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STATE OF PLAY: BRAIN INJURIES AND DISEASES OF AGING

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C O N T E N T S

C O N T E N T S

STATEMENTS FOR THE RECORD (CONT'D)

STATE OF PLAY: BRAIN INJURIES AND DISEASES OF AGING

WEDNESDAY, JUNE 25, 2014

U.S. SENATE,
SPECIAL COMMITTEE ON AGING,
Washington, DC.

The Committee met, pursuant to notice, at 1:17 p.m., Room 562, Dirksen Senate Office Building, Hon. Bill Nelson, Chairman of the Committee, presiding.

Present: Senators Nelson, Blumenthal, Warren, Donnelly, and Collins.

OPENING STATEMENT OF SENATOR BILL NELSON, CHAIRMAN

The CHAIRMAN. Good afternoon. Today, we are going to have to be a little creative because we are going to have a series of votes at 2:30, so, what I will do is recess the Committee and we will go over and vote until the very last vote, and we will cast the vote at the very beginning of the last vote and then race back over here so that we can continue the hearing.

There is also some breaking news. Just an hour ago, the NFL agreed to eliminate the $675 million cap on concussion-related claims available to thousands of players as part of a major lawsuit, and so, without objection, I will enter the NFL's statement in the record.

Part of what we are going to discuss today is traumatic brain injuries—a bump, a blow, a jolt to the head or a penetrating head injury that disrupts the normal function of the brain. More mild TBIs, more commonly referred to as concussions, have been the center of increasing discussion within the sports community in recent years as a growing number of current and former athletes say that they are suffering from memory loss and other impairments caused by repeated blows to the head, and, of course, we are seeing the TBIs that are coming home from overseas with our men and women in uniform in the performance of their duties, as well.

The Centers for Disease Control and Prevention have looked at 1.6 to 3.8 million sports and recreation-related TBIs, and they say that they occur in the U.S. each year. Such head injuries are not limited, obviously, just to one sport. They occur in a wide range of sports, and most recently, we were reminded of that in the story in the New York Times with the graphic pictures of the games going on in Brazil right now, in which one of the soccer players was completely knocked out.

Over the last few years, much has been done to increase awareness of the risk posed by sports-related concussions, and thanks to a number of partnerships and initiatives, research is underway to help us better understand the cause and the long-term impact of concussions and what we can do to prevent them. These initiatives involve a number of organizations, so, while we are making progress, it is important to note that much more research is needed and to see all of the links to other things, such as Alzheimer's.

Today, we are going to hear from two former professional athletes who had their careers cut short due to concussions, and now they are going to wonder about their function in the future. We are going to take testimony from two prominent medical researchers who will discuss the latest research, and I am going to give that privilege of introduction to Senator Warren after I turn to our great Ranking Member, Senator Collins.

OPENING STATEMENT OF SENATOR SUSAN M. COLLINS, RANKING MEMBER

Senator COLLINS. Thank you very much, Mr. Chairman.

I very much appreciate your calling this important hearing so that we can better explore the relationship between traumatic brain injury and diseases associated with aging, such as Alzheimer's, Parkinson's, and Lou Gehrig's disease, also known as ALS.

Traumatic brain injury, or TBI, affects five million Americans at an annual cost of more than $76 billion. As the Senate Co-Chair of the Alzheimer's Task Force, I am particularly interested in the research conducted over the past three decades that has linked moderate and severe traumatic brain injury to a greater risk of developing Alzheimer's disease and other forms of dementia.

One troubling study cited by the Alzheimer's Association found that older individuals with a history of moderate traumatic brain injury are more than twice as likely to develop Alzheimer's than are seniors with no history of brain injury. Those with a history of severe traumatic brain injury were found in this study to have a 4.5 times greater risk.

Finding a way to prevent and effectively treat Alzheimer's disease is among my highest priorities as a Senator and has been a focus of this Committee's work. In many ways, Alzheimer's is the defining disease of the Baby Boom generation. If we are to prevent it from becoming the defining disease of the next generation, we must strengthen our commitment to research leading to a better understanding of this devastating disease.

While researchers still have a great deal to learn about how head injuries affect an individual's risk of developing neurological diseases like Alzheimer's later in life, there is increasing evidence of a relationship. Women, even more than men, may be even more likely to experience long-term symptoms, such as cognitive and visual impairments, after sustaining a severe head injury. We know that, currently, almost two-thirds of Americans living with Alzheimer's are women.

There are many important research projects being conducted on TBI and the link to neurological diseases. For example, the National Institutes of Health and the National Football League have

embarked upon a $60 million, four-year, public-private partnership to advance research that may lead to the improvement of TBI diagnoses through better imaging technologies and also improved treatment for those who have sustained serious head injuries.

Indeed, while those who have participated in contact sports or served in the military may face a particular risk for TBI and related health conditions, the leading cause of TBI among seniors is falls. According to the CDC, individuals over age 65 have the highest rates of TBI-related hospitalizations and death.

More research is required to establish definitively the link between head injuries and neurological diseases, but it is clear that this important research could lead to a better understanding of such devastating diseases as Alzheimer's, Parkinson's, and ALS. This critical research could also benefit our veterans and troops on the ground, far too many of whom have experienced TBI and its painful, lasting effects.

Again, Mr. Chairman, thank you for holding this hearing. We have a great panel of witnesses and I look forward to getting their insights and learning more about the current research on this topic.

The CHAIRMAN. Thank you, Senator Collins.

I want to especially recognize Kevin Turner. Kevin was a star fullback at the University of Alabama. He played eight seasons with the New England Patriots and the Philadelphia Eagles in the 1990s. Since being diagnosed in 2010 with ALS, Lou Gehrig's disease, Kevin has worked tirelessly to raise awareness about the disease and its possible connection to traumatic brain injuries, and so, Kevin, we thank you very much for being with us here today. Thank you.

Senator Warren, if you will introduce two of our panel.

OPENING STATEMENT OF SENATOR ELIZABETH WARREN, COMMITTEE MEMBER

Senator WARREN. I will do that. Thank you very much, Mr. Chairman and Ranking Member Collins, for having this hearing today.

I am pleased to have the opportunity to introduce Dr. Robert Stern and Chris Nowinski, Co-Directors of the Boston University Center for the Study of Traumatic Encephalopathy.

Dr. Stern is a Professor of Neurology and Neurosurgery at Boston University School of Medicine and he is the Director of the Clinical Core of the Boston University Alzheimer's Disease Center. He received his undergraduate degree from Wesleyan University and his Master's and Doctoral degrees in clinical psychology from the University of Rhode Island. Before joining the Boston University School of Medicine, he served on the faculty of Brown Medical School and the University of North Carolina School of Medicine. Dr. Stern's research has led to more than 250 peer-reviewed publications and has helped us to better understand the effects of trauma and aging on the human brain.

Now, he is here today with Mr. Nowinski, who is the Co-founder and Executive Director of the Sports Legacy Institute. This is a nonprofit organization that is focused on addressing the issue of brain trauma through education, through policy, and through re-

search. He received his undergraduate degree from Harvard University, where he played defensive tackle for the football team, and, after college, Mr. Nowinski became a professional wrestler, and his own experience in that sport with head trauma led him to co-found the Sports Legacy Institute. He currently serves as an advisor on the NFL Players Association Mackey-White Traumatic Brain Injury Committee and the Ivy League Multi-Sport Concussion Committee. Chris has received numerous accolades, including the United States Sports Academy Distinguished Service Award for his work advocating for improving safety standards in sports.

I am very pleased that Dr. Stern and Mr. Nowinski are here with us today. I know they will add enormously to our discussion, so thank you both.

Thank you, Mr. Chairman.

The CHAIRMAN. It is my pleasure to introduce Ben Utecht, who is a former NFL tight end for the Cincinnati Bengals and the Indianapolis Colts, and, if I recall, you were on one of those teams that went into the playoffs, and perhaps you can tell us the rest of that story.

Dr. Jacob VanLandingham is the Director of Neurobiological Research at Tallahassee Memorial Hospital and he is a professor of Florida State University's College of Medicine.

What we will do, we will start with you, Mr. Nowinski, and just go right down the list. Your written statement is entered into the record, so if you would just share with us for a few minutes and then we will get into questions. Mr. Nowinski.

STATEMENT OF CHRISTOPHER NOWINSKI, FORMER PROFESSIONAL WRESTLER, WORLD WRESTLING ENTERTAINMENT, AND FOUNDING EXECUTIVE DIRECTOR, SPORTS LEGACY INSTITUTE

Mr. NOWINSKI. Thank you for that wonderful introduction, Senator Warren.

Chairman Nelson, Ranking Member Collins, and members of the Committee, thank you for inviting me to speak today. My name is Chris Nowinski, Founding Executive Director of the Sports Legacy Institute, a nonprofit organization dedicated to solving the sports concussion crisis through advocacy, education, policy, and research.

I also have a personal relationship with concussion and tremendous concerns that I have increased my risk of developing a degenerative brain disease in the future. It is my hope that this hearing raises awareness of the urgent need for funding for research on traumatic brain injuries as well as the tremendous opportunities we have for the prevention of their long-term consequences.

I never had a second thought about concussions or brain injuries until I was 24 years old. After playing contact sports in high school and then at Harvard, I became a pro wrestler, technically known as a superstar, with WWE, and I got to travel the world playing a bad guy or a hell known as Chris Harvard, who would creatively insult the fans' intelligence and cheat to win. Let me remind you, this is a character I played. I rarely cheat anymore, and, it was a performance to entertain our fans and it was a lot of fun.

In a match, I was kicked in the head by my opponent and my world immediately changed. My head became throbbing. Everything got foggy, and, most importantly, I forgot the script. I could

not remember how we were supposed to finish the match, and, honestly, that was terrifying. After the match, I was stopped by our athletic trainer who asked if I was all right, and, I lied and I said, "I am fine," even though the headache was killing me.

The symptoms then expanded beyond daily headaches to include depression and sleepwalking and they would not go away, but I lied about my symptoms for five weeks, thinking I was doing the right thing.

I finally met Dr. Robert Cantu, eventually my SLI Co-founder, who helped me understand that all the dings and all the bell-ringers I had been getting over the years were actually concussions. To think that at 24, I was learning for the first time how fragile my brain was and how critical rest was after a concussion, and that I am now at higher risk for developing a degenerative brain disease. My ignorance cost me my career. It cost me at least five years of my health, with terrible post-concussion syndrome, and I do not know what it is going to cost me in the future.

CTE, chronic traumatic encephalopathy, is what I fear most. It was first named "punch drunk" in 1928 and then largely ignored. In the last decade, we have realized that it obviously affects—that we have known it affects boxers, but now we know it affects other athletes, military veterans, even members of the general public. Since we cannot diagnose it in living people, we do not know how many people have it, but early evidence indicates it is not insignificant.

At our VA–BUSLI Brain Bank, a collaboration with the CT Center at Boston University and the VA Boston Health Care System led by Dr. Ann McKee, 58 of the 62 brains of former NFL players studied have been found positive for this disease, and athletes as young as 17, and she has also—Dr. McKee has also connected to motor neuron disease, and I want to mention, having my friend Kevin Turner here in the room, who courageously is taking on this issue. I will defer the rest of the science to my colleague, Dr. Stern.

The reality is, we need answers quickly. We do not know how big this problem is, but it may be massive, with 1.7 million TBIs a year, at least 3.8 million concussions, and, we have to recognize that contact sports are constantly evolving and we still do not know what the full life effects are of exposing children to repetitive brain trauma, because the sports seven-year-olds played in the 1950s are not the ones that we are playing today, and, football helmets were different, so players did not hit each other in the head. Soccer was not as popular, so we do not know what the effects of a lifetime of headers are. Until Title IX, few women were playing contact sports, so, we do not know these answers, but it is a public health crisis.

While we work to independently fund more work, and we applaud the State laws that have changed how we play sports, it is not enough. We do not know—you know, one of the things I do is I train WWE's wrestlers on concussions, which is fun. Before they get in the ring, they now have to listen to me, but, we think we can train adults, even though it is difficult. We do not know if we can train children, and, so, the reality is, we do not know. We have kids playing contact sports who do not recognize when they have a concussion, who will never have a doctor on the sidelines, and

that means, with all the changes that we have made, CTE will continue to be a problem for athletes and most certainly will be a problem for our military veterans.

A new initiative that we announced today that we hope will help prevent this, we teamed up with the Santa Clara Institute of Sports Law and Ethics on a campaign to educate parents and coaches on the risks of heading in soccer before high school. We were joined by Women's National Team players—former National Team Players Brandi Chastain, Cindy Parlow Cone, and Joy Fawcett, who won the 1999 World Cup, along with our Medical Director, Dr. Cantu, to say the reality is we do not need these headers to happen. The current guideline is ten. It may start even earlier for many kids, but, it should not happen.

To conclude, we must not underestimate the long-term impact of brain injuries. With one in four boys and one in 16 girls in America playing contact sports, we are putting a lot of children at risk for CTE. We owe them, as well as our military veterans, greater investment into finding ways to effectively minimize the negative consequences of this inevitable brain trauma.

Thank you.

The CHAIRMAN. Thank you, Mr. Nowinski.

Mr. Utecht.

STATEMENT OF BEN UTECHT, FORMER NATIONAL FOOTBALL LEAGUE TIGHT END, CINCINNATI BENGALS AND INDIANAPOLIS COLTS

Mr. UTECHT. Well, first of all, thank you so much for this opportunity. It is truly a privilege to be here before you to speak about something that has impacted my life in ways that are very scary and unknowns that, as a husband and father, have put me in a situation where I do not know what my future is going to look like.

As a river kid from a small town in Minnesota, Hastings, Minnesota, I do not know how it happened, but I found my way into the NFL, six years. I had an opportunity to play in the Super Bowl Championship of 2006 with the Indianapolis Colts, before I went on to play two years with the Cincinnati Bengals. I am now a husband and a father of three beautiful girls, so, thankfully, I do not have any football players in the family right now, but the new perspective of a father has really become a part of my life.

Right now, I have just taken the National Spokesperson position for the American Academy of Neurology, which is the largest association of neurologists in the world. Twenty-seven-thousand now make up the Academy. They are the leaders in neurology in the world, along with their national foundation, the American Brain Foundation, whose goal is to cure brain disease through exactly what Chris talked about, the importance of raising money for research.

I hope I never forget the night of February 4, 2007. It was an amazing night in Miami, Florida, as we stepped onto the Dolphins Stadium, onto the biggest stage in the world. I do not even know how to put it into words to describe it to you. Over 100 million people tuned in to watch the Indianapolis Colts face off against the Chicago Bears.

I will never forget, two weeks prior, our All-Pro kicker, Adam Vinatieri, telling the team, "Don't you dare blink at kickoff." Now, Adam has already won three Super Bowls, so he has quite the experience, but, there I am on the field, standing in between future Hall of Fame quarterback Peyton Manning and future Hall of Fame coach Tony Dungy, and I remember Adam's words. "Don't you dare blink at kickoff."

There Adam is, walking off the steps. The whistle blows. His hand drops, and he releases the players, and he places his foot on the ball and I have never in my life seen so many flashing lights. I mean, it would rival the experience of Neil Armstrong. It truly felt like I was dancing with the stars. It was the greatest experience of my life. We won the game, 29 to 17, and forever, I will be able to wear this ring on my finger in remembrance of that game. It was a dream come true.

Two years later, that dream was shattered when I woke up face down on a training camp field in Georgetown, Kentucky, being strapped to a board and put onto an ambulance because of my fifth documented concussion. For the first time in my life, my brain became a priority, and, the reason why it became a priority is because at 29 years old, I started to have memory problems, and, it took losing my mind to care about my mind.

My memories began to fade away. In fact, one story I have shared is going home to Minneapolis and spending time with friends of ours. My wife and I were sitting around a table, and Matt, my friend, brought up his wedding and I said, "Well, why was I not able to be there," and I got the strangest look from him, and, the table got quiet and his wife brought over their photo album from their wedding, and page after page, there I was as a groomsman in his wedding, and I sang a song in his wedding, and I have no memory of that experience. It is completely gone.

Then, there are behavioral changes. There is hearing my five-year-old daughter tell our family practice doctor that, at times, she is afraid of me. As a father, it puts the idea of the effects of traumatic brain injury on a completely different level.

I cannot help now but throw myself into a new target, neurology, to tackle a new opponent, brain disease, and particularly traumatic brain injuries and concussions. I have been impassioned through advocacy to fight for lives being ripped apart by brain disease, Alzheimer's, Parkinson's, epilepsy, and chronic traumatic encephalopathy.

We need a national revival of funding to go into these issues so that we can find the answers. You, as Senators, can really become our new coaches. You can help decide the game strategy, put in the countless hours of work and research into creating policies that can change this nation, connecting people to their most valuable asset, their mind. It is not just education and awareness, but it is changing the nature of a person. It is getting them to truly care so that they can take the education and awareness and implement it because they are passionate about who they are, which comes from their brains.

I will not stop in the pursuit of finding cures for brain disease and creating an emotional connection between the world and neurology, because neurology, our neurologists who cradle the miracle

that makes us human, our brains. It is time for all of us to realize how special our brains really are.

I have a number of policies I would love to share with you in question and answer time. Thank you.

The CHAIRMAN. Thank you, Mr. Utecht.

Dr. VanLandingham.

STATEMENT OF JACOB W. VANLANDINGHAM, PH.D., DIRECTOR OF NEUROBIOLOGICAL RESEARCH, TALLAHASSEE MEMORIAL HEALTHCARE NEUROSCIENCE CENTER, AND ASSISTANT PROFESSOR, FLORIDA STATE UNIVERSITY COLLEGE OF MEDICINE

Dr. VANLANDINGHAM. Thank you, Mr. Nelson, and thanks to the Committee for giving me the opportunity to speak today about traumatic brain injury.

I am a researcher. In 1995, I had my own personal experience with brain injury. I was not playing football. I was actually assaulted. I was down in Gainesville and there was a vagrant who assaulted me and I had three hemorrhages in my brain. I spent two weeks in intensive care and 18 months with amnesia. I was one of the lucky ones. I got my memory back. Most people who experience what a lot of us have experienced are not that lucky.

I went on to do a degree, a Ph.D., in neuroscience and focus on research. Most of my clinical and basic research over the last 17 years has been focused on traumatic brain injury. Recently, I put—the last five years—more focus into concussions and mild traumatic brain injury.

To give you a little background, after—what causes a concussion is the brain sort of slings forward and is accelerated, and it is going to hit against the inner skull on the frontal part of the brain and then it is going to be kicked back the other way, and it is going to go through this sort of acceleration, deceleration, rattling inside the skull.

A lot of people think that the brain is only damaged by hitting the inner part of the skull, but actually, the brain is sort of like Jell-O and it stretches. The accelerating frontal portion of the brain goes faster than that back portion of the brain and it stretches the brain in between, and it is that stretching that causes a sort of breakdown in metabolism in the brain and it makes it where the brain's functions are slower. Electricity does not run in the brain quite as well as it used to. When we have had a concussion, often, we will be able to get to the right answer. We are just delayed. Our thought processes are delayed in getting to that correct answer.

I think it is important that we also note that not only are we having concussions in athletics, we mentioned the military earlier, we mentioned the elderly and the falls epidemic that we have in the elderly, and we also have a problem with falls in children. We do not want to forget the pediatric population. By midnight tonight, nearly 30 children in this country will die from a traumatic brain injury, and, a lot of folks will continue—a lot of these kids—to have problems for the remainder of their life, so, it is very important that we put the focus across the age span, across the lifespan, if you will.

If we think about pediatric traumatic brain injury, we will notice that they often take a lot longer to get better after a concussion.

What may take an adult like myself seven to ten days to get better, it may take them seven to ten months. They get behind in school. They do not graduate with their fellow schoolmates. A lot of issues with pediatric brains that are different and need to be respected as different when coming up with treatments when compared to the adult. The same goes for the elderly.

When we think about sports, we always go to the NFL and professional sports. I believe that we have an even worse problem, if you will, in high school athletics because it is still an immature brain. The brain is not fully developed. If you do not have a fully developed brain and it is injured, it has a harder time recovering. That means if we have got a high school player playing football who is 240 pounds—still big—hits with a tremendous amount of force, and is engaging in having head contact with an immature brain, and that makes it that much worse.

After you have a concussion, most everybody thinks if you go rest, you just get better. About 20 percent of people do not get better. They end up with what is called post-concussion syndrome, which Chris alluded to earlier and how that ruined his career. It takes months to years to get over post-concussion syndrome.

What we also see when we have post-concussion syndrome is we see a lot of sleep difficulties. If I had a dime for every person I knew that had had a head injury that had sleep problems—and the sleep problems, we never recognize that. We never put effort into trying to improve sleep patterns, and that is such a huge part of getting better, getting the appropriate sleep at night so that brain can repair.

Unfortunately, concussions are notorious for being difficult to diagnose and treat. Each injury may have a different constellation of findings, and these findings can be very subtle. While each injury may be subtle and unique, the common factor is that when folks are injured and they are athletes or they are in the military, they do not want to actually tell the truth. They want to sort of intentionally mask it.

The same thing goes with an elderly patient. An elderly patient does not want to lose their independence. They are not engaged in wanting to give up driving or whatever it may be. The World Health Organization has stated that as the lifespan increases, we are going to see that TBI will surpass many other diseases as the major cause of death and disability by the year 2020.

In conclusion, I would like to say that TBI transcends generations and populations, from the infant to the elderly. A concussion is compounding. If you have one concussion, you are more likely to have two, and so on and so forth. In my professional opinion, we are dealing with two major research and development issues—two. First, because concussions are compounding, we need to develop new acute pharmaceutical treatments. We treat everything else with drugs. Why do we not put a focus on developing a drug for this condition. If we can give an acute treatment after a concussion, we can reset the brain, cure it at that point, and then it is not a compounding issue. You are not more likely to get a second concussion, and so on and so forth.

The other thing that we are up against, and I know Dr. Stern will speak more to, is the issue of chronic traumatic

encephalopathy, Alzheimer's disease-like pathologies. These pathologies are also being seen down in the spinal cord and leading to Lou Gehrig's disease, or anterior lateral sclerosis. We need to put a precedence on developing drugs that can stop this pathology, so, we need to stop concussions in the beginning, prevent it from being compounding, and then we need to put a focus on new drugs that can stop or halt the progression of the pathologies associated with chronic traumatic encephalopathy.

Our company, Prevacus, is currently developing an acute treatment for concussion. We will design it as a field deliverable. It will be a nasal inhalant to get more of the drug to the brain, and a medic, an ambulance technician, an athletic trainer can give it immediately and we can stop the pathological consequences in their tracks. We also hope to be developing two new neurosteroid drugs this summer, which will be focused on Alzheimer's and Lou Gehrig's disease.

I would like to thank you once again for the time you have given me to speak. Thank you, Senator.

The CHAIRMAN. Thank you, Dr. VanLandingham, and, we have to deal with issues up here like the cuts in funding to NIH and having to restore those, so, we are very sensitive to what you say.

Dr. Stern.

STATEMENT OF ROBERT A. STERN, PH.D., PROFESSOR OF NEUROLOGY, NEUROSURGERY, ANATOMY AND NEUROBIOLOGY, CLINICAL CORE DIRECTOR, BU ALZHEIMER'S DISEASE CENTER, BOSTON UNIVERSITY SCHOOL OF MEDICINE

Dr. STERN. Good afternoon, Mr. Chairman, Ranking Member Collins, and distinguished members of the Committee. It is a great honor to appear before you today.

My name is Dr. Robert Stern. I am a Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology at Boston University School of Medicine. I am also the Director of the Clinical Core of the Boston University Alzheimer's Disease Center, one of 29 centers funded by the National Institute on Aging.

For the past 25 years, I have been conducting clinical neuroscience research into issues pertaining to the aging brain, in particular, Alzheimer's disease. Since 2008, my research has focused on the long-term consequences of repetitive brain trauma in athletes. In particular, I have been studying the neurodegenerative disease chronic traumatic encephalopathy, or CTE. CTE is a progressive brain disease that can lead to dramatic changes in mood, behavior, and cognition, eventually leading to dementia. It is similar to Alzheimer's disease, but it is a unique disease, easily distinguished through post-mortem neuropathological examination.

