dr. Noble that determining the seriousness of a concussion on the field can be a challenging process.

"A definition of concussion is difficult because of the lack of objective clinical and radiographic findings," says Dr. Härtl. "There are usually no findings on routine imaging, such as CT, which makes the definition of concussion less clear than for other types of brain injury. Symptoms may be subtle so it's critical to work closely with the team physicians who are very familiar with each and every player's history. In some cases, you may not realize there was an injury because it may have occurred out of the line of vision, or players may be reluctant to admit a possible injury. Unlike in years past, any player who we suspect of having a concussion is out of that game."

Dr. Roger Härtl

In concert with the team physicians, a progression of testing for concussion starts right on the field if the player presents with loss of consciousness, headaches, nausea, vomiting, and a general feeling of dizziness. The exam continues on the sidelines with the assessment of basic neurological function, including speech, memory, and balance. More extensive neurological testing may take place in the locker room with the aid of standardized tools such as the Sports Concussion Assessment Tool 2. A few days after the injury a more sensitive neuropsychological test is administered by the team psychologist to determine if there is still an impact from that particular injury on cognitive function.

The ambiguity of the concussion disease process, however, has led physicians and researchers to look into alternate modalities – including diffusion tensor imaging (DTI) – to be able to objectively measure the severity of a concussion. "DTI is an MRI with specific sequence software that enables us to acquire scans of the nerve tracts in the brain and determine if they have been injured or disrupted," says Dr. Härtl. "There are reports of DTI being a sensitive marker of a concussion in patients who otherwise would have completely negative CT scans."

The Giants and their team physicians are very committed to research to better understand brain injury, brain trauma, and brain concussions. For the last three years, they have been actively participating with Dr. Härtl to collect DTI scan data from players between seasons to establish baseline data. If a player has a concussion during a game, the DTI is repeated soon after the injury and again a few months later. The research is ongoing – 40 players have been scanned to date – and both the Giants and Dr. Härtl, with major support from Russell F. Warren, MD, an orthopedic surgeon at Hospital for Special Surgery and Giants team physician, are hopeful that it will add to a growing knowledge base on short- and long-term consequences of head injuries."

Return to Play or Not to Play?

Once players recover from concussion when do you let them go back to physical activities continues to be the overriding question facing neurologists, neurosurgeons, and team physicians. "You gradually increase a player's level of activity," says Dr. Härtl. "If they can tolerate that without having any headaches, nausea, or vomiting, at some point you let them return completely. But clearly, a comprehensive understanding of concussion and its related risks is important in making return-to-play decisions and developing league policy."

Dr. Härtl and his colleagues recently completed a review of the literature on current findings related to recognizing and managing sports-related concussion to help sort this out. "The existence of 'second-impact syndrome,' in which a first minor head injury predisposes an athlete to later catastrophic injury, remains controversial," says Dr. Härtl. "Athletes still suffering from concussion may be at increased risk of injury due to delayed response times and, as after an initial traumatic brain injury, are at increased risk of future concussion." Additionally, Dr. Härtl advises that even if a patient with concussion has negative head imaging, further imaging is warranted in those with severe mechanism, significant loss of consciousness, focal neurologic deficit, or worsening symptoms. "It is clear that concussion can have serious effects on a player and should be considered carefully in return-to-play decisions."

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Dr. James J. Riviello Named Chief of Child Neurology at NewYork-Presbyterian/Morgan Stanley Children's Hospital

Dr. James J. Riviello, Jr.

James J. Riviello, Jr., MD, a noted authority in pediatric epilepsy, clinical neurophysiology, and pediatric neurocritical care, has joined NewYork-Presbyterian/Morgan Stanley Children's Hospital as Chief of Child Neurology.

Dr. Riviello brings three decades of experience as a clinician, researcher, teacher, and administrator. He has been involved in the development of national and international guidelines for pediatric epilepsy surgery, evaluation and management of status epilepticus, and continuous EEG monitoring for neonatal seizures.

"The Division of Child Neurology at NewYork-Presbyterian/Columbia University Medical Center has a long tradition of excellence in clinical care, teaching, and research," says Dr. Riviello. "In fact, the medical center's Neurological Institute of New York played a major role in establishing the field of child neurology. It is a great honor to lead this division."

Dr. Riviello joins the Hospital from NYU Langone Medical Center, where he served as Director of the Pediatric Neurology Division and was a member of the Comprehensive Epilepsy Program.

Board certified in pediatrics, child neurology, and clinical neurophysiology, Dr. Riviello is a member of numerous professional societies, is the past chair of the Section on Child Neurology of the American Academy of Neurology, and a charter member of the Neurocritical Care Society.

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Feil Family Brain and Mind Research Institute Established at Weill Cornell Medical College

The newly established Feil Family Brain and Mind Research Institute at Weill Cornell Medical College serves as a unique, multidisciplinary translational neuroscience research hub. Under the direction of Costantino Iadecola, MD, a leading neuroscientist in the field of cerebrovascular diseases, stroke, and dementia, the Institute will work to develop novel therapeutics for neurological diseases and conduct investigations designed to enhance current treatments and bridge the existing gap in translational medicine. Research will focus on neurodegenerative conditions such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, stroke, and vascular dementia. Brain developmental disorders, pain, addiction, and neuroimmunological diseases also will be investigated.