Originally called "punch drunk" or dementia pugilistica in the early 1900s, when it was believed to only occur in boxers, CTE has now been found in individuals from age 17 to 98, including youth, college, and professional contact sport athletes, such as football, hockey, soccer, and rugby players.

Research suggests that in some individuals, repetitive impacts to the head trigger a cascade of events leading to a progressive destruction of brain tissue, and these changes in the brain can begin years or even decades after the last trauma or after the end of ath-

letic involvement, and can lead to memory loss, poor judgment, impulse control problems, aggression, rage, depression, suicidality, movement problems, and, yes, dementia.

I have had the great privilege and honor to interview the family members of approximately 100 deceased former athletes who were diagnosed with CTE after death by my colleague, Dr. McKee, and her team. From these interviews, I have begun to learn about the clinical course and presentation of this disease, but more importantly, I have learned about the tremendous pain and suffering the family members experienced while their loved one's life was destroyed by CTE.

I have also been privileged to meet over 70 former NFL players who have come to Boston to participate in my NIH-funded DETECT study. I hear their stories. I speak with their family members, and, I listen to their fears that they have CTE or that their fellow former football players have or will get the disease. They have all witnessed firsthand the tragic downward spiral of CTE that sadly seems to have become an expected consequence of playing the game they loved.

The goal of the DETECT study is to develop objective biological tests, or biomarkers, to diagnose CTE during life. Just as a separate note, right now, today, in the next half-hour, the first NFL player—former NFL player in our study is going to undergo a very exciting new PET scan that is designed to detect the abnormal deposition of the tau protein found in this disease in a human being while they are alive. That is happening this afternoon.

This will, hopefully, improve our ability to diagnose CTE, and that, indeed, the ability to diagnose CTE during life, is the next critical step. It will lead to the ability to answer important questions about this disease, such as how common is it? What are its risk factors? How can it be prevented? How can we treat it? In other words, at this point, we actually know very little about this disease.

One thing we do know is that concussions are just the tip of the iceberg. You have been hearing today a lot about concussions. We have been hearing a lot about concussions in sport and in the military, but, the thing I am most concerned about are what we refer to as sub-concussive blows, or hits to the head that rattle the brain and likely do the same type of thing that Dr. VanLandingham has mentioned to those neurons, but without causing the same symptoms of concussion, and, those can happen many, many more times than anyone ever expects, a thousand to 1,500 times in a typical football lineman, perhaps a thousand times during heading in a season in soccer. That is what scares me.

In order to tackle the complex issue of CTE, we must expand upon current approaches to conducting research in neurodegenerative disease. We must break down the traditional silos of individual research labs, institutions, and disciplines, and begin to conduct multi-disciplinary, collaborative research across research centers, bringing together the very best scientists, novel methodologies, and state-of-the-art technology.

I fear that we have a major public health crisis looming and we must act now. Alas, as you have been hearing, this requires tre-

mendous financial support, and, as all of you know all too well, current NIH funding is, indeed, tragically low.

I want to express my gratitude toward this Committee for leading the recent effort in increasing NIH funding for Alzheimer's disease research. However, we must now have additional funding to support research focusing on CTE, and, because of their similarities, new discoveries about CTE will inform and expand our knowledge of other neurodegenerative diseases, like Alzheimer's, Parkinson's, and Lou Gehrig's.

In closing, many of our most cherished games in our country, such as football, hockey, and soccer, often involve repetitive blows to the head, potentially leading to a progressive brain disease. We must learn as much as possible as quickly as possible in order to determine who may be at increased risk for CTE and to develop methods of preventing and treating the symptoms of CTE.

I want to close by thanking the Committee for your interest in addressing this important issue and for your commitment toward improving the health and well being of older Americans. Thank you.

The CHAIRMAN. Thank you, Dr. Stern.

Senator Collins.

Senator COLLINS. Thank you, Mr. Chairman.

First, I want to thank all four of our witnesses for truly exceptional testimony.

Mr. Utecht, your statement was so moving and so riveting. You mentioned during the course of your comments that when you were strapped to that stretcher, that was your fifth documented concussion. What happened after the previous four? Were you treated each time? Did you try to conceal that you had had a concussion, such as Mr. Nowinski mentioned? Tell us what happened.

Mr. UTECHT. Sure. Thank you for those questions. A number of answers. Have I ever concealed that I have had a concussion? Yes, I have. There is tremendous pressure in professional sports to want to continue to play, not only you do not want to let down your teammates, who become your family, you do not want to let down your coaches, who you work countless hours with to put together a successful plan, and an injury can remove you from that plan and you do not want that to have an effect on the team, and, so, yes, I was put in a position where I wanted to play and I—and that pressure kept me from being honest, and I regret that.

Each concussion got worse, as the doctors have talked about today. My third concussion was simply a player jumping over me in pursuit of a tackle, as his foot lightly braised my helmet and I was knocked out unconscious for 20 seconds. I have watched the film and I see myself get up and run off to the sideline, and I have no memory of that. It was the first time I had ever experienced amnesia, and that was midway through the first quarter against the Denver Broncos in 2007, and I do not remember anything from that game until we went in at halftime, and, that really became—once the time that I began experiencing short- and long-term memory issues, which led into my final concussion that was an eight-month rehabilitation process.

Each team at that time was set up differently. For the Indianapolis Colts, they did have a neurosurgeon who was one of our team

doctors who treated the players that had concussions. In Cincinnati, it was a neuropsychologist who treated players with concussions, and, so, I think that is really one of the things we have really wanted to change, is making sure that players are actually seeing a neurologist who are those that—are the experts that can diagnose and manage concussions properly.

Senator COLLINS. Mr. Nowinski, the comments we have just heard remind me of when I first learned about the link between traumatic brain injury and neurodegenerative diseases, and it was when I met with a neurologist from Maine, Dr. Bruce Sigsbee, who had a patient come to him who was a veteran and he was being treated for post-traumatic stress syndrome at the VA in Maine, and, the doctor, the neurologist asked him if he had ever had a concussion, and it turned out that he had had several concussions and traumatic brain injuries while he was in Iraq, and, he had been misdiagnosed as having post-traumatic stress when, in fact, he had a TBI, and, it turned out that the TBI was causing him, or caused him to have a form of epilepsy, which the neurologist then treated him for.

My question to you is, is it your experience that patients with neurodegenerative diseases often have a difficult time in getting a proper diagnosis?

Mr. NOWINSKI. Thank you, Senator, Collins, for that question. It is a great question, and the answer is there is no question that former athletes are having a very hard time getting the right diagnosis, because CTE is so new that we are not—we have not been training for it in medical school and it has been widely ignored in continuing education, and, so, I mean, interestingly, when you go through our Brain Bank records, most everybody who eventually Dr. McKee diagnoses with CTE was originally diagnosed with Alzheimer's, or an abnormal type of Alzheimer's, or some other similar disease, but almost, you know, until the last couple years, it was none of whom were getting CTE as a diagnosis, meaning that they were probably being mistreated.

As Dr. Stern alluded to, how just horrible this disease is for the individual and especially their families, it is important that we at least do a better job of trying to treat them while they are alive so that they can live a better life, because—and that is something that I hope for myself, because I am 35 now and the average onset of symptoms is usually for these people in their 40s, so, there is not that much time left for me and there are certainly ticking clocks for a lot of people.

Senator COLLINS. Thank you.

Dr. Stern, I was struck when I heard you talk about the new imaging, and you mentioned that individuals with CTE have the tau protein, and, I know from my work on Alzheimer's that the tau protein is present in the brains of people with Alzheimer's, also, so, are we talking about the same protein, and is there a link here?

Dr. STERN. That is a wonderful question, and it is one of the things that is so exciting about working in this disease, because there is a definite link, but yet they are completely distinct. The difference is that in Alzheimer's disease, there are two proteins that start accumulating in an abnormal fashion and it is an abnormal form of those proteins. One is called tau and one is called

amyloid, and, in CTE, we do not see the amyloid, and when we do see it, it is not in the same kind of plaques that we see in Alzheimer's disease, and, so, CTE is very specifically a tau disease, and, the type of formation of the tau and the places in the brain where the tau starts to accumulate is quite distinct from what we see in Alzheimer's disease.

To answer the question, we have to understand that we cannot right now diagnose these neurodegenerative diseases accurately while people are living, including Alzheimer's disease. We have been studying Alzheimer's disease since 1905, when it was first discovered, and yet we still cannot truly diagnose it during life, but, fortunately, we are getting very, very close, in large part to the help that this Committee has given to support research, but, we still cannot do it.

With CTE, we have only been studying it really in depth for the last five, six years, but, what we are able to do, and what we are doing with my research right now, is exploiting what we have learned with Alzheimer's disease to learn about CTE, so, studying the tau now with a method that was originally developed for Alzheimer's disease and other neurodegenerative diseases, we can quickly come to answers about CTE.

Senator COLLINS. Thank you.

The CHAIRMAN. Well, is there something that we need to be aware of with regard to helping you in the experimentation on living patients?

Dr. STERN. Yes. Money, money, money. That is what it comes down to, but, it is not just the responsibility of the Federal Government. This needs to be a partnership of the Federal Government, foundations, and the private sector. These types of research studies and to answer the questions the right way cost tremendous amounts of money, and in order to get to some answers quickly, we must have the adequate resources to do so.

Indeed, we need continued assistance in increasing the budgets, not just reducing the cuts, but increasing the budgets at the National Institutes of Health for neurodegenerative disease research in general, but, I would hope for and ask you to start a special line of research for supporting chronic traumatic encephalopathy so we can really understand the distinction between this disease that may affect countless people in the future and diseases that have already been receiving funding, like Alzheimer's disease.

The CHAIRMAN. Senator Blumenthal.

Senator BLUMENTHAL. Thank you, Mr. Chairman, and thank you for having this very important and enlightening hearing, and thank you to the members of the panel for contributing so importantly to our discussion, and each of you has really been extraordinarily insightful in your own way, based in part on the experience and the research that you bring to this table.

Just to add to the Chairman's question, money, money, money, is often very important, but it is also how the money is spent——

Dr. STERN. Yes.

Senator BLUMENTHAL. [continuing]. Also, what can be done to prevent CTE. One of the areas is education.

Dr. STERN. Yes.

Senator BLUMENTHAL. The Korey Stringer Institute at the University of Connecticut has released, as you know, a list of nine recommendations for lessening the incidence and reducing the long-term effects of traumatic brain injuries, and the experience of the States in adopting those recommendations is very, very mixed. Connecticut has implemented only four. Most other States have implemented fewer of them, so, there is a lot of work to be done here in educating parents, trainers, but also public officials as to what can be done.

You know, one of the areas of injury that was unknown to me concerns horseback riding, which is, in fact, the leading cause of sports-related traumatic brain injuries out of all the recreational sports. Think of it, horseback is the leading cause of sports-related traumatic brain injuries. Why? Because a lot of young riders are wearing helmets made of velvet with no real protection. Think of a football player wearing a velvet helmet, nothing more.

In fact, I am planning to introduce a measure which I am naming for a young woman, Christen O'Donnell from Darien, Connecticut, who was thrown from a horse while riding, suffered a traumatic brain injury, and died the next day. She wore one of these traditional velvet hunt caps, and it was sold alongside safety-certified helmets, but her parents had no idea that they were buying a velvet decorative helmet rather than a real protective gear.

The bill that I will introduce, Christen O'Donnell Equestrian Safety Helmet Act, would require equestrian helmets produced and sold in the United States to meet minimum safety standards. I do not want to go too much into the details because I have a limited amount of time, but I want to thank you for the support in terms of the factual background that you provided for this kind of measure, which I think can be replicated in other sports areas, as well, and I am sure that we will be talking about them in the near future.

I would like to ask Mr. Nowinski, you are now 35. Your injury occurred when you were 24. How are you feeling now?

Mr. NOWINSKI. Well, thank you for asking, Senator Blumenthal. I—it is up and down. I mean, these days, I still get way more headaches than I would like to. The last two days were actually very tough. Today, right now, I feel pretty good, but, you know, as part of Dr. Stern's Legend Study, I did my annual phone call, longitudinal study testing my cognition, and there was stuff I was proud of and there was stuff that I did not feel so good about, so, I am happy where I am, but I am always wary of where I am going.

Senator BLUMENTHAL. The kick in the head that caused your injury was, in a sense, a routine part of the sport, correct?

Mr. NOWINSKI. It was an accident. We are not supposed to actually do that, just so you know.

Senator BLUMENTHAL. But, accidents in that sport——

Mr. NOWINSKI. Sure.

Senator BLUMENTHAL. [continuing]. Frequently occur. In fact, they are sort of part of the routine, because—well, you say it in your own words, but when you are in a contact sport of that kind, particularly where the routine, so to speak, is to actually do damage, at least fake damage——

Mr. NOWINSKI. Right.

Senator BLUMENTHAL. [continuing]. To another person, it is easy to make a mistake, just like if you are throwing a fake punch, if you do it in the wrong way, you are going to hit the person——

Mr. NOWINSKI. A real punch.

Senator BLUMENTHAL. [continuing]. With a real punch, so—and this must have happened to you repeatedly before that one. As you say in your testimony, you suffered repeated blows to the head in the course of sports and so forth. In your experience, are people in that sport—call it a sport for the moment——

Mr. NOWINSKI. Mm-hmm.

Senator BLUMENTHAL. [continuing]. WWE Wrestling, or similar kinds of sports, aware of this repeated impact and effect of the routine blows that are struck?

Mr. NOWINSKI. Actually, yes. WWE has become actually a close partner in the last few years with SLI. We actually honored them with our annual Impact Award last year because they have become a real leader on this issue.

Senator BLUMENTHAL. And you actually participate in some of the educational sessions.

Mr. NOWINSKI. Right. I got to—I go back and train the whole roster, and then when they hire new wrestlers, I come down and train them on concussions before they get in the ring. They made a $1.2 million unrestricted gift to support our research at Boston University, so, it has been very rewarding to see that culture change so quickly so that the people—and many of them, my friends, are still wrestling there—are in a much safer place and they have protections in place that will, hopefully, minimize the risk of long-term damage.

Senator BLUMENTHAL. In terms of the contact sport area generally—and any of the other folks on the panel should feel free to comment, as well—how is the insurance coverage for that sport and others, so far as you know, relating to this kind of injury, which, as you have just said very dramatically and compellingly, is not just a one-month or a one-year recovery period, but it can be, literally, a lifetime.

Mr. NOWINSKI. Yes. You know, it is difficult for me to speak to all insurance programs because I know there have been a lot of changes, especially very recently, in many sports to provide for more medical care long-term, but, I think you make a good point that it is just extraordinarily expensive to deal with these consequences long-term, so I can pass that down the panel, but it is a significant issue.

Senator BLUMENTHAL. Thank you.

Dr. VANLANDINGHAM. I will comment real quick. We have HMOs in the State of Florida that will not even reimburse for a concussion diagnosis, even in the Tallahassee area, the largest HMO. To get reimbursement, we have to come up with other things, like claim that there is memory impairment, and we get reimbursed based on that code, but, there is still not a specific code, and multiple HMOs that will not even reimburse this concussion in the civilian world.

The CHAIRMAN. Is that true in Medicare, as well?

Dr. STERN. In Medicare, people are definitely supported for dementia-related conditions and assessments, but, often, what we are

seeing with this disease of chronic traumatic encephalopathy is that it does not present exactly the same way as Alzheimer's disease and other dementias. There could just be really dramatic behavioral changes, or mood changes, without the memory problem initially, and, in those cases, they might be treated as having a psychiatric disease or illness, and, so, the funding is quite different in those cases and much more limited.

The CHAIRMAN. Senator, before I return to you, I want to get an understanding of how could concussions have an effect upon Lou Gehrig's disease, ALS, that our special guest is afflicted with.

Dr. STERN. Again, I just want to underscore that it is not necessarily concussions. It is the overall repetitive brain trauma, including all those sub-concussive hits that do not result in someone at all being knocked out or having changes in symptoms. It is the little hits over and over again that may start this cascade of changes in the brain cells that lead to the deposition of this abnormal tau that leads to the destruction of the brain as people live longer.

What we have seen is that in some cases, the abnormal tau and another protein called TDP–43 is not just in the brain of an individual with a history of repetitive trauma, but it also is in the spinal cord, and in those cases, it leads to the same types of alterations in motor functioning, in strength and weakness, as one would see in run of the mill ALS.

It is not that it leads to the same type of ALS that might be caused by another underlying factor. It results in the same type of motor neuron disease caused by repetitive brain trauma, is what we currently think.

The CHAIRMAN. Senator, please continue.

Senator BLUMENTHAL. Thank you. You know, Mr. Chairman, you are very, very gracious. I am over my time, out of my time, and I am going to yield to some of my colleagues in light of the vote that we have coming up, but thank you very much.

The CHAIRMAN. Senator Warren.

Senator WARREN. Thank you very much, Mr. Chairman and Ranking Member.

Research at places like Boston University that focus on traumatic brain injury has revealed that athletes and veterans with chronic traumatic encephalopathy, or CTE, exhibit structural changes to their brains that are similar to the patterns of brains from people with Alzheimer's disease and that the patients exhibit similar symptoms, and, I know we have been talking some about this, but I want to ask the question a little bit differently.

We do not know the root causes of these conditions because not everyone with a history of head trauma develops CTE, and not everyone develops Alzheimer's disease as they age, but, we also currently lack effective diagnostic tools or treatments for either disease, so, the question I would like to ask for Dr. Stern and Dr. VanLandingham is how can you use what you learn about traumatic brain injuries to inform the study of other age-related neurodegenerative diseases? Dr. Stern.

Dr. STERN. Senator Warren, thank you for that question. That is the question that led me to get involved in the study of chronic traumatic encephalopathy. As an Alzheimer's researcher, I was

never really interested in traumatic brain injury, except one day I happened to be giving a lecture saying that traumatic brain injury was a risk factor for dementia, and Chris Nowinski's roommate was in the audience and we then connected and it led me to find out about what was a burgeoning topic of this chronic traumatic encephalopathy.

The reason why I got excited about it was just for that reason, that it is a close enough cousin to Alzheimer's and other diseases that had been studied that it could—we could exploit what we find out about one to learn about the other.

Senator WARREN. Mm-hmm.

Dr. STERN. With chronic traumatic encephalopathy, we know the necessary variable for developing this disease. The necessary variable is repetitive brain trauma——

Senator WARREN. Right.

Dr. STERN. [continuing]. Like you very articulately said. That is not the sufficient variable. Not everyone who hits their head is going to develop this disease, but, we know that everyone who has this disease has had a history of repetitive brain trauma.

By that nature, we are able to then look at a group of people at high risk, very high risk for developing this disease and study them longitudinally and use new diagnostic tests to be able to detect when the disease might start and then follow them until death and have my colleague, Dr. McKee, and other neuropathologists examine them.

That is a very unique thing. In Alzheimer's disease, we do not have that ability. We do not know who is at very high risk for getting it until later on, when we might be able to do now a special kind of PET scan that can detect the amount of amyloid in their brain. Well, now, we can use both sides of this picture to inform the other and make us get to answers so necessary in a much faster fashion.

Senator WARREN. Dr. VanLandingham, did you want to add anything to that?

Dr. VANLANDINGHAM. Yes. Well, just reiterate a little bit that no one brain is the same. One of the most common questions I get from parents are, well, when should I make my son or my daughter stop playing this sport? How many concussions? And, you know, I am, like, well, everybody is different. You know, you would like to say, well, after three, they are predisposed to CTE, so, it is a very complicated answer, but I agree with Dr. Stern that it is a special population that can be measured in the years to come and you will get closer to the right answer.

I would like to add one more comment to the Lou Gehrig's issue. I work—I do a lot of pre-clinical research with animals and we can give concussions, even one single concussion to an animal, and we find the tau protein in the cerebral spinal fluid, and, that fluid not only bathes the brain, but also it bathes the spinal cord, so, it could be an issue of transferral from the brain that has been damaged of these pathological proteins down into the spinal canal and some level—but we do not know yet, but, it is definitely bathing the spinal cord after a brain injury.

Senator WARREN. Well, you know, your comments, both of you, Dr. Stern and Dr. VanLandingham, remind me that the wonderful

thing about science is that discoveries do not occur in isolation, that what we learn by studying one disease can pay dividends in shedding light on other diseases.

The Director of the National Institute of Mental Health, Dr. Tom Insel, told the HELP Committee last year that we are on the cusp of a revolution in brain research because of the incredible tools that are now available that had not been there before, and yet, at this critical moment, we are cutting back on NIH funding. Year after year, adjusted for biomedical inflation, NIH's budget has shrunk to the point that we are now investing less in research with NIH than we were in 2001.

Let me ask the question this way. If we could double the budgets of your centers, what could you do and how much faster could you do it?

Dr. VANLANDINGHAM. Do you want to go first?

Dr. STERN. I will go first.

Senator WARREN. You have got to show us the aspiration here, Dr. Stern.

Dr. STERN. With a doubled budget, we would not just double the speed at which we could answer important questions. It would be an exponential increase.

Senator WARREN. Yes.

Dr. STERN. One of the things that has been happening across the nation has been the loss of young investigators and senior investigators. Young investigators, because there are no jobs for them, because of NIH cuts, there are no jobs for young post-doctoral fellows or new researchers trying to get an assistant professorship. Senior investigators who have been working for decades are having to close their labs because, for the first time ever, they have no funding, because of that, we cannot have continuity in research. We cannot have the numbers of people to be able to focus on a particular question at any given time, so, that is one of the starting points, why we would be able to have much faster answers is because if we had more money, we would be able to have a real meaningful staff to answer the questions.

We would also be able to do much more with technology, and that is what is so wonderful about doing this type of research in 2014. While Senator Warren was out, I was mentioning that just right now, this moment, we are putting one of our former NFL players in a PET scanner to be able to look at tau protein in their brain. It is the first time we are doing it. It is very exciting. By being able to have support for that, to double our budget, to be able to continue that research, not to close it down, we would be able to diagnose CTE during life very, very accurately within the next five years.

Senator WARREN. That is amazing.

Dr. VanLandingham.

Dr. VANLANDINGHAM. I will start by saying that I work for two different nonprofit companies, for a for-profit company, and I am a professor at an academic institute, so there are various thoughts that go through my mind to answer this question.

I think if we had funds from the Federal Government, let us say, that would sponsor private companies, that it would be easier for private companies to get investors. It would improve the value to

the investor by having Federal Government support. That is a little out there.

Big pharmaceutical companies do not do R&D anymore. Smaller companies are now the ones that have to go out there and either raise the money or fight for the grants just to be able to get this to a point where it can go into clinical trials.

Professors in academic institutes have wonderful ideas, but they never, hardly ever try to commercialize them because they do not have the means in which to do that.

Your question on how much money, doubling the budget, for $20 million, in a year, I could be in a Phase 2 clinical trial for concussion, a first drug. If I had $20 million today, in a year, I could have us in a Phase 2 clinical trial.

Senator WARREN. Okay. I appreciate it. You know, we talk a lot on this Committee, for example, about Alzheimer's, and the Alzheimer's Association says that as our nation continues to age, Alzheimer's disease is projected to cost our nation $1.2 trillion a year by 2050. Over and over, we understand the importance of research, and ultimately, the importance, not just for people's lives, but the importance in terms of how much money we have to spend to care for people.

I just want to make it again clear. We cannot stand by and do nothing. We must increase our Federal investment in medical research, not slash it. This is our only chance to bring costs in the future under control and to give people a better quality of life.

Thank you very much for your work. Thank you so much for being here to raise awareness around this issue, and, thank you, Mr. Chairman, for letting us go over.

The CHAIRMAN. Amen to your comments about research, Senator.

I am going to try to squeeze us in before we have to go to vote, and the vote will be called momentarily, but we do not have to go right at that time, and I will wait until the last possible minute, so, let me see if I can handle quickly a number of questions that are still left.

Dr. Stern, how does a TBI differ in a military combat injury versus a sports injury?

Dr. STERN. The brain does not know what is hitting it. However, there is something new that has been occurring in the last 12 years in the military theaters of Iraq and Afghanistan and that is these roadside blast injuries that occur to our military servicemen and women, and, these blast injuries are not a direct hit to the brain or to the head, but through the blast waves, and often, what happens during that type of injury, the person not only has the effect of the blast on their brain and those brain cells, but the person is also thrown and hits their head within their vehicle, on the ground, et cetera.

That is a different type of injury. That is a double dose on an individual who has already been exposed, perhaps, to similar injuries, but, just like the stories you hear of our football players and other athletes who want to hide their injuries to be able to help their team be strong, our military personnel do the same all too often, and, so, what we need to do is to be able to make sure that we reduce the repetitive nature of those types of injuries.

The type of injury that one gets, let us say, in a football stadium is not necessarily going to be that same type of blast followed by hitting, but it is still going to be some kind of impact to those brain cells like was described earlier, the stretching, the shearing of those neurons that lead to this metabolic crisis within the nerve cells. It does not matter how the hit happens. That same type of change is going to occur, leading to the same type of acute symptoms.

The CHAIRMAN. I want to ask Mr. Nowinski and Mr. Utecht, do you have any observations about player suicide?

Mr. UTECHT. Well, clearly, it is a concern, whether it is in wrestling or whether it is in the NFL. That is—that is the last thing you would ever want to see occur. I think, at this point, there is just not enough information to be able to say that they are connected, and I think that is one more thing that funding into research would really be able to help us to provide, is more context between a relationship with depression and traumatic brain injury, but at this point, it is not there yet, and, so, when we look at some of these players who have come to that point, it is really hard to be able to, I think, to make that connection yet today, between traumatic brain injury and suicide.

Mr. NOWINSKI. Thank you for the question, Chairman Nelson. You know, suicide is extraordinarily complicated, but there are some things we do know. One is that acute concussion, acute traumatic brain injury does increase your risk of suicide or suicidal ideation within the next year, certainly, from some studies, and, we actually have a lot of brains in our Brain Bank from teenagers who have taken their lives within, some 36 hours, some within a year, while still suffering post-concussion symptoms, so, there is something going on there.

Then, with long-term cases and people committing suicide with CTE, you know, it is hard to know if their suicide was linked to, maybe, anxiety or depression issues that the disease brought on. Certainly, what is consistent in a lot of cases is that it has alienated them from their families and they are not able to work and they become isolated. You sometimes wonder if the guilt and the destruction of their life had some role to play in the conscious decision to take their lives, but, I think it just shows just how much this disease does affect families.

Dr. STERN. If I could add something to that, just talking about the science of it, suicide is a very complex, very tragic occurrence, but, what we do know is that the parts of the brain that are affected in chronic traumatic encephalopathy can, indeed, lead to changes in emotion and to changes in impulse control. Those are two of the big things that are affected by this disease, the amygdala, which is really the home of emotional regulation, and the bottom parts of the frontal lobes, where we control our impulses, where we stop our inappropriate behavior, and, if you have an individual who has this rage and sadness and emotional discontrol and then they have the inability to stop an impulse, that may lead to that very tragic recipe that could eventually turn to suicide.

The CHAIRMAN. Are women more subject to this type of injury than men?

Mr. NOWINSKI. The data would say yes. In sports like soccer and basketball, where the rules are very similar, women do suffer more concussions, and, the prevailing theory on that is it is likely biomechanical, the sense that they have thinner, less muscular necks, so their head—it takes less of an impact to move their head rapidly and cause their brain to move quickly, but, because of Title IX and because women have not been playing organized sports as long, we do not know what the long-term consequences are. We only have a handful of women—of female brains in our Brain Bank and we do not have a positive case yet of CTE, so we are not sure what we are going to see there, but, it is concerning.

The CHAIRMAN. If you are the team's coach or the doctor, what is your best way to make an assessment as to whether or not your player should be able to continue?

Dr. VANLANDINGHAM. I would say, first, you do a memory and attention test there on the sidelines, and nowadays, we know that a lot of issues after a concussion are related to balance impairment because of inner ear damage during the concussion, that a quality test for balance as well as sort of quick thinking, memory, attention things on the sideline is probably the most common thing today.

The CHAIRMAN. Does that get into that IMPACT, the Immediate Post-Concussion Assessment and Cognitive Testing?

Dr. STERN. The IMPACT test is the most common cognitive assessment for sideline—not really sideline testing, but for athletic testing. It is used most commonly as a baseline test before a season, and then after someone is injured, it is used again to compare the performance, but, it would not be used on the sideline. It takes too long. The environment is not appropriate, and, what is very important to know is that many of the symptoms of concussion are not immediate. They may not occur for hours or perhaps until the next day.

If you are a coach trying to make a decision, first of all, have adequate medical staff on hand, whether that be athletic trainers or team doctors who are well trained in concussion assessment, and those medical professionals should take it very seriously and be independent of the coaching decisions so they are not pushed in any way, shape, or form to send someone back to play before they are ready.

Mr. UTECHT. One other thing to note on the IMPACT test, too, is we are finding that athletes are now failing the IMPACT test on purpose so that their baseline is now lower to start out with, so that if, in fact, a concussion occurs, they do not have to get back to what truly is their normal baseline, but one that has been fabricated because of choices they have made during the test taking.

This is about changing the nature of this injury, as well, and really getting people to care about their brain so that they do not make choices like that.

The CHAIRMAN. In this case, you mean that that enables them to get back out on the field.

Mr. UTECHT. Well, correct. It takes their baseline and lowers it so that their results do not have to come back to what really would be their normal baseline.

The CHAIRMAN. I see.

Dr. VANLANDINGHAM. They would not be taking that IMPACT until the day after.

Mr. UTECHT. Correct.

Dr. VANLANDINGHAM. You are doing sort of a quick and dirty on the sidelines to decide whether they can go back in immediately or not. Then, you are holding them out and doing that check towards baseline the day after, and every seven days until they return to normal.

The CHAIRMAN. All right. Now, there have been a number of athletic organizations that are getting involved in the business of donating millions of dollars to research, some through NIH. How can the public be sure that these donations do not buy us the outcome of the research?

Dr. STERN. I can speak to the NIH donation by the National Football League. The NFL gave $30 million to the Foundation for NIH, which is an organization associated with the National Institutes of Health to accept money from the private sector to then be used for peer-reviewed research, and, so, there is this firewall between accepting the money and then the review that is done through NIH, not through FNIH.

The goal of the NFL giving that money was so that it did not have any conflict of interest, so there was not any playing favorites. It was there to be able to truly support research so it can be peer-reviewed and funded just like any other NIH research, so, in that case, I strongly support it.

The CHAIRMAN. Okay. Now, final question. A recent medical journal said emergency room visits for these sports-related TBIs have increased by 92 percent over a ten-year period. You are a parent. You have a child. They want to play sports. If it is a contact sport, do you let them play? Let us just go right down, right down. Mr. Nowinski.

Mr. NOWINSKI. Sure. You know, after doing this for a long time——

The CHAIRMAN. I am going to keep you short——

Mr. NOWINSKI. All right.

The CHAIRMAN. [continuing]. Because we have got to go vote.

Mr. NOWINSKI. Yes. I am saying, definitely no contact sports with repetitive brain trauma before high school, and then after that, you know, I have time, I do not have kids yet, so we will see, but, I think, I would say, do not let them get hit in the head hundreds of times a year before high school.

Mr. UTECHT. I would have to agree with Mr. Nowinski. In fact, there is a high school in Texas who has now gone to pretty much flag football up until high school, and, really, you see even players in the NFL who did not play football in college. They were basketball players, but they have become Pro Bowl players in the NFL, so, can you, in fact, remove contact sports until high school and still teach fundamentals, still teach even correctly how to tackle but removing the contact? I really believe that you can.

The CHAIRMAN. Doctor?

Dr. VANLANDINGHAM. I agree. I just—I still have my concerns about as large and as fast as high school players have gotten today, that there still will be a major issue, but, at least we have removed anybody under the age of 15 or 16 from being engaged in it.

The CHAIRMAN. Dr. Stern.

Dr. STERN. I think we have had a tremendous knee-jerk response in our society to limited research that has led to a lot of, perhaps, scary stories that are passed along, and that is before we have adequate science. However, we also have to think rationally and make rational decisions. I think people are now understanding that hitting your head over and over again is not necessarily a good thing for you, so, I would agree with everyone else that, at the very least, contact sports with repetitive hits to the head should be limited to as late as possible.

The CHAIRMAN. We especially want to thank our special guest, Kevin. We want to thank all of you——

Senator BLUMENTHAL. Mr. Chairman——

The CHAIRMAN. [continuing]. Most illuminating.

Senator.

Senator BLUMENTHAL. I apologize for interrupting, but I am wondering whether the record could be kept open. This has been such a phenomenally——

The CHAIRMAN. Absolutely.

Senator BLUMENTHAL. [continuing]. Good panel. I have some additional questions I would like to submit.

The CHAIRMAN. The record will be kept open for five days.

Senator BLUMENTHAL. Thank you.

The CHAIRMAN. The meeting is adjourned.

[Whereupon, at 2:41 p.m., the Committee was adjourned.]

APPENDIX

Prepared Witness Statements

Prepared Statement of Christopher Nowinski, Founding Executive Director, Sports Legacy Institute

Introduction

Chairman Nelson, Ranking Member Collins, and Members of the Committee, thank you for inviting me to speak today before the Committee. My name is Chris Nowinski, and I am the founding executive director of the Sports Legacy Institute, known as SLI, which is a non-profit organization dedicated to solving the sports concussion crisis through education, advocacy, policy, and research. I am also a cofounder of the Boston University Chronic Traumatic Encephalopathy (CTE) Center and serve on the executive committee of the Boston University School of Medicine Alzheimer's Disease Center, which houses the CTE Center.

I serve as a volunteer advisor to the National Football League Players Association, Major League Lacrosse, and The Ivy League. I also have a personal relationship with concussion, and tremendous concerns that I have increased my risk of developing a degenerative brain disease in the future. It is my hope that this hearing raises awareness of the urgent need for funding for research on traumatic brain injuries, as well as the tremendous opportunities we have for prevention of their long-term consequences.

I never had a second thought about concussions or brain injuries until one day when my world changed so drastically that I would never go a day without thinking about my brain again. It happened late in my competitive athletic life—I was 24 years old. After playing contact sports in high school and at Harvard University, I had become a professional wrestler, known as a Superstar, with WWE. I got to travel the world playing a bad guy, or "heel," known as Chris Harvard who creatively insulted the fans' intelligence and cheated to win. Let me remind you that this was a character than I played; it was a performance to entertain our fans, and it was fun.

In a match at the Hartford Civic Center, I was kicked in the head by my opponent Bubba Ray, and my world immediately changed—my head began throbbing, everything got foggy, and most importantly, I forgot the script. I couldn't remember how we were supposed to finish the match. It was terrifying.

We created a new finish, and on my way back to the locker room I was stopped by our athletic trainer, who asked if I was alright. By that time, my memory had begun to come back, so I answered instinctually with, "I'm fine." But I wasn't—I went down a hallway and lay down on the ground, holding my head as if I was trying to keep my brain from falling out.

The symptoms, which expanded beyond daily headaches to include depression and sleepwalking, would not go away. I traveled from doctor to doctor until I met Dr. Robert Cantu, my cofounder at SLI. He was the first person to ask me "How many concussions have you had?" I told him, "One."

Dr. Cantu was the first to then ask, "How many times have you been hit in the head and become confused, dazed, or considered yourself 'dinged?' I said "Doc, that happens all the time." I had been playing contact sports my entire life. I played soccer from age five to thirteen. I played football from age 13 to 21. I wrestled for three years. I probably suffered over 10,000 blows to the head, and at this point I can remember nine concussions since the age of 19, but can't remember what happened prior because I never knew the dings were worth remembering.

Dr. Cantu went on to tell me, "The symptoms you are experiencing are likely the result of cumulative trauma. In addition, the fact that you never took a day off for those injuries means that each one was more damaging than it needed to be. Had you chosen to rest, you would have probably recovered by now."

There I was, at 24, learning for the first time how fragile my brain was, and how critical rest is after a concussion. I wish I would have recognized my concussions, reported them to a medical professional, and then rested both physically and cognitively. My ignorance cost me—a career, five years of health before the daily symptoms went away, and who knows what else in the future. Dr. Cantu shared with me his concerns about the risk of progressive brain degeneration that may manifest mood disorders, behavioral problems, cognitive impairment and memory deficits, and eventually dementia. All this from a couple of head knocks that seemed perfectly innocent at the time.

The Long-Term Effects of Brain Trauma

Scientists have been writing for nearly 100 years that brain trauma can lead to a degenerative process in the brain, but it has only been in the last seven years that we have had a focused national conversation on the problem.

Of concern is the growing evidence that brain degeneration continues after the injury without any additional trauma—the brain essentially continues to rot away. The disease we are most concerned with is Chronic Traumatic Encephalopathy (CTE), which Dr. Ann McKee, Professor of Neurology and Pathology at Boston University School of Medicine and Director of Neuropathology Service for the New England Veterans Administration Medical Centers, has now discovered in over 100 former contact sport athletes and military veterans at our VA-BU-SLI Brain Bank. Studying brains post-mortem is currently the only way to diagnose CTE, which also means we don't know how many people have it. Unfortunately, 58 of the first 62 donated brains of professional football players that we examined ended up having it, and we have found the beginnings of the disease in football players as young as 17.

My colleague Robert Stern, PhD, Professor of Neurology and Neurosurgery at Boston University School of Medicine, has submitted testimony on the science behind CTE and brain degeneration, so I will focus my remaining testimony on the ethical and policy implications of the work.

Moving Forward

What the scientific evidence appears to be telling us at this point is that the human brain, while magnificent and resilient, is particularly vulnerable to brain trauma. The working theory is that too much brain trauma, in the form of a severe injury or repetitive mild injury, can spark disease.

What is special about this brain disease is that we think we know the primary cause—concussive or subconcussive brain trauma. *In fact, no one has ever been diagnosed with CTE who wasn't exposed to significant brain trauma*. Therefore, unlike Alzheimer's disease, Parkinson's, or many other neurodegenerative disorders—we may be able to effectively prevent CTE by limiting or eliminating exposure to brain trauma.

While the majority of CTE cases have been found in professional athletes, it has also been found in many athletes that never played beyond high school, and only played sports as minors. *Through participation in sports, we are giving some children a preventable degenerative brain disease*

We must act to recognize and minimize this risk. This is not a war on football, this is not a war on sports, but it is a war on brain injury.

There are a number of meaningful policy solutions that are slowly being implemented across sports, including:

1. Education, so that athletes, parents, coaches, and medical professionals can accurately recognize and respond to concussions.
2. Better tests and return-to-play protocols, so that athletes can recover before being exposed to another injury.
3. Better equipment, so that plastics, rubber, and foam can help absorb impact and draw it away from the brain.

It has been rewarding to watch WWE embrace brain trauma research and implement innovative concussion management, education, and prevention programs. In recent years, WWE has banned certain moves added full-time doctors to tour with talent, added computerized baseline testing, and annual seminars for all talent, referees, producers and medical personnel on concussions. In fact, I travel to the WWE Performance Center in Orlando where they train new recruits and conduct an educational seminar for all new hires on concussions before they step foot into the ring, emphasizing the urgency of preventing concussions along with the health and career advantages of reporting them. WWE is also one of the largest corporate donors to CTE research.

However, as we implement these changes, they expose the gaps that we may never be able to close, and that call into question how effective our policy changes will be in changing outcomes for athletes, including:

1. *Current education for athletes does not appear to be effective*. While we change their knowledge of concussion signs and symptoms, we still struggle to convince them to report their injuries.[1]
2. *We may not be able to educate the youngest athletes, pre-high school*, to even recognize the signs and symptoms of concussion enough to report when they are injured.
3. *We still do not have a biomarker for concussion*, and have imperfect ways of determining when an athlete is injured, or when it is safe to return. Children

[1] Kroshus E, Daneshvar DH, Baugh CM, Nowinski CJ, Cantu RC. NCAA concussion education in ice hockey: an ineffective mandate. BJSM. 2013 Aug 20.

are more vulnerable: widely used return-to-play tests for adults and teenagers simply do not work for children.

4. *Adding doctors and athletic trainers* to the sideline dramatically improves the odds of recognizing a concussion, yet only about half of high schools have an athletic trainer, and they are rarely available prior to high school. Without them, likely 85 percent–95 percent of concussions go undiagnosed.[2]
5. *Young athletes have biomechanical and developmental differences* that make them more vulnerable to concussions and their negative consequences.

Most of these gaps are not ever going to be closed directly—we will never have a doctor on the sideline of every athletic event, and we will never be able to teach every child how to recognize when they have a concussion and report it to their parent. While we wait for technology to close those gaps, the best solution is prevention, and prevention is far too often missing from this discussion.

The little research we have indicates that people at greater risk for trauma-linked brain disease start *younger, play longer, and receive greater cumulative brain trauma (concussions plus subconcussive impacts)*.

We can reduce cumulative brain trauma, and some sports are working to decrease the frequency of brain trauma. Indeed, SLI has developed the Hit Count® Program which is designed to use sensors to create a Pitch Count for the brain, and eventually provide guidelines and limits.

However, the one option we have the most control over is when athletes start receiving repetitive, voluntary brain trauma. This does not refer to accidental, rare brain trauma, the kind that can occur when someone trips and falls. It refers to regular, unavoidable brain trauma, the kind that occurs when a football player makes a tackle or block, or purposeful, repetitive brain trauma, like heading a soccer ball.

The curious thing about repetitive brain trauma in sports is that most people don't think it is a good idea to hit a child in the head. In our culture and in our legal system, outside of the context of sports, it is considered abuse. Deep down, we know there is something inherently disconcerting about children being hit in the head, and the science is now finally catching up and putting numbers where before there was only intuition.

I don't believe we should continue to tolerate repetitive brain trauma in sports for children. Children should play games for fun, exercise, and life lessons. They should not just be playing the sports that professionals play, which we watch on television for entertainment and that are organized for profit.

Some governing bodies of youth sports have taken notice of the long-term risks of brain trauma and made logical changes. USA Hockey raised the age of the introduction of checking from 11 to 13, in part to reduce the number of concussions, and US Lacrosse continues to change its rules and penalties to eliminate all purposeful hits to the head for youth.

But not every sport is reacting quickly. Current guidelines in soccer which are not well enforced, recommend introducing headers at age 10. This week, SLI is teaming up with the Santa Clara Institute of Sports Law and Ethics (ISLE) on a campaign to educate parents and coaches on the risks of headers in soccer prior to the high school level.

Former US Women's National Team player and ISLE board member Brandi Chastain and former teammates Cindy Parlow Cone and Joy Fawcett are leading the campaign along with SLI medical director and concussion expert Dr. Robert Cantu, to educate parents and coaches that the risks of introducing heading prior to high school have to be weighed against the rewards of more skilled heading among children.

Chastain, Parlow Cone, and Fawcett, former professionals who are now parents and coaches, don't allow their children or players they coach to head the ball before high school, as they don't believe the risk is worth it. I hope the rest of the world follows their lead.

In many ways, the risks involved with brain trauma mimics smoking cigarettes. The more cigarettes one smokes, the greater the risk of lung disease. As a society, we determined that no child should smoke before age 18, when they have the capacity to understand the long-term risks involved, and we have immense campaigns to discourage children from smoking.

We should view purposeful brain trauma in children in a similar fashion, as both lung disease and brain disease are expensive problems to care for down the road, and will negatively impact our health care system and our economy.

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[2] Echlin PS, Johnson AM, Riverin S, et al. A prospective study of concussion education in two junior ice hockey teams: implications for sports concussion education. Neurosurg Focus 2010;29:E6.

Conclusion

We must not underestimate the long-term impact of brain injuries. With one in four boys and one in 16 girls in America playing contact sports, we are putting a lot of children at risk for CTE. We owe them, as well as our military veterans, greater investment into finding ways to effectively minimize the negative consequences of inevitable brain trauma.

We must also take what we have learned about brain injury and take advantage of opportunities we have to prevent brain trauma and prevent CTE, and it begins with changing the culture of sports. I look forward to working with you to protect those at risk.

Prepared Statement of Ben Utecht, Former National Football League Tight End, Cincinnati Bengals and Indianapolis Colts

Concussed

"I'm in here counting the days while my mind is slipping away. I'll hold on as long as I can to you. I may not remember your names or the smell of the cool summer rain, everything and nothing has changed, nothing has changed."—Ben Utecht

I remember my first tackle vividly: digging the toe of my foot into the soft grass, giving my young athletic body the best chance for speed that it had. With complete abandonment, I took off toward my target and threw myself into the chest of my dad, who enveloped me in his arms as he was falling backwards onto the ground from his knees. Playing catch in the backyard with dad in 3d grade is when it all began. Then came the pads in 4th grade along with full contact nine-year-old aggression. When I look back at my complete experience in tackle football from nine years to twenty-nine years of age, I am shocked to say that I had a twenty-year career playing the game of football. What a career it was . . .

The night was February 4th of 2007. There was a cool Miami Florida mist filling the Dolphins stadium as I stepped on to the largest professional sports field in the world on that night. It was hard to believe that a river rat kid from Hastings, MN was now one of the starting tight ends in the biggest game in history. Roughly 100 million viewers tuned in that night from around the world to watch Super Bowl XLI, the Indianapolis Colts vs. the Chicago Bears. I'll never forget two weeks prior when our Pro-Bowl place kicker, who had already won three Super Bowl rings, told the team "don't blink, don't you dare blink" at kick-off, so there I was standing between future Hall of Fame head coach Tony Dungy and future Hall of Fame quarterback Peyton Manning watching our kicker about to lay his foot into the sweet spot on that NFL pig skin ball, when I remembered his words. The whistle blew and the players let loose their speed and our kicker crushed the ball. I kept my eyes as wide open as humanly possible and experienced a light show I'm sure would rival that of Neil Armstrong's. It was truly amazing, as if I was dancing with the stars. It was a very special cinematic slow motion picture moment that I hope is never taken from me. We went on to defeat Chicago 29?17, and the Indianapolis Colts became world champions. It was my dream come true.

That dream was shattered two years later when I woke up face down on a training camp field in Georgetown Kentucky, playing for the Cincinnati Bengals. Next I was strapped down to a gurney and rushed to the hospital after my 5th documented concussion. That began an 8-month rehabilitation processes that led to my retirement from the NFL due to traumatic brain injury. My post concussion symptoms were numerous, including amnesia, sleeplessness, night sweats, dizziness, fatigue, and some behavioral changes, to name several. However it was a gift I took for granted that would become my greatest concern and priority . . . My memory.

My memories began to fade away along with pieces of my identity. My wife Karyn and I, along with our three beautiful daughters, visited one of my best friends and roommates from college. Matt and Kim began sharing favorite moments from their wedding as Karyn nodded in remembrance while I sat in mental darkness trying to understand why nothing sounded familiar. I stopped Matt mid-sentence, asking him, "Why wasn't I able to be at your wedding?" He looked at me awkwardly and continued, but again I asked the same question. This time Matt, Kim and Karyn stopped talking and studied me looking for a comedic reaction, but nothing came. I continued, "When was it . surely I wasn't busy?" Kim got up from the table and retrieved their wedding photo album. Page after page—I was in disbelief, seeing myself in numerous pictures, as a groomsman and singing for them a song. To this day I still have no memory of that event. Unfortunately for my family and me, that is only one of multiple memory gaps in my 32-year-old brain.

What is my greatest fear? It's to be trapped inside the coffin of my mind. To wake up one morning and not remember the faces and names of the people I cherish the most. I was asked by a good friend to do something very difficult. Write a love letter to my wife and girls from the perspective of the 50-year-old NFL'er who doesn't remember them any more. I wrote the letter, on a plane ride home with the brim of my hat over my eyes to hide the tears as they began to flow. This letter produced the song that will forever let my wife and three beautiful girls know that no matter what brain disease may take from me in the future, it can never take their love.