> **"By bridging the translational bench-to-bedside gap, the Feil Family Brain and Mind Research Institute promises to have a transformative impact on current care paradigms and change the landscape of neuroscience medicine."**
> **— Dr. Costantino Iadecola**

The Institute, named in honor of long-time benefactors Gertrude and Louis Feil and created with a generous $28 million gift from the Feil Family, is headquartered in the new Belfer Research Building, a focal point for disease-oriented research at Weill Cornell. The Institute is designed to rapidly accelerate the translation of breakthrough research discoveries from the laboratory to the neurological patient's bedside, developing the most advanced personalized therapeutic solutions for patients with brain diseases. Central to its mission, the Institute will develop innovative preventive and diagnostic tools, leveraging advances in neuroimaging, genetics, genomics, epigenetics, metabolomics, computational biology and bioinformatics technology, as well as biomarkers for early disease detection and intervention.

Dr. Costantino Iadecola

Dr. Iadecola works with a team of leading physician-scientists, including Matthew E. Fink, MD, Neurologist-in-Chief at NewYork-Presbyterian/Weill Cornell Medical Center. "There is a rising tidal wave of age-related brain diseases striking our maturing population, especially the 77 million baby boomers who will all need care for age-related brain diseases at the same time," says Dr. Iadecola. "Brain and mind diseases are a growing health challenge worldwide and a major contributor to loss of life and severe disability. By bridging the translational bench-to-bedside gap, the Feil Family Brain and Mind Research Institute promises to have a transformative impact on current care paradigms and change the landscape of neuroscience medicine."

The Institute will also recruit leaders in the field of neuroscience and serve as a mentoring center for faculty and clinical and basic neuroscientists. It will train medical students, fellows, and residents to be the future generation of physician-scientists in translational medicine. To that end, the Leon Levy Foundation has awarded the Institute a $1.5 million grant for training and development of translational neuroscientists.

"Quality of life depends on brain health," adds Dr. Iadecola. "We intend to take the vital steps to chart new paths to prevent neurological diseases and minimize their devastating impact on patients' lives."

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Clinical Trials Update

NewYork-Presbyterian/Columbia and NewYork-Presbyterian/Weill Cornell to Lead NIH Regional Coordinating Stroke Center

Dr. Randolph S. Marshall

NewYork-Presbyterian/Columbia University Medical Center and NewYork-Presbyterian/Weill Cornell Medical Center have been awarded a grant from the National Institute of Neurological Disorders and Stroke (NINDS) to establish one of only 25 Regional Coordinating Stroke Centers funded in the United States as part of the NINDS Stroke Trials Network or StrokeNet. The nationwide network of stroke centers is intended to improve the efficiency of stroke research. As a regional stroke center, the New York Stroke Trials Network of Columbia and Cornell will lead NIH-sponsored clinical trials in stroke prevention, acute stroke treatment, and stroke recovery.

"For the first time, the three main facets of comprehensive stroke care – stroke prevention, acute stroke treatment, and stroke recovery and rehabilitation – will be integrated into an NIH-funded national clinical trials network," says co-principal investigator Randolph S. Marshall, MD, Chief of the Stroke Division at NewYork-Presbyterian/Columbia. "The New York Stroke Trials Network of Columbia and Cornell will benefit from the expertise of our physicians and scientists in all three areas." At the national level, Dr. Marshall will co-direct the Education and Training Core for the Stroke Trials Network; he also has been appointed to the StrokeNet Executive Committee.

NewYork-Presbyterian Hospital treats one of the highest volumes of stroke and cerebrovascular disease patients in the world and the highest in New York City. Stroke patients treated at high volume centers with specialty-trained physicians demonstrate the best recovery and survival rates. "This grant will allow us to provide our stroke patients with the most up-to-date, cutting-edge treatments available through high quality clinical trials," adds Dana Leifer, MD, Associate Professor of Neurology at Weill Cornell Medical College, who serves as a co-principal investigator with both Dr. Marshall and Matthew E. Fink, MD, Neurologist-in-Chief at NewYork-Presbyterian/Weill Cornell. "A team of more than 30 co-investigators at NewYork-Presbyterian Hospital will participate in developing well-designed trials that will test new treatments for stroke patients and then will conduct these trials along with the other StrokeNet centers to produce practical improvements in stroke patient care."

In addition, the New York Stroke Trials Network of Columbia and Cornell is one of only four StrokeNet centers with neurosurgeons as co-principal investigators. Serving in this role are E. Sander Connolly, Jr., MD, Surgical Director of the Neuro-Intensive Care Unit at NewYork-Presbyterian/Columbia, and Philip E. Stieg, PhD, MD, Neurosurgeon-in-Chief at NewYork-Presbyterian/Weill Cornell. NewYork-Presbyterian's Stroke Trials Network will also include a unique sub-network of academic stroke rehabilitation sites and a sub-network of acute stroke hospitals in New Jersey and Brooklyn with capabilities for acute endovascular stroke therapy.

Patient enrollments are expected to begin in Fall 2014.

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