"I can still feel you here in this place beyond all tears, where love does what it does, it stay, yes it stays, and I will remember your smiles and your laughter long ever after this moment is gone . . . Seasons turned and turned again, till they became remember when. The love in your hearts made this man complete, my Cin-

derella's you danced on my feet. You will always be my girls, you're the beauty of my world and no matter how tomorrow unfurls, till the moment I am dome with this world, my yesterday babies in curls. You will always be my girls"—You Will Always Be My Girls, Ben Utecht/Rick Barron

I can't help but to throw myself into a new target . . . Neurology. To tackle a new opponent, brain disease, and particularly TBI/Concussions. I have been impassioned through advocacy to fight for those lives being ripped apart by brain diseases and disorders. We need a national revival for funding research that will help us find the cures. You as Senators can become my new coaches: you can help decide the games strategy and put in the countless hours of work and research into creating policies that can change this nation connecting people to their most valuable asset, their minds. We can become world champions on a new gridiron, the field of our identity. I will not stop in the pursuit of finding cures for brain disease, and creating an emotional connection between the world and neurology because neurology is what cradles the miracle that makes us human, our brains. It's time for all of us to realize how special our brains really are!

Concussion Insurance Policy Proposal

I urge Congress to mandate that the NFL and any other tax exempt non-profit sports organization, who are making millions and billions of dollars off of athletes sacrificing their brain health, to pay premiums on a long-term health care and disability insurance policy specifically surrounding Traumatic Brain Injury and Concussions. One solution to the concussion crisis, which has now impacted the entire globe athletically and beyond, is to provide a security blanket that can cover the future brain health of our athletes. You must see clearly that you cannot have professional contact sports without traumatic brain injuries. Therefore athlete's brains should be covered under a Concussion Policy.

Keys to Success

A mandate that makes all of the billionaire owners, franchises, and Professional sports organizations invest in the future brain health of their players.

Traumatic Brain Injury and Concussions are an epidemic that effects the entire population, which means this insurance policy could also be made available for the general population specifically our youth in contact sports who are injuring their brains during the most important developmental stages of their brain maturation.

Underwriting will be essential to the success of the policies.

The insurance policy could also provide annual Neurologist consultations or physicals that would allow all athletes and general population under the policy to start a relationship with a brain expert who can best diagnose and manage a TBI/Concussions. This annual physical would be most important to the management and care of our youth who are active in contact sports.

These policies would also provide accountability by battling the issue of athletes withholding critical information regarding a TBI/Concussion they have sustained. Athletes lie about symptoms in part because they lack job security. A concussion policy would provide them with future financial security regarding their brains.

The Premiums should be made tax deductible.

Written Testimony of Jacob W. VanLandingham, Ph.D., Director of Neurobiological Research at Tallahassee Memorial Healthcare Neuroscience Center, Assistant Professor in the Department of Biomedical Sciences at Florida State University College of Medicine, and Founder and President of Prevacus Incorporated, Tallahassee, Florida

Mr. Chairman and Members of the Committee, thank you for the opportunity to appear before you today to discuss the current State and future needs for improving the treatment and management of mild traumatic brain injury.

Background

According to the most recent statistical data from the Center for Disease Control and Prevention (CDC), approximately 1.6 to 3.8 million people experience a traumatic brain injury (TBI) in the United States each year alone, resulting in 52,000 deaths. TBI was the leading cause of combat deaths in both Operation Iraqi Freedom and Operation Enduring Freedom; estimates range from 15 percent to 25 percent of all injuries sustained in warfare during the previous century involved TBI. Of significant concern for this Committee, pediatric patients struggle more than any other age group to return to function after a brain injury. Most relevant to this hearing: over 50 percent of deaths associated with falling in the elderly are due to TBI. Although interest in severe TBI has long dominated research studies, we now know the number of TBIs of mild to moderate severity far outnumber those with severe injury. In fact, annually it is now known that more than 1.7 million people are treated and released from emergency departments. Recent evidence suggests that participation in sports involving contact and/or collisions may alter regional brain metabolic processes and increase the risk of catastrophic neurodegenerative diseases, including chronic traumatic encephalopathy (CTE) which has been linked to repetitive concussion brain injuries. Over 300,000 sports injuries a year have a brain injury component. When considering the burden of TBI on our healthcare system consider that in the US each year over 70 billion dollars are spent from lost work days to intensive care units.

Health-Consequences-of-Concussion

Contact sports are synonymous with mild TBI (mTBI), which is also known as concussion. As the brain accelerates and subsequently decelerates inside the skull its sensitive processes are stretched and damaged. Additionally, bruising presents at sites where high speed impact occurs against the inner skull. Returning to play too soon after a concussion increases the risk of experiencing another more serious TBI that can be caused by less force. Not to mention, those athletes who have experienced more than two concussions are at higher risk for permanent to prolonged symptomology. Recent findings supported by the NIH have shown that repetitive concussions may lead to progressive decline in brain functions over the life span. It is becoming more evident that athletes who have sustained multiple concussions are at risk for clinical depression and subsequent suicidal ideation. These athletes also tend to have memory and attention impairment with delayed information processing speed. Some reports State that of all the people engaged in athletics 19 percent may suffer a concussion each year. Individuals who experience concussions have up to a 20 percent likelihood of developing Post-Concussion Syndrome (PCS). Unlike the concussed who return to normal within two weeks, patients with PCS have long term disability with prolonged symptoms including: chronic headaches, fatigue, sleep difficulties, personality changes, sensitivity to light or noise, dizziness when standing quickly, and decreases in short-term memory, problem solving and general academic functioning. Clearly, anyone who has sustained a concussion needs to be immediately evaluated and treated by a physician, and closely monitored thereafter. Also, the individual should visit and be evaluated by a neuropsychologist, a specialist who can best monitor the athlete's symptoms and immediately put appropriate treatments in to play.

Mild-Concussion-Defined; Challenges-With-Diagnosis

A mild concussion, is characterized by a confused or disoriented State lasting less than 24 hours; loss of consciousness for up to thirty minutes; memory loss lasting less than 24 hours; and structural brain imaging (CT scan) that yields normal results. Concussions are notoriously difficult to diagnose and treat. Each injury may have a different constellation of findings, and such findings can often be very subtle in their presentation as well as intentionally masked by the patient. Current side-

line tests have multiple limitations, including low sensitivity, environmental factors, ease of implementation and equipment restrictions. Furthermore, return to sports participation, work, and military duty criteria are based on symptomatic resolution and normalization of neurocognitive function. With the former, reliance on the patient's report is required, and patients will frequently do whatever it takes to get back to their prior activities, including the use of deception. With the latter, baseline testing is needed for comparison, and many individuals will attempt to "sandbag" their baseline in order to be able to more easily pass the test. This is to say, just as you would expect a young athlete or soldier to do what it takes to return to the field, the elderly also tend to do what it takes to preserve independence.

Finally, many technologies used for concussion diagnosis and clinical assessment have different limitations; including technically difficult application, diagnosis-only (i.e. inability to inform return-to-play decisionmaking), poor sensitivity, and high costs.

A Compounding Injury

As a compounding injury, a significant consequence of not properly treating mTBI is that suffering one injury makes a second more likely; and the second injury will most likely be worse than that first; and so on and so forth. Chronic traumatic encephalopathy (CTE), a form of neurodegenerative disease, has been recently shown to be associated with repetitive concussions. CTE is characterized by a progressive taupathy, neuritic threads and neuronal TAR DNA-binding protein–43 (TDP–43) proteinopathy. Tau protein aggregation and formation of neurofibrillary tangles is also associated with the loss of control of mood, emotions, and intellectual functioning. The pathological hallmarks of CTE have been recently discovered in the brains of professional athletes who suffered repetitive TBI and in brain tissue from deceased combat veterans diagnosed with psychological disorders such as PTSD and manic depression. In fact, it is now widely recognized that the behavioral sequeale of CTE can mimic Alzheimer's disease (AD) and Frontotemporal Dementia (FTD), including memory loss and depression. The severity of AD has been associated with abnormal hyper-phosphorylated tau containing aggregates of TDP–43. Repetitive TBI with the development of CTE leads to abnormal TDP–43 expression in about 83 percent of cases. Thus, it is imperative to develop a therapeutic intervention which can block the cellular and molecular cascades following TBI that lead to tau misfolding and aggregates, NFT formation and tau proteinopathy. The recent elucidation that NFT is made of tau and amyloid fibers should make it possible to select specific drugs and molecules that may stop or prevent the process from progressing, rather than simply suppressing the symptoms. That is to say, simply, concussion may not have to be a compounding injury at all. The findings of tau and TDP–43 are not only linked to CTE but also to Anterior Lateral Sclerosis (ALS). ALS is a degeneration of the motor portions of the spinal cord that allow for voluntary muscle activity. Recently, autopsied victims of brain trauma also diagnosed with ALS have shown that these pathological markers are not only in the brain but have diffused into the spinal cord.

The Aging Veteran Community

Commonly referred to as a signature wound of the last 12 years of sustained combat in Iraq and Afghanistan, TBI remains number one on the Combatant Command (COCOM) medical priority guides because of the impact on readiness and combat effectiveness, as well as the long term effect on service members' health and quality of life. According to Defense Medical Surveillance System (DMSS), Defense and Veterans Brain Injury Center, of the total 253,330 *reported* traumatic brain injury (TBI) cases between January 1, 2000, and August 20, 2012, 194,561 have been mild. As with other populations, combat-related brain injuries can result in serious neurological and psychological disorders, such as memory impairment and suicidal ideation. Additionally, and perhaps unique to the military and veteran community, concussion can amplify PTSD behaviors. Given the seriousness of this injury on both military readiness and the aging veteran population, as well as the translation of any findings to the overall civilian population, the Department of Defense and Department of Veterans Affairs are collaborating on concussion research. The majority of their research funding and effort, however, has been spent on diagnosis and prevention, rather than treatment. Given the compounding nature of concussion, as well as the enormous cost of treating our already aging veteran population, in my professional opinion more emphasis must be placed on developing treatments. There are, however, bright spots. The Army's Medical Research Material Command (MRMC) is working to fund research on treatments; the Combat Casualty Care Di-

rectorate has a staff that is attuned to their mission of treating combat injuries and, when possible, returning soldiers to the battlefield. Dr. James Kelly, Executive Director of the National Intrepid Center of Excellence, is also leading the way in efforts to treat our Wounded Warriors. The work that both of these organizations are doing right now, I believe, will yield positive results that will translate to the civilian population just as other areas of military research have ultimately done so. Given the translational nature of this research, this Committee, the Committee on Veterans Affairs, the Armed Services Committee and the HELP Committee should continue to emphasize, across Committee jurisdictions, the importance of the effort to find a treatment for concussion.

Kids and Concussion; the Unknowns

By midnight tonight, nearly thirty children in the U.S. will have died from head injuries incurred today and many more will develop lifelong disability from their TBI. Even more will exhibit at least transient impairment of learning, development, and behavior. Although head injury is the leading cause of death and disability in children, there are only general management guidelines, and no Class I evidence supporting any standard therapy. While only a modest number of pediatric clinical trials for traumatic brain injury (TBI) have been conducted, nearly all pediatric trials and over 100 adult TBI trials have failed to show significant neuroprotective benefits of any specific therapy. More attention to the potential risks associated with TBI in the developing brain is needed to develop proper management and treatment strategies. While we do not fully understand the vulnerability of a child exposed to repeated TBIs in sports and household settings, we do recognize that this population struggles even more than the adult population to recover from a single TBI, because the brain is not fully developed until people are in their early 20's, the risk for serious brain injury is greater for those athletes who are younger than 25. The risk may be particularly great for high school athletes because they are big and strong enough to hit each other with tremendous force, but their brains are certainly not mature. Therefore, dangers in the near and long term are clearly highest in a younger population of athletes.

Brain Injury in the Elderly; Dramatic Increases With Prolonged Life Span

In the opinion of the World Health Organization, TBI will surpass many diseases as the major cause of death and disability by the year 2020. Approximately 10 million people worldwide are affected by TBI per year. Often neglected, elderly TBI patients are going to be an increasing financial burden to the society as our population continues to age. The CDC has identified concussion as a silent epidemic and the elderly portion of this diagnosis the silent population. Falls are the leading cause of TBI in the elderly. Following a TBI an elderly person has much more trouble returning to normal. The aged brain is not equipped to recover from trauma like more youthful adult brains. Additionally, the elderly have a much harder time recovering when left non-ambulatory and from avoidance of other transmittable conditions associated with trauma as their immune system is weaker with age. Often following a TBI an elderly patient will be transferred directly to long term housing. Many of the elderly are on blood thinners for other conditions and therefore more likely to acquire a hematoma with increased intracranial pressure following a blow to the head. The CDC has made a strong effort to educate caregivers on how to reduce falls in the elderly however studies are still needed to determine specific treatment and management strategies for the elderly who have sustained a TBI which tends to present differently than in younger adults.

Research Methods

Recent workshops of the TBI and stroke scientific communities have examined why agents with preclinical therapeutic efficacy have failed to translate to clinical success. In addition to challenges imposed by the heterogeneity of TBI and differences between rodents and humans, they concluded agents should be tested in multiple animal models, using clinically relevant outcomes, short-term and long-term endpoints, and histological and functional metrics, because of marked differences in maturation, morphology, and injury mechanisms, current and popular rodent TBI preclinical therapy trials must be complemented by additional preclinical trials. Pig models are highly developed and currently should be considered the top choice. Research is needed to develop time-courses and mechanisms associated with focal and diffuse injuries that will identify time intervals and targets for

future clinical care to develop management and treatment strategies. Further research is needed to develop clinically relevant imaging and neurointensive care monitoring methods in animal models.

Conclusions

Concussions and other forms of TBI will no longer be a silent epidemic as we continue to shine light on the negative effects of the disorder. TBI transcends generations and populations from the infant to the elderly and from athletic fields to battlefields. In our fast-paced and too often violent world it is no surprise that head injuries are becoming all too common. The current cost to society to care for TBI patients is over 70 billion dollars per year in the US alone. From lost work for the victim as well as their family members to surgical procedures to reduce pressure on the brain, the consequences of TBI are catastrophic to so many involved. Research to date has focused on identifying the pathology of the injury and diagnosing based on individual presentation. Further funding has gone to prevention to try and improve protective gear and educate caregivers/coaches/commanders on removing risks. Unfortunately, no funding has focused on developing new treatments from a pharmaceutical or rehabilitation perspective. As many more parents are keeping their kids out of sports these days due to fear of concussion this may lead to other disorders such as obesity and juvenile diabetes as a result of lack of activity. Furthermore, no one wants to see rule changes to our favorite past times which reduce the excitement of the games. Even more disturbing for the safety of our country would be a reduction in armed forces enrollment.

In my professional opinion we are dealing with two major issues that need our complete focus and this focus requires research and development funding and collaboration. First, concussions are compounding. In other words, if you have one you are more likely to have two and they become additive when it comes to pathological findings and subsequent negative presentation. Therefore we need to develop new acute pharmaceutical treatments that are delivered immediately after the concussion to prevent the compounding nature of subsequent concussions. By developing new rehabilitative techniques they can be used as an adjunct to these drug treatments. Second, we have a population that currently has or is predisposed by multiple prior concussions to AD and ALS-like pathologies. Therefore we need to develop new chronic pharmaceutical treatments that can block the progression of these pathologies and stop the disease process in its path.

Prevacus Incorporated is positioned today to develop a pharmaceutical for the acute treatment of concussion and prevent the compounding effects of brain trauma. Designed as a nasal inhalant the drug will be readily available in the field for use by athletic trainers, medics and ambulance technicians. The lead candidate is a neurosteroid and in toxicology studies. Clinical trials are designed to start in January, 2015 if sufficient funding is acquired. We have also designed 22 other neurosteroids and are poised to start preclinical studies with two of them this summer in animal models of AD and ALS. Now is the time for leaders in science, medicine and government to come together to advance new treatments for concussion and halt the progression of others who are already facing the TBI-associated pathology.

Written Testimony of Robert A. Stern, Ph.D.

Professor of Neurology, Neurosurgery, and Anatomy & Neurobiology
Director, Clinical Core, BU Alzheimer's Disease Center
Co-Founder, Center for the Study of Traumatic Encephalopathy
Boston University School of Medicine

Before the Special Committee on Aging
United States Senate

Hearing on "State of Play: Brain Injuries and Diseases of Aging"

Wednesday, June 25, 2014

Good afternoon, Mr. Chairman, Ranking Member Collins, and distinguished Members of the Committee. It is a great honor to appear before you today for this hearing on "Brain Injuries and Diseases of Aging." My name is Dr. Robert Stern. I am a Professor of Neurology, Neurosurgery, and Anatomy & Neurobiology at Boston University School of Medicine. I am also the Director of the Clinical Core of the Boston University (BU) Alzheimer's Disease Center, one of 29 Alzheimer's research centers funded by the National Institute on Aging. In 2008, I co-founded the BU Center for the Study of Traumatic Encephalopathy (now referred to as the BU CTE Center) with Dr. Ann McKee, Dr. Robert Cantu, and Mr. Christopher Nowinski who is also testifying before you today.

For the past 25 years I have been conducting clinical neuroscience research, primarily focused on the cognitive, mood, and behavioral changes of aging, in general, and in neurodegenerative diseases, in particular. I have been on the faculties of the University of North Carolina School of Medicine, Brown Medical School, and, for the past 10 years, Boston University School of Medicine. In my role in the BU Alzheimer's Disease Center, I oversee all clinical research pertaining to Alzheimer's disease (AD), including studies aimed at the diagnosis, genetics, prevention, and treatment of this devastating disease.

Chronic Traumatic Encephalopathy (CTE)

Since 2008, my research has focused on the long-term consequences of repetitive brain trauma in athletes. In particular, I have been studying the neurodegenerative disease, chronic traumatic encephalopathy or CTE. CTE is a progressive neurodegenerative disease that can lead to dramatic changes in mood, behavior, and cognition, eventually leading to dementia. It is similar to AD but is a unique disease, easily distinguished from AD and other diseases through post-mortem neuropathological examination. CTE has been found in individuals from ages 16-98, including youth, college, and professional contact sport athletes (including football, hockey, soccer, and rugby players), military service members exposed to blast trauma and other brain injuries, and others with a history of repetitive brain trauma, such as physically abused women, developmentally disabled head bangers, and seizure disorder patients. (See **Table 1.**)

Although CTE has been known to affect boxers since the 1920s (previously referred to as "punch drunk" or dementia pugilistica), it is only recently—since CTE was diagnosed in several deceased former professional NFL players—that this disease has received greater medical and media attention. However, the scientific knowledge of CTE is in its infancy. The little that is known is based primarily on post-mortem examinations of brain tissue and interviews from the family members of the deceased athletes. What these studies have shown

is that, in some individuals, early repetitive brain trauma triggers a cascade of events in the brain leading to progressive destruction of the brain tissue. The hallmark feature of CTE is the build-up of an abnormal protein called tau (See **Figure**; based on the work of Dr. McKee), one of the abnormal proteins also seen in AD (McKee et al., 2013). These changes in the brain can begin years, or even decades, after the last brain trauma or end of athletic involvement, and can lead to memory loss, poor judgment, impulse control problems, aggression, depression, suicidality, movement problems, and, eventually, progressive dementia (See **Table 2**).

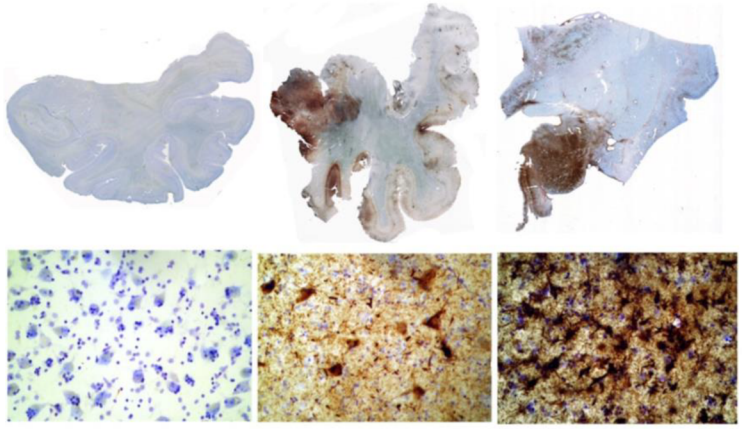

Figure of CTE Neuropathology. Left Top: Section of brain of 65 year old healthy man demonstrating no evidence of abnormal tau depositions. Left Bottom: Microscopic enhancement of same brain sample demonstrating no evidence of tau neurofibrillary tangles that would have shown up as brown from immunostain. Middle Top: Section of brain from 45 year old John Grimsley, a former NFL football player who had a five year decline in functioning (e.g., poor memory, short fuse) prior to his death from an accidental gunshot wound; brown areas are abnormal tau deposits. Middle Bottom: Microscopic enhancement of Grimsley's brain demonstrating neurofibrillary tangles. Right Top: Section of brain of 73 year old former professional boxer who died in a nursing home with clinical diagnosis of dementia pugilistica after several year decline in functioning; brown areas demonstrate widespread tau deposition. Right Bottom: microscopic enhancement of boxer's brain demonstrating widespread tau deposits

The Symptoms of CTE

Although the cognitive changes in CTE are very similar to those in AD, many individuals with CTE develop the significant changes in mood and behavior relatively early in life (Stern, et al., 2013) that can lead to significant distress for the individual with CTE as well as their family, friends, and other loved ones. These mood and behavioral impairments caused by CTE are typically misdiagnosed and attributed to routine psychiatric disorders, stress, substance abuse, or pre-existing personality traits. However, it is completely expected that the areas of the brain

damaged in CTE would lead to these problems, including depression, impulsivity, emotional lability, irritability, and behavioral dyscontrol. It is noteworthy that the much heralded "NFL Settlement" (currently in limbo while the judge examines several issues) began as a class action to address the issue of CTE in former NFL players and to provide the players and their families with appropriate compensation for the losses and distress experienced due to CTE. However, the "settlement," as it is currently written, does not provide any compensation for individuals with the mood and/or behavioral impairments so common in CTE. For example, the families of well-known former players who died of suicide and were found to have CTE post-mortem, such as Junior Seau and Dave Duerson, would not receive any benefits under the currently written settlement if they died after the acceptance of the settlement. Rather, only individuals with the memory, cognitive, and functional independence difficulties associated with Alzheimer's disease dementia would meet criteria for compensation.

Table 1. All cases of neuropathologically confirmed cases of CTE have had a history of repetitive brain trauma. CTE has been diagnosed in the following individuals:
Professional football players
College football players
High school football and other contact sport athletes
Professional soccer players
Semiprofessional soccer player
Professional rugby players
Boxers
Mixed martial art athlete
Combat military service members
Others, including a domestically abused woman, seizure disorder patients, developmentally disabled headbanger

Like other neurodegenerative diseases, CTE can only be diagnosed through post-mortem neuropathological examination of brain tissue. Dr. Ann McKee from our BU center has examined the brains of more athletes and others with repetitive brain trauma than any other neuropathologist. As part of the investigation of these post-mortem cases, I have had the great privilege and honor to interview the family members of approximately 100 deceased former athletes who were diagnosed with CTE after death by Dr. McKee and her team. From these interviews I have begun to learn about the clinical course and presentation of this disease. But, more importantly, I have learned about the tremendous pain and suffering the family members experienced while their loved one's life was destroyed by the progressive destruction of the brain. I have spoken with spouses of former professional football players who slowly lost their ability learn new information, communicate with others, dress, feed, and toilet themselves. I have interviewed

the adult children of former professional and college football and rugby players whose fathers had dramatic changes in personality, the development of aggressive and out-of-control behavior, and suicidal thoughts. And, I have spoken with the parents of young athletes in their 20's or 30's who impulsively took their own lives.

Table 2. Clinical Features of Chronic Traumatic Encephalopathy

Behavioral Features	Mood Features	Cognitive Features	Motor Features
Explosivity	Depression	Memory impairment	Ataxia
Loss of control	Hopelessness	Executive dysfunction	Dysarthria
Short fuse	Suicidality	Lack of insight	Parkinsonism
Aggression and rage	Anxiety	Perseveration	Gait Disturbance
Impulsivity	Irritability	Impaired attention	Tremor
Physical/verbal	Labile emotions	and concentration	Masked facies
violence	Apathy	Language difficulties	Rigidity
Paranoid delusions	Loss of interest	Dementia	Muscle weakness

Diagnosing CTE During Life

I also have been privileged to meet over 70 former NFL players who have come to Boston to participate in my NIH-funded research study entitled, *Diagnosing and Evaluating Traumatic Encephalopathy with Clinical Tests*, or DETECT. I hear their histories, I speak with their family members, and I listen to their fears that they have CTE or that their fellow former football players have or will get CTE. They have all witnessed firsthand the tragic downward spiral of CTE that sadly seems to have become an expected consequence of playing the game they loved. The goal of the DETECT study (which was the first grant ever funded by NIH to study CTE) is to develop objective biological tests, or biomarkers, in order to detect and diagnose CTE during life. The study involves the examination of a total of 100 former professional football players (selected based on positions played and existing clinical symptoms) and 50 same-age non-contact sport elite athletes. All research participants undergo extensive brain scans, lumbar punctures (to measure proteins in cerebrospinal fluid), electrophysiological studies, blood tests (e.g., for genetic studies and novel potential biomarkers), and in-depth neurological, neuropsychological, and psychiatric evaluations. In addition, I have recently received Department of Defense funding (with my colleague, Dr. Martha Shenton of the Brigham and Women's Hospital) and a separate grant from Avid Radiopharmaceuticals (part of Ely Lily) to examine an exciting new Positron Emission Tomography (PET) ligand (developed and owned by Avid) that is specifically designed to attach to the abnormal forms of tau protein found in CTE. Preliminary results of the DETECT study are very promising. However, it is just the first step. Future research is needed, including

longitudinal designs with much larger samples and the inclusion of newer techniques and technologies, as well as post-mortem validation of the findings during life.

To me, the ability to diagnose CTE during life is the next critical step in the study of CTE. It will lead to the ability to answer important questions about this disease, such as: How common is CTE? What are the risk factors for CTE? Can it be prevented? How can we treat it? In other words, at this point, we actually know very little about this disease (See **Table 3**). One thing we do know about CTE is that every case of post-mortem diagnosed CTE has had one thing in common: a history of repetitive brain trauma. This means that the repetitive brain trauma is a necessary factor in developing this disease. However, it is not a sufficient factor. That is, not everyone who hits their head repeatedly will develop this progressive brain disease. There are additional, as yet unknown, variables that lead to CTE, such as genetic susceptibility or specific aspects of the exposure to the brain trauma. Some have argued that brain trauma cannot possibly cause CTE, using the argument that there are many older former football players and other athletes with dramatic brain trauma history who are completely healthy. This irrational argument is analogous to those made years ago that cigarette smoking does not cause lung cancer because there are many people who smoked for decades who never develop lung cancer. An important next step in CTE research is to examine the specific additional risk factors, including genetics and exposure variables.

Subconcussive Trauma

It is important to note that CTE is not a disease restricted to former *professional* athletes. It has been found in individuals who only played their sport up through the *college* level and even just through *high school*. It has been found in warfighters who were exposed to blast trauma and other injuries. Another important issue to note is that post-mortem confirmed CTE has been found in individuals who have had no history of known or reported symptomatic concussions, but, nonetheless, were exposed to a tremendous amount of repetitive hits to the head that did not result in the symptoms of concussion. These "subconcussive" blows are quite common. It is estimated that the typical lineman in football experiences between 1000-1500 hits per season (i.e., at every snap of the ball at every play of every game and every practice), each at 20-30*g*. These hits are not just experienced by professional players. For example, a study by Broglio and colleagues (2011) found that high school football players received, on average, 652 hits to the head in excess of 15*g* of force in a single season. One player received 2,235 hits! To put this in perspective, a car going 35 mph into a brick wall experiences approximately 20*g* of force. There is now growing research evidence that even after one season, repetitive

subconcussive trauma can lead to cognitive, physiological, and structural changes to the brain. And, it appears that this exposure to repetitive subconcussive blows is associated with the development of CTE. This, perhaps, is one of the most frightening aspects of CTE. Over the past few years, there has been a tremendous increase in public awareness of *concussions* and the need to prevent and manage them. The "concussion crisis" in sports is a hot topic in the media, on playing fields, and in doctor's offices. However, when it comes to the long-term consequences of sports-related brain trauma, concussions are likely the tip of the iceberg. That is, subconcussive trauma appears to be as important or more important in the development of CTE.

Table 3. CTE Research is in its Infancy: What are the Important Questions to Address?
How common is CTE?
Is it a critical public health issue?
Above and beyond having a history of repetitive brain trauma, what are the risk factors for CTE?
Do genetics play a role in determining who gets CTE?
What types of brain trauma exposure increase risk?
Is there a certain age in childhood or adolescence when the brain is more vulnerable to brain trauma, increasing CTE risk?
How can we diagnose CTE during life?
Are there specific biomarkers that can accurately detect the abnormal tau deposition in the brain during life?
Can we distinguish between Alzheimer's disease and CTE by clinical examination?
How can we treat the symptoms of CTE effectively?
Can we modify the disease course if we intervene early?
Can CTE be prevented?
What is the biological mechanism for the development of CTE?
How does the abnormal tau move from one part of the brain to another?

Increased Funding for CTE Research

In order to tackle the complex issue of CTE, we must expand upon current approaches to conducting research in neurodegenerative disease. We must break down the traditional silos of individual research labs, research institutions, and disciplines, and begin to conduct multidisciplinary, collaborative research across research centers, bringing together the very best scientists, novel methodologies, and state-of-the-art technology. Most importantly, we must not forget that our research must focus on reducing individual human suffering and improving public health. Alas, this requires tremendous financial support. And, as you all know, current NIH funding is tragically low. The budget cuts to NIH in recent years have resulted in a tragic slowdown in the momentum of scientific discovery, and have led many scientists -- both young

investigators and older senior researchers – to leave their careers in the biomedical sciences. A recent survey by the *Chronicles of Higher Education* (Baskin & Vossen, 2014) of 11,000 senior researchers found that almost half of the respondents already abandoned an area of scientific investigation they considered key to their lab's mission. And more than three-quarters had reduced or eliminated their recruitment of graduate students and post-doctoral fellows because of reduced funding.

I want to express my deepest gratitude toward this Committee and its members for leading the recent effort to increase NIH funding of Alzheimer's disease research. However, **we must have additional funding to support research focusing on CTE and the long-term consequences of repetitive brain trauma in athletes, military service members, and other members of society**. In addition to direct federal funding, this effort will require public-private collaborative funding, such as that which supported the revolutionary Alzheimer's Disease Neuroimaging Initiative or ADNI. What might come as a surprise is that in 2012, the National Football League (NFL) donated $30 million to the Foundation for NIH to support peer-reviewed research studies on injuries affecting athletes, with brain trauma being the primary area of focus. However, that is just the beginning. We need much, much more.

In summary, many of our most cherished games in our country, such as football, hockey, and soccer, often involve repetitive blows to the head, potentially leading to a progressive brain disease with later life behavior, mood, and cognitive changes, as well as the development of dementia. We must learn as much as possible, as quickly as possible, in order to determine who may be at increased risk for CTE and other long-term consequences of the repetitive head impacts experienced by athletes at all ages, and to develop methods of preventing and treating the symptoms of CTE. I want to close by thanking the Committee for your interest in addressing this important issue and for your commitment toward improving the health and well-being of older Americans.

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Questions for the Record

U.S. Senate Special Committee on Aging
"State of Play: Brain Injuries and Diseases of Aging"
June 25, 2014
Questions for the Record
Mr. Christopher Nowinski

Senator Richard Blumenthal

World Wrestling Entertainment (WWE) has implemented the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) Concussion Management Model. This model is used to perform baseline testing on WWE athletes prior to annual contract renewal; the exam is also utilized after an athlete is suspected to have had a concussion in order to determine whether an athlete can return to a match/game. In terms of education, WWE offers an annual education seminar for coaches and participants. The organization has also eliminated props that can potentially lead to head injuries.

Question:

In the course of your interactions with WWE, have you seen data that suggests success of these prevention measures illustrated by a decrease in concussions or brain injuries?

Response:

I requested data on this topic from WWE after receiving your inquiry. I am advised that concussions at NXT (WWE's developmental program) have decreased by more than 50 percent from 2012 092014 as compared to 2009 092011, and by more than 25 percent at WWE during the same time periods. Considering that I would expect an increase in reported concussions due to consistent education on concussions, the decrease may be higher. For example, when I provided a brief educational seminar to most teams in Major League Lacrosse in 2013, concussions jumped from one diagnosed in 2012 to seven diagnosed in 2013, an increase of 600 percent. We believe that the 600 percent increase did not represent more actual concussions, but simply that players were now reporting them. I continue to be

impressed by the programs WWE has put in place to raise awareness for and help the prevention of concussions.

Question:

In your personal interactions with World Wrestling Entertainment (WWE) following your diagnosis and in your collaboration with the organization on behalf of the Legacy Institute, have you found that athletes, diagnosed with neurocognitive deficits acquired from concussions and other traumatic brain injuries, are offered adequate compensation and benefits?

Response:

I am not aware of any WWE talent or former talent who has sought compensation or benefits from WWE due to neurocognitive deficits. In my case, WWE continued to pay me for a period of 4 years following my injury, and also paid for my medical care with multiple experts of my choosing, including Dr. Robert Cantu. In fact, WWE's assistance with Dr. Cantu was the genesis of my relationship with him, which ultimately led to the formation of SLI.

Senator Elizabeth Warren

According to the Centers for Disease Control, traumatic brain injury is a major cause of death and disability in the United States. Data from numerous studies, including a 2012 publication in the journal Brain co-authored by Dr. Stern and Mr. Nowinski, suggest that multiple traumatic brain injuries, even mild ones, can lead to behavioral and cognitive problems. Because of this knowledge, traumatic brain injury is being addressed more seriously in professional sports, in the military, and to some degree in amateur and school sports. But serious, long-term consequences from brain injuries are not limited to athletes. Anyone can experience multiple injuries or accidents throughout their lives.

Question:

How could we do a better job of collecting data on repetitive traumatic brain injuries in people not participating in sports or in the military so that researchers could gain a better understanding of the effects of these injuries in the population?

Response:

I will defer to my colleague Dr. Bob Stern at Boston University.

Physical activity during childhood is important to set the foundation for a healthy lifestyle. In 2010, the Centers for Disease Control reported that there is substantial scientific evidence showing that physical activity can help improve academic achievement and decrease the risk for chronic conditions like heart disease and diabetes by helping kids maintain a healthy weight. Organized sports help many kids stay active and set a good foundation for healthy lives, but it's important that they do not come with a high risk of concussion and serious long-term injury. Concussions have a greater impact on children - kids have a lower injury threshold and poorer recoveries than adults - and even mild injuries can have developmental consequences.

Massachusetts requires that student-athletes even suspected of having a concussion are removed immediately from play - and only allows their return after receiving clearance from a licensed health professional. The Commonwealth also requires a mandatory head injury safety training program for student athletes, parents, and coaches.

Question:

What State-level strategies have been the most effective at reducing concussions and increasing awareness?

Response:

Unfortunately, there is little solid data available to understand which changes have been most effective at reducing concussions and increasing awareness. Most State-level strategies have focused on three points.

- No return to play same day of a suspected concussion.
- No return to play until cleared by an appropriate medical professional.
- Annual concussion education.

There is no question that annual concussion education is likely to increase awareness and increase the number of recognized and diagnosed concussions. However, the quality of the education matters significantly, and very few States require rigorous programming. Our team studied the athlete education provided to

six elite college ice hockey teams and found that those that were just provided a handout or received an e-mail did not improve concussion knowledge.[1] Even those athletes who received more comprehensive education, who did show improved concussion knowledge, did not show changed behavior in the form of being more likely to report concussion symptoms.

Other important groups have received even less comprehensive education. Parents are rarely required to receive education beyond a handout, and coaches are usually required to only view a 30-minute online video. More funding needs to go into research on how we effectively educate stakeholders.

The greatest opportunities we have to prevent concussions and minimize risk tend to lie outside State control, although States are starting to be more proactive. For example, the greatest opportunity to prevent concussions in football is to reduce hitting in practice. The NFLPA negotiated with the NFL to have only one full-contact day of practice per week in 2010. In 2011, The Ivy League changed their policy to allow only 2 days per week. It took years before State high school athletic associations began following suit, partially because high school athletes don't have a union through which to negotiate protections. Only recently, California became the first State to legislate practice limits at the State level (only about 10 States currently have limits) and I hope more follow their lead.

Question:

What strategies you would like to see more widely adopted to reduce our kids' risk of concussion?

Response:

I believe we are making incremental gains in education, concussion recognition and diagnosis, and managing return-to-play, return-to-school, and return-to-life. The strategy that will make the biggest difference is to change the rules of sports for youth. Many youth sports are modeled too closely to their professional or collegiate version, despite the fact that hits to the head and concussions are far riskier for younger athletes.

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[1] AKroshus E, Daneshvar DH, Baugh CM, et al. NCAA concussion education in ice hockey: An ineffective mandate. Br J Sports Med 2013.

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Some sports have made changes - USA Hockey has raised the age to introduce checking from 11 to 13, and US Lacrosse has made all head contact illegal. Our non-profit, the Sports Legacy Institute, recently partnered with the Institute for Sports Law and Ethics at Santa Clara University along with US women's soccer legends Brandi Chastain and Cindy Parlow Cone to urge parents and coaches to eliminate heading in soccer before high school. At least 30 percent of concussions, and potentially more than half, are caused by the act of heading at that age, a skill that many feel is unnecessary before high school.

In the big picture, I don't think it is appropriate to expose young children to repetitive, purposeful brain trauma in sports.

We are also excited about the potential of head and helmet sensors to create safer sports. While we don't yet have a concussion threshold where sensors could accurately warn sideline personnel about a concussive impact, the data could still be valuable. Our Hit Count® program is designed to count every meaningful impact to the head, which our experts determined is the sub-concussive level of 20g of linear acceleration, which is above normal movement of the head.

Over the next year, working with sensor companies that have passed a laboratory certification test developed in conjunction with a leading academic neurotrauma lab, we hope to understand what is a ``normal'' Hit Count® for every sport, age, gender and position. By counting Hits, we will make coaches accountable for how they designed practice and players for their technique, and the Hit Count® will reveal opportunities for changes. For example, in a recent study of 9- to 12-year-old football players by Virginia Tech, one team averaged a Hit Count® of 150, and another team averaged only 61, but was still successful. By extrapolation, this means that of the 1.5 billion Hits that occur in football each year, hundreds of millions could be eliminated.

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Mr. Ben Utecht

Senator Elizabeth Warren

Physical activity during childhood is important to set the foundation for a healthy lifestyle. In 2010, the Centers for Disease Control reported that there is substantial scientific evidence showing that physical activity can help improve academic achievement and decrease the risk for chronic conditions like heart disease and diabetes by helping kids maintain a healthy weight. Organized sports help many kids stay active and set a good foundation for healthy lives, but it's important that they do not come with a high risk of concussion and serious long-term injury. Concussions have a greater impact on children – kids have a lower injury threshold and poorer recoveries than adults – and even mild injuries can have developmental consequences.

Massachusetts requires that student athletes even suspected of having a concussion are removed immediately from play – and only allows their return after receiving clearance from a licensed health professional. The Commonwealth also requires a mandatory head injury safety training program for student athletes, parents, and coaches.

Question:

What state-level strategies have been the most effective at reducing concussions and increasing awareness?

Response:

Thank you for your question regarding the most effective state-level strategies for reducing concussions and raising awareness of concussions. I am pleased that nearly every state has a law or several laws on the books addressing this issue, most of which address (1) education of athletes, coaches and parents about symptoms and risks associated with concussions; (2) removing from play a youth

athlete suspected of a concussion; and (3) clearance by a health professional for return to play.

I specifically commend efforts to:

- Adopt evidence-based protocols governing evaluation and management of concussion;
- Require utilization of medical experts (including concussion specialists) at games;
- Limit the number of off-season practices and number of in-season contact practices;
- Provide comprehensive education/certification programs for coaches, trainers, and players; and
- Promote accountability within schools and youth sports programs to ensure that state laws, rules and other protocols are being followed appropriately.

Question:

What strategies you would like to see more widely adopted to reduce our kids' risk of concussion?

Response:

I love the game of football, and always will. I want America's favorite past time to remain as strong as it is today. When it comes to our youth, I believe that limiting the amount of contact can be an important step in reducing the risk of concussions.

Some proposals to achieve this include:

- Changes to the off-season schedule (lengthening off-season and limiting number of contact practices);
- Strongly encouraging fair play policies and enforcement of the rules; and
- Additional medical research concerning the long-term consequences of concussion among youth participants and education regarding the number of impacts and the magnitude of those impacts per week and per season.

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Questions for the Record
Mr. Jacob VanLandingham, Ph.D.

Senator Richard Blumenthal

Question:

In 2009, the National Football League (NFL) developed a stricter protocol for response to concussions. Specifically, a NFL athlete is prohibited from returning to a game, until that athlete tests normal for cognitive and motor function, if he suffers a concussion or shows signs of having suffered a concussion. Moreover, players, coaches, and trainers are now educated on how to identify the signs and symptoms of concussions.

To what extent are these precautions successful in reducing the number of concussions and other head injuries?

Response:

The NFL has developed much more stringent protocols to respond to the epidemic of concussions associated with this sport, including a major change in how players tackle. According to the NFL, the process begins prior to the opening of the season and training camp when team doctors perform "baseline" examinations to clinically assess memory, reaction time, attention span, problem-solving abilities and other cognitive skills that can be affected by a concussion. Players complete a list of current symptoms including headache, neck pain, fatigue, etc. Neuropsychological tests including the Immediate Post-Concussion Assessment and Cognitive Testing (IMPACT) test and the Automated Neuropsychological Assessment Metric (ANAM), developed by the U.S. Military, are employed. On the field, there is now "an eye in the sky", a certified athletic trainer who sits in the stadium box seat and watches the game live and via television replays to scan the field for players with potential concussive injuries who may require assistance.

As of 2013, a "Neurotrauma expert" physician unaffiliated with the team (the unaffiliated neurotrauma consultant or UNTC) is also available on the sideline as

an “extra set of eyes”. Under 2013 guidelines, players with suspected concussions are assessed by the team medical staff, including a six-item checklist by the team physician that determines whether the player should be removed immediately from the game. These tests include loss of consciousness, unresponsiveness, confusion, amnesia and other concussion-related symptoms. The remaining sideline concussion assessment tool is then administered, which include all the tests performed as part of the pre-season baseline assessment. Memory, concentration, and balance are evaluated, including how quickly and thoroughly the player can recall words presented to him five minutes earlier. Other questions are presented, including specific orientation questions. The process, as stated by the NFL, currently takes about “8-12 minutes” Currently, an NFL player is prevented from returning to a game until he tests “normal” for cognitive and motor function and any player diagnosed with a possible concussion is required to leave the filed for the locker room.

These guidelines, in my opinion, represent a major, but incomplete, step forward towards the protection of professional athletes from re-injuring a brain made vulnerable by concussion by remaining on the field of play. Nearly 1/5 of NFL players surveyed by the Associated Press admit to hiding or playing down the side effects they are experiencing in order to remain in the game. We must protect the players from themselves and their ultra-competitive desire to continue competing at any future cost to their health and well-being. While little data exists to confirm that the actual number of concussions AND the number of players allowed to return to the field with a suspected concussion has decreased since these guidelines were put into place, these are not laurels that the world of professional sports should rest on. Concussion are often an “insidious foe” exactly because their signs are not visible. Slurred speech, impairment in recall, loss of muscle control does not always occur for every concussion. “Subconcussive” changes- those that occur in the brain with no outward behavioral signs or correlates- may occur with impacts on the field that will only reveal themselves with advanced testing and often much later down the line. Impacts that are not viewed as having the potential to cause concussion may, actually, be exacerbated when the player’s head hits the ground, creating a second impact that may push things over the line into a true concussion. Since these impacts occur with such frequency in American Football and given the self-professed “8-12 minute” timeline (which, realistically speaking, would probably be more like 20-30 minutes), the sideline medical staff would be overwhelmed trying to conduct concussion testing on multiple players every set of downs. Moreover, the “eye in the sky” unaffiliated athletic trainer may be called to the sideline and requested to perform an evaluation, but these are not documented, and it remains unclear how much additional time this would add before the player

was deemed “eligible” or “ineligible” for further contact. The UNTC physician is required to be positioned at the 25 yard-line, away from team personnel and can only enter the personnel area to evaluate a player if he is called to do so by the team physician. No data is available as to how frequently this occurs and whether the addition of the UNTC has facilitated on-field concussion diagnoses. Stricter compilation of data by the NFL would be helpful in our ability to determine whether the newly created guidelines are effective in accurately diagnosing concussion and preventing “second impact” syndrome and other damaging sequalae of on-field impact.

The connection between traumatic brain injury and Lou Gehrig’s Disease, or ALS, has been called into question.

A 2010 New York Times article stated that many times these injuries can be classified as Chronic Traumatic Encephalopathy (CTE). A 2013 NFL settlement brought by 4,500 retired players resulted in a total $765 million compensation package put a value on each diagnosis. The settlement allocates a higher compensation value to those diagnosed with ALS. Less money is given to players who have been diagnosed with CTE and even less to those with other neurocognitive benefits.

Question:

Is the difference of treatment based on diagnosis in this compensation package comparable to similar to any general benefits and compensation given to athletes with neurocognitive deficits resulting from sporting injuries?
Can you explain why certain athletes are compensated more when diagnosed with ALS?

In the absence of a legal settlement, what compensation is available to athletes with long-term cognitive or physical effects related to their play in the NFL?

Response:

Distinguishing definitions are helpful here at the outset:

- Amyotrophic lateral sclerosis (ALS) - also known as Lou Gehrig's Disease or motor neuron disease. This is a progressive neurodegenerative disease that destroys the nerve cells in the spinal cord and brain. Motor neurons reach from the brain to the spinal cord, and from there to all our muscles.

The progressive deterioration of the motor neurons eventually causes death. The death of motor neurons leads to the loss of muscle control. In the later stages of the disease, patients become completely paralyzed.

- Alzheimer's disease - a progressive neurologic brain disease which leads to irreversible loss of neurons and cognitive abilities, including memory and reasoning.

Recent studies reporting a six-fold increase in the prevalence of ALS in soccer players prompted a similar investigation in NFL players. A retrospective analysis conducted online indicated that 8 of 3,891 players who played after 1960 had ALS, a prevalence of 206 per 100,000 and a *40-fold higher* prevalence rate than that for the general U.S. population (5 per 100,000). Subsequent studies reported in 2012 have reported that NFL players are three times more likely to die from neurodegenerative diseases than the general U.S. population and four times more likely to die from Alzheimer's Disease (AD) and ALS. This study analyzed data from a cohort of 3,439 NFL players who played at least five seasons between 1959 and 1988. Analysis showed that NFL players had a significantly increased mortality from neurodegenerative disease – three times greater than that of the general U.S. population and, similar to the original studies, a *four times* greater mortality rate for AD and ALS. One study found that "speed" positions (62% of the cohort- quarterback, running back, halfback, fullback, wide receiver, tight end, defensive back, safety and linebacker) are at higher risk of neurodegenerative mortality compared with lineman or "nonspeed" position players. More recent studies suggest that chronic traumatic encephalopathy (CTE), a distinct disease with symptoms resembling other neurodegenerative diseases, may have been the true primary or contributing cause of death in many of these cases. Since CTE is a recently discovered diagnosis, it has not been traditionally included on players' death certificates. A brain autopsy is necessary to distinguish CTE from AD or ALS. While CTE is a separate diagnosis, the symptoms are quite similar to those of AD, ALS and other neurodegenerative diseases. There have been several high-profile NFL players who have developed ALS, including Steve Gleason, who played for eight seasons and developed ALS at age 34.

Under the recent settlement, individual awards will be capped at $5 million for men with Alzheimer's disease; $4 million for those diagnosed after their deaths with CTE; and $3 million for players with dementia, according to the lead plaintiffs' lawyer Christopher Seeger. For any player to collect compensation before his medical situation reaches the level of CTE, the settlement proposal requires that they suffer from specified levels of dementia. Although their clients suffer from serious and disabling symptoms, attorneys for the NFL players have

noted that none of them have reached the stage of dementia that would qualify them for a payment under the settlement proposal. Presumptively, the differences determined by the NFL Commission with respect to compensation for athletes with ALS vs. other neurodegenerative diseases may have to do with the fact that this disease, because it disrupts motor neuron pathways and influences spinal cord and motor function, may require more chronic care, equipment, respiratory, urinary tract and other physiological disabilities which other neurodegenerative diseases that affect primarily cognitive function do not.

Question:

According to data from the National Electronic Injury Surveillance System-All Injury Program and analyzed by the Centers for Disease Control, horseback riding has the highest rate of traumatic brain injury-related emergency department visits, out of all recreational sports. Why might TBIs among equestrians be occurring at such an alarming rate? Why do accidents among horseback riders and equestrians tend to be more serious than in other sports?

Data shows that the rate of injury among horseback riders is higher than even bicyclists and motorcyclists. Do you think there should be a federal minimum safety standard for equestrian helmets, as there is for bicycle helmets?

What research do you think should be funded that would help inform helmet safety standards and make sure that they incorporate the most advanced science and technology?

Response:

Each year, roughly 70,000 people are treated in emergency rooms because of equestrian related injuries. The average age of an injured equestrian is between 10 and 19, while riders with 5 or more years' experience are more likely to be injured. The most frequent cause of death and serious injury for mounted and dismounted horse-related activities is TBI and, according to the CDC, horseback riding cause the highest proportion (11.7%) of TBIs among sports-related recreational activities. Amazingly, a motorcyclist can expect one serious accident for every 5,000 hours of riding but an equestrian, on the other hand, is likely to sustain a serious accident in just 350 hours of riding. Brain injuries comprise 18% of all equestrian injuries and are the number one reason for horse-related hospital admissions and the leading cause of death (NIIC) and the proportion of brain injuries in sports-related emergency visits is highest for horseback riding (CDC). TBI is the cause of death

in 60% of all equestrian fatalities. To put it in perspective, on average, there are 8 TBI-related deaths each year in contact sports such as football but 60 TBI-related equestrian deaths annually.

Riding injuries occur most frequently in riders younger than 21 years of age. In 1999, 15,000 horse injuries to children ages 15 and under required ER visits. Falling or being thrown from a moving horse account for the majority of mounted injuries, while being kicked or trampled accounts for most dismounted injuries. Interestingly, evidence suggests that dismounted injuries require hospitalization approximately 42% of the time, while mounted injuries require hospitalization in only 30% of incidents.

We believe that the incidence of TBI among horseback riders and equestrians is more serious and prevalent than in other sports because, like household falls, the brain is subjected to rotational, slow-shearing forces as it strikes the ground that cause both focal and diffuse brain injury. Indeed, it is known that the height of the fall from horseback is the most significant factor in predicting injury severity (probably related to the force of the head striking the ground). The effect is likely to be amplified during equestrian activities since the rider is being thrown from a fast-moving horse, which superimposes the complicating and additive dimension of acceleration into the impact/rotation/impact scenario. This likely adds to the severity of brain injury forces.

Currently, there are no experimental models of equestrian TBI and the development of laboratory models of acceleration-fall injuries should be promoted to better understand the underlying mechanism of injury morbidity and mortality. Gender difference studies with respect to outcome should also be solicited and supported, since women are much more likely to experience a horseback related TBI (vide supra) and more likely to suffer a concussion and permanent disability vs. male riders. The Committee is encouraged to support additional data collection on equestrian injury – the influence of the height of the jumps, speed of the horse, etc. Better data collection is necessary.

I believe that prevention is one of the keys to this significant health problem. Only 20% of equestrians wear protective headgear every time they ride. There is a *four-fold* increase in mortality for injured, non-helmeted riders suggesting that the use of approved helmets is associated with a decline in severe TBI. We agree that federal minimum standards for equestrian helmets should be instituted, effective immediately. Better awareness and research that improves safety standards for

equestrian helmet safety incorporating the most recent scientific advances should be strongly encourage.

Senator Elizabeth Warren

According to the Centers for Disease Control, traumatic brain injury is a major cause of death and disability in the United States. Data from numerous studies, including a 2012 publication in the journal *Brain* co-authored by Dr. Stern and Mr. Nowinski, suggest that that multiple traumatic brain injuries, even mild ones, can lead to behavioral and cognitive problems. Because of this knowledge, traumatic brain injury is being addressed more seriously in professional sports, in the military, and to some degree in amateur and school sports. But serious, long-term consequences from brain injuries are not limited to athletes. Anyone can experience multiple injuries or accidents throughout their lives.

Question:

How could we do a better job of collecting data on repetitive traumatic brain injuries in people not participating in sports or in the military so that researchers could gain a better understanding of the effects of these injuries in the population?

Response:

In the United States, the number of people 19 and under treated in emergency rooms for concussions and other traumatic brain injuries linked to sports and recreational activities jumped from 150,000 in 2001 to 250,000 in 2009. Many of these people are sent home with aspirin, advice for rest and a checklist for the telltale signs of concussion. Even amongst the general population, there is a "culture of resistance" for reporting the signs and symptoms of a concussion. Our culture, particularly with respect to males, emphasizes the stoic, tough-it-out response to getting one's "bell rung". Moreover, recent evidence suggests that experiencing one concussion makes a person much more likely to have a second or third brain injury. So repetitive mild TBI is truly an unreported epidemic in the general population. The most recent data suggests that 5 of 10 concussions go unreported or undiagnosed. Current imaging may miss the existence of brain damage up to 70% of the time. Better diagnostic tools to uncover and detect mild TBI and/or concussion are greatly needed. More sensitive metrics and rapid tests need to be developed to diagnose a sub-clinical mild TBI. The advent of recent

exploration of blood- born "biomarkers" of concussion and brain injury – chemicals that are released by the brain after even the slightest impact and find their way into the bloodstream- suggests that this area of research is critical for development. A rapid blood-stick and test to diagnose concussion is not the stuff of future science-fiction and these studies need to be funded and promoted urgently.

Emergency room physicians must be educated and trained to report any suspected person who visits the ER and who is suspected of having a concussion, even if they are triaged and sent home without being admitted. The establishment of a central National database for ER/urgent care clinic visits for concussion would greatly facilitate the collection of data. Private physicians should also be educated to report possible concussion in patients who choose not to visit the hospital ER but seek medical attention with their private-practice doctors.

Physical activity during childhood is important to set the foundation for a healthy lifestyle. In 2010, the Centers for Disease Control reported that there is substantial scientific evidence showing that physical activity can help improve academic achievement and decrease the risk for chronic conditions like heart disease and diabetes by helping kids maintain a healthy weight. Organized sports help many kids stay active and set a good foundation for healthy lives, but it's important that they do not come with a high risk of concussion and serious long-term injury. Concussions have a greater impact on children – kids have a lower injury threshold and poorer recoveries than adults – and even mild injuries can have developmental consequences.

Massachusetts requires that student athletes even suspected of having a concussion are removed immediately from play – and only allows their return after receiving clearance from a licensed health professional. The Commonwealth also requires a mandatory head injury safety training program for student athletes, parents, and coaches.

Question:

What state-level strategies have been the most effective at reducing concussions and increasing awareness?

What strategies you would like to see more widely adopted to reduce our kids' risk of concussion?

Response:

All physical activity involves some risk of injury. Although it will be impossible to prevent all future sports-related concussions in young people, specific measures can be developed and employed to reduce the risk of these injuries. The State of Washington House Bill 1824, also known as the Zackery Lystedt law, was signed into law in May 2009 and is widely recognized as the first statewide advocacy effort focused on concussion prevention to formally result in the passage of legislation. Most states have since followed suit, resulting in adoption of laws addressing concussions in youth sports across the United States. In fact, since 2009, all 50 states and the District of Columbia have introduced formal bills before their legislatures with language addressing youth concussions.

Consideration of these bills has resulted in either codified statute or statewide administrative regulation in 49 states and the District of Columbia. The one exception is Mississippi; concussion legislation was last introduced in the Mississippi legislature in January 2013, but it did not pass through committee. Although state concussion laws do not focus on the primary prevention of concussion, they do aim to increase *awareness* about concussion signs, symptoms, and outcomes and to reduce the risk and consequences of multiple concussions and potentially to promote quicker recovery. State law-mandated use of protective and preventative equipment such as helmets has been shown to reduce both mortalities and severity of brain injury. According to a recent NIH report *"Sports-Related Concussions in Youth: Explaining the Science, Changing the Culture":* "Helmets are designed to mitigate the likelihood of head injuries from an impact to the head by dissipating and distributing the energy of impact and protecting the head from penetration. Early helmets were designed to prevent such injuries as skull fractures as well as moderate to severe brain injuries such as focal contusions and hemorrhages. The typical helmet has a comfort liner, an impact energy attenuating liner, a restraint system, and a shell. Some helmets, such as those used in motor sport, bicycling, and alpine skiing, are designed to attenuate a single impact. Once one of these single-impact helmets has sustained an impact, it must be replaced. Other helmets, such as those used in ice hockey, football, and lacrosse, are designed to withstand multiple impacts over a season of games and practices (Hoshizake and Brien, 2004). Part of the difference between single-impact helmets and multiple-impact helmets lies in the materials used. For example, multiple-impact helmets, such as those for hockey and football, use materials that do not permanently deform but rather compress and return to their original dimensions. Inner shells can be made of vinyl nitrile or expanded polypropylene, and outer shells use lightweight plastics and composites for durability and protection. Single-

impact helmets contain materials that are frangible and deform or fracture permanently upon impact as part of their energy management strategy…Epidemiological evidence that helmets mitigate concussion primarily comes from the bicycle helmet literature. In a review of five case-control studies from the literature, Thompson and colleagues (2000) concluded that bicycle helmets reduce the risk of head injury (defined as any injury to the brain or skull) by 69 percent, the risk of brain injury by 69 percent, and the risk of more serious brain injury (a score of 3 or more as measured by the Abbreviated Injury Scale score, or AIS) (see AAAM, 1998) by 74 percent as compared with control groups consisting of individuals who visited emergency departments after bicycle accidents in which they were not wearing helmets. Furthermore, when they used a control population of all cyclists who crashed, they documented even stronger benefits (85 percent reduction of head injury, 88 percent reduction in brain injury). Although these studies do not specifically separate out concussion injuries, approximately 70 percent of the brain injury subgroup in the study sustained injuries of an AIS 2 level, most of which were likely concussions. The studies they reviewed did not focus exclusively on children, but about two-thirds of the population studied were children and adolescents." Moreover, "In soccer the only formal epidemiological evaluation of headgear in the literature was conducted by Delaney and colleagues (2008), who reported that among Canadian male and female soccer players ages 12 to 17 (n=278) those who did not use headgear were 2.6 times more likely to sustain a concussion than those who did." However, advances in helmet test standards that incorporate the newest data and new injury criteria for concussion that include the evaluation of potential protection from both linear and rotational loading forces are called for.

The preventative use of mouthguards represents a simple but seemingly effective technique for reducing the risk of concussion and mild TBI. According to the NIH report cited above, "It has been speculated that mouthguards may reduce the risk of concussions caused by impact to the jaw by positioning the jaw to absorb some of the forces that would otherwise be transferred through the base of the skull to the brain (Knapik et al., 2007; Takeda et al., 2005). One biomechanical study found that when hits to the mandibular undersurface of a mechanical skull were applied, the presence of a mouthguard significantly ($p < .01$) decreased surface distortions related to deformation or fractures to the mandibular bone (by 54.7 percent) and significantly decreased linear acceleration of the head (by 18.5 percent) compared to when a mouthguard was not in place. Nonetheless, the authors of this study acknowledged that further well-designed research is needed on the relationship between mouthguards and concussion risk. Another group of researchers, who worked with a cadaver model, found that having a mouthguard in place reduced by

50 percent the amplitude of bone deformation and intracranial pressure that followed a hit to the chin (Hickey et al., 1967)." Additionally, facial protection, including face shields and visors, have been shown anecdotally to reduce the incidence of concussion and facial/head damage associated with ice hockey.

State-level strategies could also include better regulation of playing surfaces and playgrounds. According to the recent NIH report, "From 2001 through 2008 there were an estimated 1,786,608 emergency department (ED)–treated injuries associated with playground equipment, of which 30,578 (2 percent) were concussions. (The actual number of playground-related injuries, including concussions, is likely much higher, given that many such injuries are not treated in an ED.) The greatest share of playground injuries of all types (44 percent) involved falls from, into, or onto equipment, followed by injuries involving equipment breakage, tip over, or poor design or assembly (23 percent) (CPSC, 2009). To reduce the likelihood of head injuries on playgrounds, it is important to consider the impact-attenuating properties of the surfacing under and around the playground equipment (CPSC, 2010). The Consumer Product Safety Commission (CPSC) and ASTM International have developed guidelines for playground surfacing. The most recent CPSC handbook for public playgrounds states that playground equipment should not be placed over asphalt, concrete, dirt, grass, or carpet not tested to ASTM F1292. ASTM standard F1292 provides a "critical height" rating for playground surfaces that approximates the fall height below which a life-threatening head injury would not be expected to occur. The rating assigned to a given surface should be greater than or equal to the fall height of the highest piece of equipment on the playground. Preferred surfacing includes unitary surfaces (rubber tiles, mats) tested to ASTM F1292; loose fill materials (pea gravel, sand, wood mulch not treated with chemical preservative, and wood chips) maintained at a minimum depth of 9 inches; or shredded or rubber mulch maintained at a minimum depth of 6 inches (CPSC, 2010).4 Recent nationwide data on the safety conditions of playgrounds are not available. A 2004 survey of 3,000 school, childcare, and park playgrounds in the United States resulted in overall grade of B– for fall surfacing and, within this category, a grade of F for appropriate depth of loose fill materials (National Program for Playground Safety, 2004). There currently are no national safety standards for outdoor play equipment." Currently, only a relatively few states mandate compliance with the CPSC guidelines.

Cheerleading is another youth activity whose risk of concussion, while poorly studied, could benefit from greater regulation of surface material. According to the NIH report, "Concussions and other closed-head injuries account for 4 to 6 percent of all cheerleading injuries (Labella and Mjaanes, 2012). Although concussion

rates in cheerleading (0.06 per 1,000 exposures) are low compared with other sports, from 1998 to 2008 concussion rates in cheerleading increased by 26 percent each year, which was a greater rate of increase than for any other sport played by female youth at the high school and college levels. This increase is thought to have been due to the increasing difficulty of stunts (Labella and Mjaanes, 2012; Shields and Smith, 2009a). Falls and stunts that involve interaction with the surface (e.g., tumbling) account for a sizable share of all injuries in cheerleading (Marar et al., 2012; Schulz et al., 2004; Shields and Smith, 2009a). The potential for concussions and other injuries can be minimized by increasing the shock-absorbing capacity of the surface on which cheerleaders practice and perform (Shields and Smith, 2009b)."

According to the recent NIH report, "States also vary on their education and release requirements for parents and youth athletes. Although laws in the majority of states require that parents be provided with concussion education materials, several states do not require parents to read and sign an information sheet describing the nature and risks of concussion as a prerequisite to their children's participation in sports. Many states' laws do not require youth athletes themselves to read and sign a concussion information sheet (Tomei et al., 2012). CDC's Heads Up initiative materials are explicitly mentioned in some state's laws as the guideline for creating educational materials for parents and athletes…. Similarly, laws in the majority of states require that a youth athlete be removed from play when a concussion is suspected. In a handful of states, the laws are more specific, stating that athletes should be removed from play when signs, symptoms, or behaviors consistent with concussion are observed (Tomei et al., 2012). North Carolina's law (House Bill 792), for example, states that "if a student participating in an interscholastic athletic activity exhibits signs or symptoms consistent with concussion," he or she should be removed from the activity at that time. Some states' laws name coaches, officials, or athletic trainers as the parties responsible for removal of an athlete from play, while most say nothing about who has this authority. Texas law specifies that parents and guardians are among the individuals who may call for the removal of a youth athlete from play (House Bill 2038). The removal-from-play requirements of concussion laws highlight the importance of education on signs, symptoms, behaviors, and other indicators (e.g., a hard impact to the head or body) of concussion for coaches, athletes, parents, and others who participate in or attend youth sporting events….Another way in which states vary considerably is the types of health care providers who can provide clearance for return to play. Laws in several states specify that a licensed health care provider trained in concussion diagnosis and management may provide clearance for athletes to return to play. Other states allow any licensed health care provider to

make such decisions, and still others say nothing about who is allowed to evaluate concussions. In states that are more specific about the types of health care providers who may make return-to-play decisions, all allow physicians to evaluate concussions, and many allow physician assistants and nurse practitioners to do so.

Some states allow athletic trainers, psychologists with training in neuropsychology, or physical therapists to provide clearance for return to play. Figure 6-2 shows the types of providers who were permitted to clear youth athletes for return to play according to a review of state laws as of December 2012 (Tomei et al., 2012). As these laws are continually being updated, there may have been some shift in states' provisions regarding the types of providers who may make return-to-play decisions since the review was published." Clearly, greater standardization between states regarding concussion prevention and education would greatly enhance our ability to reduce the risk of concussion and increase public awareness.

Our specific recommendations include:

- Direct CDC to determine how to capture, and then provide technical assistance to states on collecting the information through their registries (42 states have TBI or trauma registries).
- Fund several states to match 10 years' worth of outpatient data, hospital discharge data and ambulance trip data to see if people sustain multiple TBI-related injuries over time.
- Use the existing statewide TBI Model Systems to run special data set on repetitive TBIs, although this would have limitations—16 and older.
- Fund injury and violence prevention state programs in all states – right now, less than half have funding to analyze stats, develop strategies for reducing injuries in their states—although some states are funding activities through other funding sources. Having all 50 states reporting to CDC, and the same with regard to state registries, would greatly facilitate consistency for data collection/injury strategies, and the ability to evaluate impact of these prevention activities.

With respect to strategies that need to be more widely adopted to reduce concussion risk in the population, currently, all 50 states have enacted return to play guidelines with regard to student athletes/sports-related concussions. Most state brain injury associations (BIAs) conduct local workshops for school districts and/or clinics for coaches/trainers, often in collaboration with NFL teams, using CDC's Heads Up materials. This has been effective, but the CDC is often out of materials and/or some of the materials are designed to be printed locally (which

most community-based groups don't have the funds for). Our recommendation is to continue to provide and promote the CDC materials but make sure the agency is adequately funded/staffed for dissemination activities.

Most states have not passed legislation with regard to using helmets with bikes, skateboards, etc. However, NHTSA, Safe Kids, BIAs, Think First programs, WalMart and state highway safety and state health prevention funds have all been instrumental in purchasing helmets for kids and holding local events to promote safety. We believe that Congress should encourage NHTSA at DOT, OSERS at ED and HRSA at HHS to provide leadership/incentives for states to continue with enacting state laws, education/awareness of kids in schools, distributing helmets, educating parents etc.

Other specific recommendations include:

- Family physicians could help with education and promoting safety—just like they ask if you drink, smoke, etc.—they could ask—do you wear a bike helmet, use your safety belt—have you ever hurt you head when playing sports (soccer, baseball, football, etc.) – how did you feel afterwards—the American Academy of Family Physicians could lead this initiative.
- EMS training—adopting guidelines for pre-injury screening/management. CDC has guidelines that need better dissemination to the public.
- School nurses—The National Association of School Nurses should be encouraged to promote awareness, treatment/screening, etc. to assist nurses to promote prevention, attend to concussions, provide info to parents, etc.
- Insurance incentives—we encourage insurers to provide some type of reduction/incentive for the parents of youth who wear helmets (bike, skating, skiing, etc.).

U.S. Senate Special Committee on Aging
"State of Play: Brain Injuries and Diseases of Aging"
June 25, 2014
Questions for the Record
Mr. Robert Stern

Senator Richard Blumenthal

Question:

World Wrestling Entertainment (WWE) has implemented the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) Concussion Management Model. This model is used to perform baseline testing on WWE athletes prior to annual contract renewal; the exam is also utilized after an athlete is suspected to have had a concussion in order to determine whether an athlete can return to a match/game. In terms of education, WWE offers an annual education seminar for coaches and participants. The organization has also eliminated props that can potentially lead to head injuries. In the course of your interactions with WWE, have you seen data that suggests success of these prevention measures illustrated by a decrease in concussions or brain injuries?

Response:

I do not have any interactions with the WWE. I defer this question to Mr. Nowinski.

Question:

In 2009, the National Football League (NFL) developed a stricter protocol for response to concussions. Specifically, a NFL athlete is prohibited from returning to a game, until that athlete tests normal for cognitive and motor function, if he suffers a concussion or shows signs of having suffered a concussion. Moreover, players, coaches, and trainers are now educated on how to identify the signs and symptoms of concussions. To what extent are these precautions successful in reducing the number of concussions and other head injuries?

Response:

I am not directly privy to NFL medical records or data and, therefore, am not able to provide a meaningful response to this specific question. However, I am not confident that the protocol changes listed in the question would result in a change to the number of concussions and other head injuries. The specific protocols for response to concussions are meant to: (1) reduce risk of post-concussion syndrome; (2) reduce risk of second impact syndrome (SIS); and (3) overall, reduce the risk of returning to play and having a new brain injury while the player's brain is still recovering from the original injury. I am very confident that these critically important changes have now occurred and that the safety of the players has vastly improved as a result. There have also been important changes to the rules of the game implemented by the league (e.g., changing the yard line at which kick-offs are made, making specific types of tackles illegal) that have also certainly reduced the number of concussions. Perhaps the most important change the NFL has implemented was the dramatic reduction of full-contact practices in both the off-season and during season. This change has dramatically reduced the overall exposure to head impacts for every player, thus reducing the frequency of concussions as well as subconcussive trauma. It is the latter change that will likely reduce the overall risk for later life neurological change, such as the development of the neurodegenerative disease, chronic traumatic encephalopathy (CTE).

Question:

The connection between traumatic brain injury and Lou Gehrig's Disease, or ALS, has been called into question. A 2010 New York Times article stated that many times these injuries can be classified as Chronic Traumatic Encephalopathy (CTE). A 2013 NFL settlement brought by 4,500 retired players resulted in a total $765 million compensation package put a value on each diagnosis. The settlement allocates a higher compensation value to those diagnosed with ALS. Less money is given to players who have been diagnosed with CTE and even less to those with other neurocognitive benefits. Is the difference of treatment based on diagnosis in this compensation package comparable to similar to any general benefits and compensation given to athletes with neurocognitive deficits resulting from sporting injuries? Can you explain why certain athletes are compensated more when diagnosed with ALS? In the absence of a legal settlement, what compensation is available to athletes with long-term cognitive or physical effects related to their play in the NFL?

Response:

The current version of the NFL Settlement (preliminarily approved by the federal judge on July 7, 2014) is, in my expert opinion, fraught with critical deficiencies, such that the majority of the class members for whom it was originally meant to provide compensation will receive little or no compensation. Amongst the numerous problems with the Settlement are the following two which I view as the most critical:

- As detailed clearly in the Settlement (and in clear contradiction to public comments by Mr. Seeger, one of the lead attorneys for the plaintiffs), many of the most disturbing and disabling symptoms of chronic traumatic encephalopathy (CTE) will not be compensated at any level whatsoever. By way of background, the primary clinical features of CTE include changes in Cognition, Mood, and Behavior. However, only "cognitive" impairment (as measured by a required set of neuropsychological tests) will be eligible for compensation. That is, significant changes in mood (e.g., depression, suicidality) and behavior (e.g., rage, aggression, violence, impulsivity), regardless of their impact on the former player or his family, are not at all covered under the Settlement. It is noteworthy that some of the most well-known cases of neuropathologically confirmed CTE (whose families were original plaintiffs in the Settlement), such as Junior Seau (suicide), Dave Duerson (suicide), Tom McHale (drug overdose), would not be eligible for ANY compensation if they had died following the preliminary approval date; that is, even definitive cases of neuropathologically confirmed CTE will not be eligible for compensation if the death occurred after July 7, 2014, unless they were diagnosed with ALS, Parkinson's disease, or Alzheimer's disease prior to death, or if they were diagnosed with the specific cognitive impairments (defined by the mandatory test battery and associated arbitrary algorithm) prior to death.
- The threshold for compensation based on level of cognitive impairment defined by the specific test findings and algorithm detailed in the Settlement is far too severe. That is, in order to be eligible for compensation under Neurocognitive Impairment Level 1.5 or 2.0, the former player would have to be so severely impaired in several areas of cognitive functioning that they would require assistance in many activities of daily living (in Level 1.5) or be almost

fully dependent on another person for most activities of daily living, such as bathing, toileting (for Level 2.0).

In response to the specific question about why certain conditions receive more compensation, I am afraid I cannot provide a response that includes any insight into what the decision-making process was for the two sides of attorneys.

However, I do not believe that the differences in compensation amount have anything to do with differences in treatment expenses. With regard to the question about what compensation is available to former NFL players with long-term cognitive or physical effects, the most important program is the "88 Plan." Named for Pro Football Hall of Famer John Mackey (who was found to have CTE following his death in 2011 after a long battle with dementia), the 88 Plan provides retired players with up to $88,000 per year for medical and custodial care resulting from dementia as well as from ALS.

Question:

According to data from the National Electronic Injury Surveillance System-All Injury Program and analyzed by the Centers for Disease Control, horseback riding has the highest rate of traumatic brain injury-related emergency department visits, out of all recreational sports.

Why might TBIs among equestrians be occurring at such an alarming rate?

Why do accidents among horseback riders and equestrians tend to be more serious than in other sports?

Response:

Unfortunately, I am not aware of these data and cannot speculate on why these injuries may be more serious.

Question:

Data show that the rate of injury among horseback riders is higher than even bicyclists and motorcyclists. Do you think there should be a federal minimum safety standard for equestrian helmets, as there is for bicycle helmets?

Response:

My opinion is that all protective headgear for all sports should meet federal minimum safety standards. As such, I would strongly support the implementation of such standards for equestrian helmets.

Question:

What research do you think should be funded that would help inform helmet safety standards and make sure that they incorporate the most advanced science and technology?

Response:

I am not an expert in the area of safety standards and related engineering. However, there is excellent research currently being conducted at the Virginia Tech-Wake Forest University School of Biomedical Engineering and Sciences, which incorporates the most advanced knowledge and technology to examine the safety of a variety of helmets.

Senator Elizabeth Warren

According to the Centers for Disease Control, traumatic brain injury is a major cause of death and disability in the United States. Data from numerous studies, including a 2012 publication in the journal Brain co-authored by Dr. Stern and Mr. Nowinski, suggest that that multiple traumatic brain injuries, even mild ones, can lead to behavioral and cognitive problems. Because of this knowledge, traumatic brain injury is being addressed more seriously in professional sports, in the military, and to some degree in amateur and school sports. But serious, long-term consequences from brain injuries are not limited to athletes. Anyone can experience multiple injuries or accidents throughout their lives.

Question:

How could we do a better job of collecting data on repetitive traumatic brain injuries in people not participating in sports or in the military so that researchers could gain a better understanding of the effects of these injuries in the population?

Response:

This is an important question that raises many complex issues. First, there already is an excellent program aimed at tracking the recovery from, and consequences of a single traumatic brain injury. The project, funded by the National Institute of Neurological Disorders and Stroke, is called the TRACK-TBI Multicenter Initiative. It forms part of the larger global initiative InTBIR: International Initiative for Traumatic Brain Injury Research with centers throughout Europe, Canada, and elsewhere. This initiative represents a major step forward in understanding single traumatic brain injuries. However, the question of collecting data on *repetitive mild* brain trauma in people not participating in sports or in the military is an important one. There are some vulnerable groups (e.g., women subjected to repeated domestic abuse, developmentally disabled individuals with head-banging behavior, seizure disorder patients with repeated falls) who may be at risk for later life consequences (including CTE) of repeated head impacts. A registry, with longitudinal follow-up of these groups would be important, but would be very difficult to implement on its own. Rather, my opinion is that there needs to be an extensive, longitudinal study (similar to the Framingham Heart Study) of a large cohort of individuals either at risk for repetitive head impacts or who have already sustained such impacts. Ideally, this would include participants as young as elementary schoolers as well as adolescents, young adults, middle-aged adults, and seniors, across diverse demographic backgrounds. The study would involve the collection of detailed data regarding exposure to repetitive head impacts and brain trauma, through a variety of experiences, included athletics. Participants would undergo periodic evaluations of brain functioning (e.g., neuroimaging, biomarkers, cognitive assessment, mood and behavior examinations) throughout their lives. Genetic studies would also be conducted and ongoing data regarding nutrition, exercise, intellectual stimulation, social networks, and other variables would be collected in order to obtain a full evaluation of potential risk factors and protective factors for developing long-term consequences of repetitive head impacts. This type of project would require resources above and beyond those available through federal support. Rather, it would require a partnership of public, private, industry, foundation, and philanthropic support.

Question:

Physical activity during childhood is important to set the foundation for a healthy lifestyle. In 2010, the Centers for Disease Control reported that there is substantial scientific evidence showing that physical activity can help improve academic achievement and decrease the risk for chronic conditions like heart disease and diabetes by helping kids maintain a healthy weight. Organized sports help many kids stay active and set a good foundation for healthy lives, but it's important that they do not come with a high risk of concussion and serious long-term injury. Concussions have a greater impact on children – kids have a lower injury threshold and poorer recoveries than adults – and even mild injuries can have developmental consequences.

Massachusetts requires that student athletes even suspected of having a concussion are removed immediately from play – and only allows their return after receiving clearance from a licensed health professional. The Commonwealth also requires a mandatory head injury safety training program for student athletes, parents, and coaches.

What state-level strategies have been the most effective at reducing concussions and increasing awareness?

Response:

As this is not my area of expertise, I defer to Mr. Nowinski's responses.

Question:

What strategies you would like to see more widely adopted to reduce our kids' risk of concussion?

Response:

There is no single solution to reduce concussion risk. Furthermore, my concern is that we should not be focusing solely on symptomatic concussion. Rather, I am even more concerned about our children's exposure to repetitive "subconcussive trauma." Subconcussive trauma occurs when the head or the body receives a jolt or blow with adequate force to alter the functioning of the nerve cells but that do not result in the signs and symptoms of concussion. These types of traumas occur

often in certain sports (e.g., heading in soccer) and in certain positions (the repetitive helmet-to-helmet contact at the line of scrimmage by football lineman). It is estimated that these types of head impacts occur 1000 or more times per season for an individual athlete. Unlike concussions, because of the lack of overt symptoms or physical signs, these types of brain trauma do not receive the attention of athletic trainers, coaches, team doctors, parents, or even the players themselves. However, research has demonstrated that these subconcussive blows can lead to cognitive changes, as well as physiological and structural brain changes that can be detected following a season of hits. Therefore, I would recommend that strategies should focus on reducing both concussions and subconcussive trauma. Any of these changes are especially important for children prior to puberty as the developing brain appears to be more vulnerable to even minor impacts. One of the best strategies to reduce the frequency of these types of brain injury in children is to remove unnecessary hits to youth sports. For example, full-contact practices in tackle football should be reduced substantially across all levels of play. Restricting the use of heading in soccer to the high school level and beyond is another example. Removing body checking in hockey and lacrosse prior to high school may also be effective. The ultimate goal is to maintain the physical, social, and emotional benefits of participation in youth sports while also doing everything possible to remove all but accidental hits to the head or body that result in sudden movement to the head.

Statements for the Record

TESTIMONY OF JEFF MILLER

SENIOR VICE PRESIDENT, NATIONAL FOOTBALL LEAGUE

BEFORE THE

SPECIAL COMMITTEE ON AGING

UNITED STATES SENATE

JUNE 25, 2014

Mr. Chairman and members of the committee,

On behalf of the National Football League, I appreciate the opportunity to offer this written testimony to the Special Committee on Aging on the topic of concussions in sports. Attached to this statement are copies of the NFL's "2012 and 2013 Player Health and Safety Report". These documents provide substantial information on the projects the NFL is pursuing to make football safer at all levels, to assist our retired players when they leave our game and to change sports culture as it relates to head injuries. Essential for the purposes of this hearing, the reports also detail the NFL's substantial scientific research investments with world class partners – including institutions represented here today – to accelerate progress on diagnosis, prognosis, treatment and prevention of brain injury. This statement will highlight some key aspects from the report.

There is nothing more important to the NFL than the health and safety of our players. Commissioner Goodell has stated repeatedly that he spends more time on the health and safety aspects of our sport than any other issue. We also appreciate that the decisions we make impact football at all levels, other sports, as well as influence our society more broadly.

There is no better example than the NFL's commitment to support research around brain injuries. Tens of millions of research dollars already at work promise to advance the understanding of the brain; millions more are being spent to compensate retired players who have cognitive injuries. These breakthroughs will benefit public health far beyond sports.

National Institutes of Health

In September of 2012, the NFL announced a $30 million commitment to funding medical research with the Foundation for the National Institutes of Health (FNIH). The unrestricted gift is the NFL's single-largest donation to any organization in the league's history, demonstrating just how strongly the NFL believes in the pursuit of medical research into basic neuroscience.

Some areas of research to be funded by our grant include chronic traumatic encephalopathy (CTE); concussion management and treatment; and the understanding of the potential relationship between traumatic brain injury and late-life neurodegenerative disorders, especially Alzheimer's disease. All of these are topics of today's hearing.

The funding has already helped support important research projects. In December of last year, the NIH announced its first round of grants to eight institutions for the study of traumatic brain injury. In addition, the NIH announced funding for six pilot projects in sports-related concussions.

Just last month, President Obama announced the next $16 million of our commitment to the NIH at the White House's summit on youth sports safety. The NIH will pursue a longitudinal research effort into the effects of concussions. The topic of today's hearing will be benefitted by this important work.

Apart from these initiatives, the NFL has supported research and educational efforts with a variety of private and public institutions, including the Centers for Disease Control, leading equipment manufacturers and major universities.

Head Health Initiative

In March of last year, we announced with GE the Head Health Initiative, a four-year, $60 million collaboration to speed diagnosis and improve treatment for mild traumatic brain injury as well as find ways to better prevent against the injury.

The initiative includes a four-year, $40 million research and development program to evaluate and develop next generation imaging technologies to improve diagnosis that would allow for targeting treatment therapy for patients with mild traumatic brain injury.

In addition to the research program, the NFL is partnering with GE and Under Armour to launch the Head Health Challenge, which has two focus areas that seek new solutions for understanding mild traumatic brain injury. The organizations pledged to find and fund ideas that accelerate solutions for brain protection. The challenge fund could invest up to $20 million.

We received more than 400 submissions from people in 27 countries to the first innovation challenge. All of these ideas were directed toward better ways to diagnose brain injury. In January, with GE, we presented 16 winners from around the world, $300,000 each with an opportunity to win another $500,000 in the next year. The expert judges from the military, NIH and others believe that the 16 winners all have a realistic chance to make a difference in the diagnosis and prognosis of traumatic brain injury in a short time.

The second challenge which focused on methods for protecting the brain from injury, recently closed. This challenge was even more popular. The website received more than 40,000 visitors from more than 100 countries. In the end, inventors, entrepreneurs, academics and others submitted more than 450 ideas representing 19 different countries around the world. We are reviewing the submissions now with the intent of making awards this September.

Retired Players

Our efforts to promote sports safety and advance scientific research goes far beyond head injuries and far beyond football. The NFL works to ensure that everyone who plays the game or has played the game receives the best possible medical care. This includes the many retired NFL players pursuing different careers and interests long after they leave the playing field. We are pleased that retired players are living productive and healthy lives.

In 2012, a NIOSH study found that former NFL players are likely to live longer than men in the general population. Former players also had a lower rate of cancer-related and heart disease related deaths. For those players who do experience medical challenges, the NFL 88 Plan has distributed almost $30 million since 2007 to former players for assistance with for dementia, ALS and other neurodegenerative diseases. In addition to the 88 Plan, we also have comprehensive disability plan; long-term care insurance; joint replacement surgery; and players

now have the opportunity to remain in the NFL medical plan post-career. All told, the NFL distributes well over $150 million a year in pension, disability, and other post-career benefits to retired players.

In 2012, we established the NFL Life Line as a free, independent and confidential phone consultation service and website. All members of the NFL family have complete access to the Life Line and its staff of trained mental health experts 24 hours a day, every day of the year. The NFL Player Care Foundation ("PCF") provides resources for former players to take care of their mental and physical well-being. The PCF provides a free national screening program open to all former NFL players, including a series of private and confidential cardiovascular and prostate screenings, along with mental health resources and education.

Fostering a strong culture of player health, wellness and safety – that extends across all aspects of a player's life, from his football career to his family and personal growth– is a focal point for the NFL. Players are provided resources, tools and support to assist them as they move through their careers and lives, from signing with their first NFL team to having their first child to adjusting to life post-football.

On the Field

During a player's playing career, the first rule that the NFL follows in all cases is that medical decisions take precedence over competitive ones.

In recent years, we have made significant improvements to our practices and protocols to better identify and manage injuries. First, we added an athletic trainer to a skybox in every stadium for the sole purpose of quickly identifying possible injuries and relaying that information to the team medical staff. Second, the medical staff now has available the actual video of the play on which the injury occurred; they can watch that video on the sidelines almost immediately to better understand how the injury occurred. Third, with respect specifically to concussions, several special protocols are in place. Players who may have sustained a concussion are removed from the game or practice and examined by trained medical professionals. Anyone who has sustained a concussion may not return to play that game under any circumstances. A player who may be showing signs or symptoms of a concussion is taken to the locker room away from the noise and the lights of a packed stadium. There, a doctor can perform a full exam.

The sideline review is a standardized exam, consistent across all 32 teams, and is based on internationally accepted medical standards. This year, team medical personnel were aided by unaffiliated neurological consultants in making concussion diagnosis. These doctors, local concussion experts, have no relationship with a club and are there solely to offer their expertise when it is needed. We were very pleased with the program in its first year and will use it again this coming season.

If a player is diagnosed with a concussion, he may not return to play or practice until he completes a graduated protocol involving periods of rest, examination and exercise challenges, and has been cleared by his team neurological expert as well as an independent expert identified in consultation with the players association.

Players know more about concussive injuries than they have ever before. In each locker room is a fact sheet and poster designed to educate players, coaches and others at our team on concussions – what they are, what symptoms to look for, and what to do if a player suspects that he or a teammate has had a concussion. We worked closely on the poster and fact sheet with the Centers for Disease Control and Prevention. Working with the CDC and others, we have helped to design a complimentary version for all youth and high school sports, which is freely available on the CDC's website. According to the CDC, it is one of their most popular offerings and has been downloaded more than a million times.

Youth Sports Safety

In addition to the NFL's work with the CDC to educate the public about concussion injuries, we are also proud of our efforts to promote youth concussion laws in every state to make athletes in all sports safer.

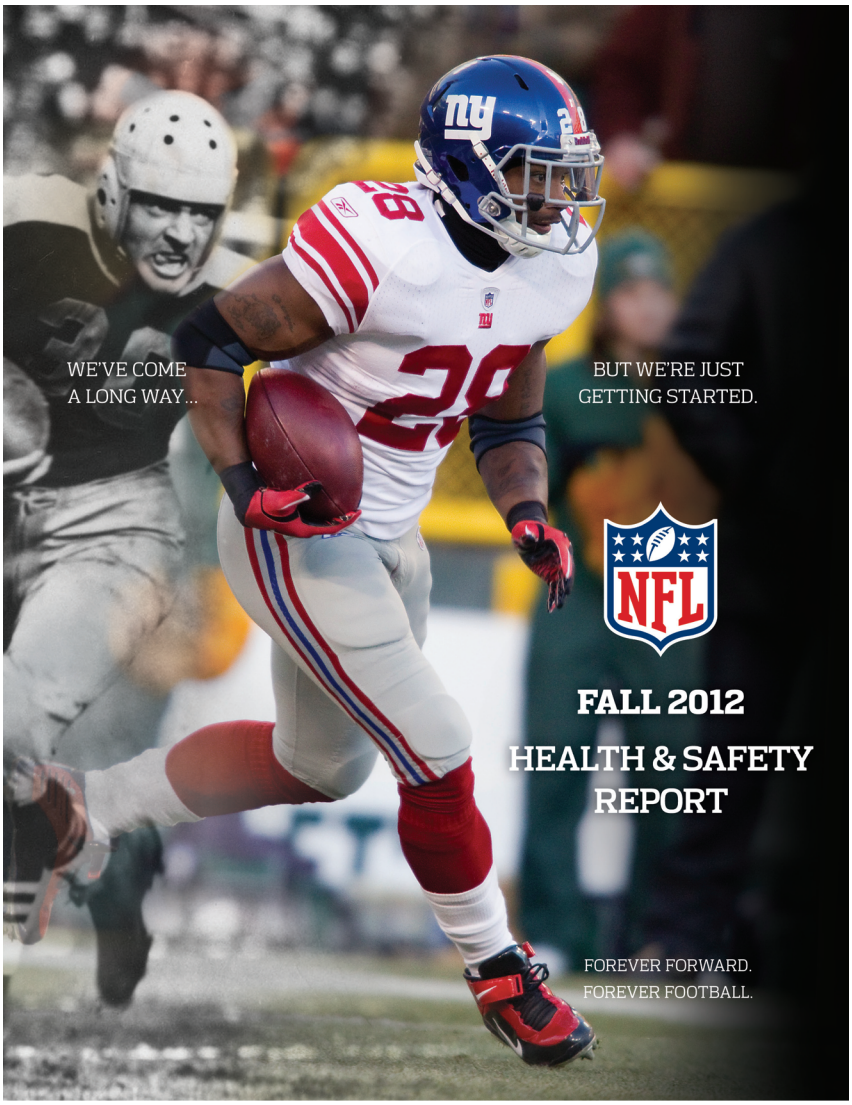
The legislative effort was inspired by Zackery Lystedt's courageous story. As a 13-year old football player, Zackery suffered tragic injuries in a football game. During his recovery, Zackery became the inspiration for legislation passed in Washington State that would become a model for youth sports concussion laws passed around the country.

The NFL committed to advocating for the Lystedt law, which had then passed in six states, until every state adopted this important protection for all youth athletes. Earlier this year, the NFL achieved its goal and today all fifty states have passed laws addressing concussion in youth sports. As a result, all youth athletes are safer and parents, coaches and teachers are more aware of concussion diagnosis and treatment than ever before.

Finally, in support of USA Football's Heads Up Football program, the NFL committed $45 million to promote Heads Up Football and make it the gold standard for youth and high school football. This program insists that every coach is certified in teaching the game correctly, in concussion and heat exposure education and in equipment fitting. More than half of all youth leagues have already signed up for Heads Up Football as it enters its second year. Hundreds of high school programs are signing up this year in the first year of the high school version of the program.

Mr. Chairman, this is a brief summary of the NFL's efforts advance scientific research and sports safety. Please consider the attached reports for further information on the NFL's efforts.

Thank you.


WE'VE COME
A LONG WAY...
BUT WE'RE JUST
GETTING STARTED.
NFL
FALL 2012
HEALTH & SAFETY
REPORT
FOREVER FORWARD.
FOREVER FOOTBALL.

toc

Foreword

We continue to make significant strides in promoting a culture of safety for NFL players and, through our leadership, for football players and other athletes at all levels.

Our focus is on the total health of athletes – from when they start playing the game as youngsters through their entry and participation in our league to their transition out of the game. We also know that what we do sets an example for all sports and can have a very positive impact.

We are guided by a few simple principles:

- **Leadership.** We are not waiting on science to tell us the answers. We will continue to make rule changes, provide the best equipment, and give our medical staffs the tools to protect player health and safety and make our game as safe as possible.
- **Research.** We will fund pioneering medical research to help scientists and doctors find the breakthroughs that will benefit all athletes. Putting this principle into action, we recently announced a $30 million unrestricted grant to the Foundation for the National Institutes of Health to accelerate the pace of discovery in topics directly related to player health and safety.
- **Advocacy.** We will continue to emphasize awareness and education and to fight for legislation that better protects youth athletes from the potential consequences of head injuries. Safer sports means better sports for our young people.
- **Transparency.** It is important that we continue to share our information with the broadest possible audience because the potential benefits go well beyond the game of football.
- **Partnerships.** We will continue to work with leading organizations in the health sciences and sporting industries to support research and drive innovation to enhance the safety of players at all levels of the game.

Why is this such an important priority? We want our players to have long, successful careers so that fans can enjoy their extraordinary talent. Equally important is that we want our players to be successful in their lives off the field and after they leave the game. We also want to continue our tradition of leadership in sports to promote safe and fair play at all levels.

The resources available to support player health and safety continue to evolve and improve. We want you to know about all of our initiatives and welcome your ideas. This is a total team effort and we will not relent.

On behalf of everyone in the NFL, thank you to the many individuals and institutions that are not only contributing to making our sport safer, but also having a deeply positive impact on all of sports and wellness.

Roger Goodell
NFL Commissioner

Welcome to the Fall 2012 NFL Health & Safety Report

Distinguished researchers, medical professionals, including a MacArthur Genius Grant winner, and neurosurgeons at the top of their field are all a part of NFL University, the term I use to describe the network of medical resources devoted to making football and other sports safer at all levels. From helmet research to injury tracking, rule changes to cutting-edge medical studies, NFL University is hard at work every day.

The NFL not only has a long-standing commitment to the health and well-being of its players, but also to players active in collegiate, high school and youth programs. While this report is new, the NFL's commitment to health and safety is not. For nearly forty years, the NFL has funded a wide range of research through NFL Charities, various medical committees and joint efforts like the Partnership for Clean Competition. In the last few years, we have committed nearly $22 million to a wide range of research to improve player health and safety. Our new collective bargaining agreement takes this commitment one step further with plans to invest more than $100 million over the next 10 years in medical research. On September 5, 2012, the NFL announced a $30 million unrestricted grant to the Foundation for the National Institutes of Health to advance medical research, the single-largest donation to any organization in the league's 92-year history. In the last year the NFL also changed kickoff rules, resulting in a 40 percent reduction in concussions on kickoffs; and continued to improve in-game procedures, introducing enhanced concussion protocols and adding sideline video monitors for reviewing and treating injuries.

The league also continues to support former players with programs that provide them with financial assistance to meet their medical needs. This includes the 88 Plan, which helps support former players struggling with dementia, amyotrophic lateral sclerosis (ALS) or Lou Gehrig's disease, Parkinson's disease, and Alzheimer's disease, and the NFL Player Care Foundation, which addresses a variety of medical needs.

The NFL recognizes the importance of helping to improve safety in all sports, which is why it has been active in advocating for youth concussion laws in every state. These laws better protect young athletes in all sports with respect to concussions and return to play. They require that parents, coaches and players learn about concussions and that a player who has suffered a concussion cannot return to play or practice until he or she is cleared by a medical professional. Currently, 40 states and Washington, D.C., have passed youth concussion laws, many with the support of the NFL.

As chairman of the newly created NFL Owners Committee on Health and Safety, I take pride in NFL University, and all that we have accomplished so far. We have more to do — advancing research, continuing partnerships with organizations like USA Football and the Centers for Disease Control and Prevention, creating new relationships and supporting continued improvement in injury prevention and treatment. We look forward to providing players and fans with a game that is as safe as possible and even more exciting and fun in the years to come.

John York, M.D.
Co-Chairman, San Francisco 49ers
Chairman, NFL Owners Committee on Health and Safety

Executive Summary

The 2012 NFL Health and Safety Report offers an up-to-date summary of the programs and initiatives in place **today** to protect and enhance the health and safety of players; a look forward to **tomorrow**; and an acknowledgement of the many partners who work **together** with the NFL on these programs.

The goal of this and future reports is simple: provide those who care passionately about the game of football and its players with a comprehensive look at the league's health and safety efforts, and illuminate where important progress has been made in the past year — and where further improvements can be made.

The key pillars of the NFL's player health and safety program that are detailed in this report include:

I. Health and Safety Culture: Advancing a culture wherein the health and safety of players is paramount requires much more than just a set of game rules. It requires ongoing education, dialogue and monitoring. It requires constant assessment and consistent reinforcement of policies. And it requires an unstinting commitment to everyone involved in the game – players, coaches, administration, medical staffs and the NFL Players Association.

The combination of these efforts, in conjunction with league-wide rule changes and safety equipment updates as outlined in this report, have measurably improved player health and safety. There is perhaps no better recent illustration of the league's commitment to health and safety than in the area of concussions. The NFL has taken considerable steps to reduce both the occurrence and health impacts of head injury, including concussions.

In 2011, the league continued these efforts by updating rules and enforcement policies meant to reduce head injuries, and by educating players about what to do if they experience concussion-related symptoms through educational videos, and a fact sheet and poster distributed to all teams, and presentations from the officiating department. The league also added further enhancements to its in-game concussion-related policies, instituting a new tool for sideline concussion evaluations, and more. The NFL also continued to promote safe play at all levels of football, working closely with the Centers for Disease Control and Prevention, USA Football and other leading organizations to educate young athletes, their parents and coaches about the importance of head injury awareness.

II. Advocacy: The NFL recognizes and takes very seriously its role in encouraging health and safety awareness and action at all levels of football and in youth sports. As part of this commitment, the NFL is a passionate advocate for the passage of youth concussion laws in every state. As of September 2012, 40 states and the District of Columbia have youth concussion laws, and the league is committed to supporting passage in all 50 states.

III. Safety Rules: The NFL's efforts to improve the safety of the game through rule enhancements extend back to its formation nearly a century ago. Prior to the start of the 2011 season, the NFL Competition Committee enacted four more rule changes to provide additional protections to players. One of the most notable rule changes – the move in the restraining line for the kicking team from the 30- to the 35-yard line – contributed to a 40 percent reduction in the number of concussions occurring during kickoffs when compared to the previous season.

IV. Research: The NFL has a long-standing commitment to fund important research into new and better ways to protect players at all levels of the game, and to drive new discoveries to improve player health. The engine of this effort is NFL Charities, a nonprofit organization created by the 32 member clubs of the National Football League, which has funded nearly $22 million in medical research grants in the areas of sports injury prevention and treatment. These grants support research conducted at some of the country's most prestigious institutions, including the Cleveland Clinic, Johns Hopkins University and Massachusetts General Hospital. In 2012, the NFL took this commitment to greater heights with a grant of $30 million for medical research to the Foundation for the National Institutes of Health.

V. Equipment: Correctly using the latest in protective safety equipment is one of the fundamental ways to help prevent injuries. The NFL's Head, Neck and Spine (HNS) Committee and its Subcommittee on Safety Equipment and Playing Rules, comprised of experts in the fields of medicine and sports science, identify trends in injuries and develop recommendations for enhancing playing equipment. In the last year, the committees have been focused on supporting research to identify improvements to equipment that can provide additional protection to the head and neck as well as the feet and ankles of players. The HNS Committee is currently studying the use of accelerometers for a pilot program that will collect head impact data to better understand the amount and types of hits players sustain.

The programs and initiatives in this report represent the work and dedication of hundreds of individuals, including volunteer members of NFL medical committees, team doctors and trainers, and many of the best minds from the scientific and medical communities.

The NFL and its teams would like to extend their deep gratitude to the men and women whose efforts are detailed in this report and to all those who are committed to a safer playing environment in the NFL, college and youth football — and all sports.


TODAY
The NFL continually strives to improve the health and safety of all those who play the sport, from youth players to current and former NFL players. This commitment includes continuous enhancements to player safety rules, support of community outreach programs to provide health and safety resources to all athletes and their communities, and support for legislation that protects young athletes — all of which contributes to a culture focused on doing everything the NFL can **today** to create an even better, healthier and safer **tomorrow**.

HEALTH AND SAFETY CULTURE

The NFL has made health and safety an integral part of the culture of football, and a vital component of the game itself. The NFL is proud to use its reach and influence to spread this culture beyond our game, through partnerships with leading institutions, programs reaching youth, and research that can improve lives well beyond the playing field.

The NFL's health and safety efforts are guided and supported by many leading research and medical professionals. The league's commitment to protecting players is demonstrated through player education, policies and a variety of health and safety programs. NFL culture continues to evolve and advance along with the sport, informed by experience, improved understanding and the latest scientific and technological discoveries.

The Culture of Leadership

Support for health and safety at the NFL spans all levels of the organization, from the commissioner's office, to the players on the field, to the club owners, to the coaching and medical staffs on every team. In addition, the NFL has gathered independent experts with relevant medical expertise to consult, conduct research, gather and analyze NFL injury data, and provide recommendations for improving player health and safety. These experts participate in committees and panels focused on specific health and safety topics, as well as consult directly for individual clubs. They are affiliated with some of the most prestigious academic, research and medical institutes across the country.

NFL medical consultants are affiliated with top-tier organizations around the country including:

National Institute of Neurological Disorders and Stroke

DARPA

FNIH Foundation for the National Institutes of Health

Mayo Clinic

Through regular committee meetings and annual events, these medical experts exchange knowledge and key learnings, and recommend specific actions where needed. One such gathering is the annual meeting of the NFL Physicians Society (NFLPS). The NFLPS was formed in 1966 as a way for team physicians to share information and collaborate on solutions to common injuries and health matters of NFL players. The NFLPS has grown to more than 130 members representing the 32 clubs of the NFL, and is led by President Anthony Yates, M.D., FACP, Co-Director of the University of Pittsburgh Medical Center Corporate Health Program and Head Team Physician for the Pittsburgh Steelers. Members of the NFLPS gather annually during the NFL Combine to address issues common to the membership such as orthopaedic injury, heat and hydration issues, controlling substance abuse problems among players, other medical concerns, and helping to develop effective health and safety policies for NFL players.

Sharing Culture through Education

Educating NFL players about the importance of protecting themselves and other players on the field is a critical part of building a health and safety-focused culture. From rule changes to playing equipment updates, the NFL educates players about the reasoning behind its decisions and reinforces the fact that health and safety considerations are as important as any other aspect of the game.

All NFL rookies are required to participate in the NFL Rookie Symposium, during which medical professionals speak about important health and safety matters, followed by the NFL Rookie Success Program, which takes place during the first 12 weeks of the regular season. The Rookie Success Program consists of nine required classes on matters including money management, social responsibility, emotional intelligence including stress management, transitioning into and out of the NFL, and avoiding high risk behaviors. The material is presented by a combination of league experts, medical experts, coaches and former players. Resources and benefits offered to players, such as free counseling sessions and mental health resources, are reviewed throughout the season, for both rookies and existing players, by directors of player engagement at each club.

In addition to player orientation, the NFL routinely provides players with information, instruction and updates on important health and safety issues through the Rookie Playbook, the NFL Player Engagement website, periodic health alerts, and monthly newsletters for current players, with a separate newsletter addressing the needs of former players. Topics include notification of new health benefit offerings, finding balance in your personal life, planning for life after football, and more.

NFL Total Wellness

In 2012, the NFL Total Wellness program was launched as a platform to help empower players to make positive long-term health decisions; promote support-seeking behaviors in connection with behavioral and mental health issues; and provide health and safety education for players and all members of their support network, including spouses, parents, and children. The platform expands on a number of NFL Player Engagement programs and service offerings.

Among the program's services is NFL Life Line, a free, independent and confidential 24/7/365 phone consultation service and website developed and manned by third-party mental health professionals. NFL Life Line provides support and referrals to all members of the NFL family in times of need and is administrated by a group of national mental health experts who also operate a program for military service members with the Department of Veterans Affairs (VA).

Player Education

The league has also expanded education with respect to concussions. A poster and related player fact sheet was developed in partnership with the Centers for Disease Control and Prevention (CDC), NFL Players Association (NFLPA), NFLPS and Professional Football Athletic Trainers Society (PFATS), to educate players about the possible consequences of concussions and advise them to report any related symptoms they may experience to team staff. The poster emphasized the NFL's concussion management guidelines for return to play, which require players to be fully asymptomatic, both at rest and after exertion; pass normal neurologic and neuropsychological exams; and be cleared by both the team medical staff and an independent neurologic consultant. A similar poster, endorsed by 16 national governing bodies for sport, was developed for young athletes and made available through the CDC to display in youth team locker rooms, gymnasiums and schools nationwide. The poster was distributed to approximately 300,000 coaches, parents, schools and sports leagues in 2011.

During that same season NFL Commissioner Roger Goodell distributed a memo to all 32 teams in the league, emphasizing the focus on further reducing contact to the head and neck. Commissioner Goodell stated that further action by the league would be taken to educate players about safe and controlled playing techniques.

The NFL develops educational videos for players to provide a detailed explanation of major rule changes and points of emphasis. The videos detail the changes going into effect, highlight plays from previous seasons, and explain why the rule changes were made. For example, at the start of the 2011 season, a video was produced explaining the new kickoff rule.

Three additional instructional videos distributed throughout the 2011 season focused on illustrating illegal plays and clarified rule changes. Illegal plays from the first half of the season were reviewed and explanations were given on why each was considered illegal. Topics discussed included the definition of a defenseless player and illegal helmet-to-helmet hits.

Coaches and players are also given rule presentations from members of the NFL officiating department each year during training camp. A League Policy for Players manual is distributed to players each year

to serve as a quick reference guide for some of the most commonly applicable policies. Topics in the document include player safety and equipment guidelines and disciplinary measures for violating game-related player health and safety rules.

The NFL will continue to educate players about protecting themselves on the field, and work to improve health and safety at all levels of the game and in all sports.

The Role of Policy and Programs

Policies are reviewed on an ongoing basis to ensure they meet the highest standards in protecting player health and safety. The policies often include practice and game procedures, but also extend beyond the field to policies and programs for current and retired NFL players.

For example, players are educated on league policies prohibiting substance abuse and the use of anabolic steroids and other performance-enhancing substances. The policy helps to preserve the integrity of the game, protect players against the adverse health effects of using the substances, and send a message to athletes of all ages that substance abuse is not acceptable.

Game-Related Policies

Game-related policy updates made prior to and during the 2011 season included:

- The first league-wide policy for sideline concussion evaluations was developed and updated during the season based on lessons learned through its initial implementation.
- Players displaying concussion-like symptoms were removed from the game and not allowed to return to practice or play until being cleared by an independent neurological consultant.
- Mandatory conference calls were conducted by league officials and medical advisors prior to the start of the season to review key health and safety guidelines and policies. One call included all head coaches and general managers while a second call was held with all team trainers and doctors. Hydration and heat-related illness and the revamped concussion protocol were among the subjects reviewed on the calls in preparation for players returning to the practice fields.
- Points of emphasis for officiating were announced prior to the start of the season and included a continued focus on removing illegal hits to the head and neck area; illegal contact with a player's facemask; horse collar tackles; and illegal low blocks such as chop blocks and clips.
- To reinforce the concept of club accountability, teams were advised that they would be fined for players who commit multiple flagrant hits that result in fines for the player.
- An independent certified athletic trainer was added to each game to monitor play of both teams and provide medical staffs with any relevant information that may assist them in determining the most appropriate evaluation and treatment. This athletic trainer is stationed in a booth upstairs with access to video replay and direct communication to the medical staffs of both teams. In most cases, the athletic trainer is affiliated with a major college program in the area or was previously affiliated with an NFL club. The athletic trainer's role is to provide information to team medical staffs that might have been missed due to a lack of a clear view of the play or because they were attending to other players or duties. The athletic trainers work independent of the clubs, all of their fees and expenses are paid by the NFL main office.
- Starting in the 2011 season, club medical staffs were permitted to use their cell phones during games for purposes of obtaining information relating to the care of an injured player. This is not limited to concussions and is intended to assist team medical staffs in addressing a variety of injuries.
- Clubs were reminded of the importance of team coaching and medical staffs continuing to work together to ensure that full information is available at all times to medical staffs, that players do not take steps to avoid evaluations, and that concussions continue to be managed in a conservative and medically appropriate way.
- Sideline video monitors were installed to allow medical staffs to review the network video of any play during which a player was injured in order to properly manage their care.

"We have emphasized minimizing contact to the head and neck, especially where a defenseless player is involved. It is clear to me that further action is required to emphasize the importance of teaching safe and controlled techniques, and of playing within the rules."

- NFL Commissioner Roger Goodell in a 2010 memo to all 32 NFL teams

Post-Career Health and Safety Initiatives

The NFL's commitment to player health and safety extends beyond the playing field to retired players. To support retired players, the NFL owners, in partnership with the NFLPA, Pro Football Hall of Fame, and the NFL Alumni Association, created the NFL Player Care Foundation (PCF) in September 2007.

The PCF is an independent organization dedicated to helping retired players improve their quality of life. The PCF addresses all aspects of life – medical, emotional, financial, social and community – providing programs and assistance in each area. The PCF provides free health screenings to all former players, and fiscal grants to qualified former players in need of financial and medical assistance. Support includes joint replacement surgery and rehabilitation services, neurological care, and non-medical assistance.

Screenings

Since its inception in 2007, the PFC has dedicated more than $2.8 million to underwrite medical research and health screenings for former NFL players.

In 2008, the PCF partnered with the American Urological Association Foundation (AUAF) to offer free prostate screenings for retired NFL players across the nation. Since then, more than 1,200 retired players have been screened for prostate cancer through this program.

Cardiovascular screenings are offered to former players through partnerships with the Boone Heart Institute and the Living Heart Foundation. Since the PFC began sponsoring cardiovascular screenings in 2008, more than 1,300 former players have participated in the program.

Joint Replacement

The NFL provides financial contributions for eligible former players who need knee, hip and shoulder joint replacement surgery. Nearly 250 former players have been reimbursed for costs associated with joint replacement surgery. The PCF assists qualified players with joint replacement expenses.

Joint replacement program centers include:

- St. Vincent's Birmingham /Andrews Sports Medicine & Orthopaedic Center, Birmingham, AL
- Broward Health Broward General Medical Center, Ft. Lauderdale, FL
- Centinela Freeman Regional Medical Center, Marina del Rey, CA
- Cleveland Clinic Foundation, Cleveland, OH
- Lenox Hill Hospital, New York, NY
- MedStar Health – Georgetown University Hospital and Union Memorial Hospital, Washington, D.C. and Baltimore, MD
- The Methodist Hospital, Houston, TX
- The Mount Sinai Medical Center, New York, NY
- Northwestern Memorial Hospital, Chicago, IL
- OASIS MSO, Inc., San Diego, CA
- St. Joseph's Hospital-Atlanta, Atlanta, GA
- Texas Orthopedic Hospital, Houston, TX
- University of Pittsburgh Medical Center, Pittsburgh, PA

Neurological Care Program

The NFL provides eligible retired players with access to comprehensive evaluations at six top-tier medical centers recognized for their expertise, high-quality service and reputation. Each center has a team of specialists, led by a neurologist who serves as the program director and point of contact for retired players.

Neurological care program centers include:

- Morehouse School of Medicine, Atlanta, GA
- Mt. Sinai School of Medicine, New York, NY
- Tulane University, New Orleans, LA
- University of California, San Francisco, CA
- University of California, Los Angeles, CA
- Washington University School of Medicine, St. Louis, MO

Since 2010, the league has also sponsored 14 events around the nation for retired players to discuss mental health issues, led by Dr. David Satcher, former U.S. Surgeon General and director of the Satcher Health Leadership Institute at Morehouse School of Medicine. Dr. Satcher serves as a mental health advisor to the NFL.

Spine Treatment Program

The NFL spine treatment program makes available spine specialists at five hospitals across the country to evaluate and treat spine-related conditions among retired players. Each hospital provides an orthopedic spine surgeon who serves as point of contact for the player, and program director who coordinates the services of a team of healthcare professionals and specialists in the evaluation and, if warranted, treatment of eligible former players. The team includes a neurosurgeon and a physiatrist (rehabilitation physician).

Spine treatment program centers include:

- Mt. Sinai Medical Center, New York, NY
- Emory Spine Center, Atlanta, GA
- Washington University Medical Center, St. Louis, MO
- University of California Medical Center, San Francisco, CA
- University of California Medical Center, Los Angeles, CA

88 Plan

As a part of the collective bargaining agreement between the NFL and the NFLPA, the "88 Plan," named for Pro Football player and legend John Mackey (who wore number 88 for the Baltimore Colts), provides retired players with as much as $100,000 per year for individual care; up to $88,000 for home custodial care in addition to costs pertaining to certain physician services; durable medical equipment; and prescription medications resulting from dementia, Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis (ALS). Since the program's inception in February 2007, more than $18 million has been distributed to qualifying retired players and their families.

Player Health Plans

The NFL is committed to ensuring the health of its players and their families both on the field and off with comprehensive health benefits. Highlights include:

Current Players:

- *Complete health care coverage with **no premium***
- *No lifetime cap on medical coverage*
- *Free life insurance of up to $1.6 million*
- *Vested players receive 5 years of continued free health insurance after leaving the league, plus eligibility to remain in the plan for life*

Former Players:

- *Continued health insurance for 5 years after leaving the NFL*
- *Access to top-tier neurological care and spine treatment centers*
- *Financial assistance for knee, hip or shoulder replacements*
- *Free health screenings*
- *Bert Bell/Pete Rozelle NFL Player Retirement Plan provides free long term care insurance for eligible players*
- *Up to $100,000 per year for individual care and up to $88,000 for home custodial care for players with dementia, Alzheimer's disease, Parkinson's disease and ALS in the Bert Bell/Pete Rozelle NFL Player Retirement Plan*

ADVOCACY

The NFL is dedicated to making a positive impact on the health and lives of players and fans in the communities of the 32 teams of the league, and across the nation through targeted outreach programs. The programs focus on protecting the health and safety of youth athletes through education on a variety of topics, and by raising awareness of public health issues such as breast cancer. The NFL collaborates with a variety of partners to implement programs focused on increasing awareness and understanding of health and safety issues, and to raise funds for nonprofit organizations such as the American Cancer Society.

Youth Awareness and Outreach

Concussion Awareness and Education

According to the Centers for Disease Control and Prevention (CDC), in the last decade there has been a 60 percent increase in visits to emergency departments for sports- and recreation-related traumatic brain injuries (TBIs), including concussions, among children and adolescents. While this increase is partially due to an increase in awareness of these injuries and related symptoms, it is also a reminder that concussions are a serious public health issue going well beyond the NFL. The NFL understands this and champions concussion awareness, education, prevention and effective diagnosis and treatment through a variety of targeted outreach programs to coaches, trainers, youth athletes and their parents, and through advocacy for laws and policies to protect young players.

The Zackery Lystedt Law

Zackery Lystedt is a young man from the state of Washington who suffered a significant brain injury after returning to play in a middle school football game after sustaining a concussion. Zackery, his family and a broad range of medical, business and community partners lobbied the Washington state legislature for a law to protect young athletes in all sports from returning to play too soon. The Lystedt law contains three essential elements:

- Athletes, parents and coaches must be educated about the dangers of concussions each year.
- If a young athlete is suspected of having a concussion, he/she must be removed from a game or practice and not be permitted to return to play. When in doubt, sit them out.
- A licensed health care professional must clear the young athlete to return to play in the subsequent days or weeks.

"When we watch a NFL game we see it so differently than others. The penalties you don't like or the score you aren't happy with are so insignificant. We know how impressionable the game is on our youth and are so proud of the NFL's push for safety and the concern for their players."

- Victor Lystedt, father of Zackery

After NFL Commissioner Roger Goodell met Zackery and his family, he committed that the league would support promotion and adoption of the Lystedt law in all 50 states to make youth sports safer.

Since the passage of the Lystedt law in the state of Washington in May 2009, many other states have passed similar laws to protect youth athletes. The NFL has worked to raise awareness about the importance of adopting these laws. Commissioner Goodell has contacted governors of states without laws protecting young athletes, encouraging them to pass legislation similar to the Lystedt law. Commissioner Goodell has stated his belief that sports and political leaders can preserve the benefits of organized sports, while simultaneously raising awareness of concussions and ensuring proper and effective treatment. Currently, 40 states and Washington, D.C., have passed youth concussion laws, many with the support of the NFL.

NFL and USA Football

The NFL's dedication to health and safety extends beyond the professional field into youth football leagues, reaching players, coaches, clinicians, parents and administrators through its commitment and partnership with USA Football. Endowed by the NFL and NFL Players Association (NFLPA), USA Football is the sport's national governing body, an independent nonprofit organization, and the Official Youth Football Development Partner of the NFL and the NFLPA.

"All of you are football players and all of you love the game of football, but it is also important no matter what sport you play that you play it safely. That means understanding the rules; that means understanding your equipment; and that means understanding your body to make sure when you are not feeling well that you get the proper medical care."

– NFL Commissioner Roger Goodell, at New York Jets youth fan forum

The NFL and USA Football collaborate on programs and resources to address key health and safety issues. They work with leading medical organizations, including the CDC, the American College of Sports Medicine (ACSM), and USA Football's Football and Wellness Committee members. Representatives are affiliated with organizations such as the American Red Cross, the University of Nebraska Medical Center, Duke University Medical School, University of Washington Medicine/Harborview Medical Center/ Seattle Children's Sports Concussion Program, U.S. Olympic Committee's Sports Medicine Advisory Committee, and others. This collaboration provides educational resources, including:

- Free concussion education and management resources, including dozens of articles, downloadable documents and videos.
- Free educational materials about hydration, conditioning, tackling techniques, nutrition, protective equipment, injury prevention and emergency care, and general player health and safety. Materials include articles, videos and other resources.
- The first online youth football coaching course, which includes comprehension quizzes encompassing concussion education and management, heat and hydration preparedness, tackling techniques, and equipment fitting guidelines. The course has helped train more than 80,000 youth coaches.
- The promotion of safe and healthy play through more than 100 annual football training events and national campaigns.
- An instructional video series to aid coaches in teaching players how to tackle properly.

In addition, the NFL and USA Football have partnered with the Atlantic Coast Conference on national programs aimed at youth health and safety, including **Put Pride Aside for Player Safety** - a campaign to increase awareness of the seriousness of concussions. The campaign has been successful in raising awareness among youth players, coaches and parents of the importance of removing athletes from play when they are suspected of sustaining a concussion. The campaign has been supported by public service announcements (PSAs), videos for youth football coaches and educational sessions across the country hosted by NFL teams and USA Football for local youth and high school football coaches. The PSA aired during every college football game throughout the 2010 and 2011 seasons on the Atlantic Coast Conference Network, and was included in the pregame programming for many NFL clubs.

USA Football's Youth Football Safety Surveillance Study, with funding from the NFL, will be conducted in the fall of 2012 to examine player health and safety in organized youth tackle football across the United States. USA Football has commissioned The Datalys Center of Indianapolis to lead the independent scientific study, the first of its scope in youth football's 80-plus year history. The study's findings will advance player safety and further strengthen USA Football's widely used development resources, employed by youth leagues in all 50 states and Washington, D.C.

USA Football's Tackle Progression Model helps youth coaches teach the sport's fundamentals in a safe and smart way. The innovative teaching method gradually introduces young players to contact to foster better learning and to limit incidental contact with the helmet. Developed with the help of football experts within youth, high school, college

"Participation in sports is a great way for kids and teens to be active. However, young athletes, and especially their parents, need to know about concussions and the danger they pose. We commend the NFL on its commitment and look forward to partnering with them to help prevent injuries among young athletes."

– Dr. Ileana Arias, CDC's Principal Deputy Director on the release of the NFL-CDC youth concussion poster

and NFL football, the Tackle Progression Model is endorsed by medical experts specializing in the treatment of sports injuries, including head trauma.

The NFL and NFLPA also created the **Youth Football Fund** (YFF) in 1998 to support the game at the youth level. YFF collaborates with USA Football on a number of health awareness and education programs, including an annual sports safety summit for youth and high school football coaches. YFF also supports a **Coach Smart** awareness initiative, which supplied online health and safety materials to 2010 NFL Player and Coaches Football Camp Grant recipients. From 2010 through 2011, more than 500 coaches associated with the NFL Player and Coaches Football Camp Grant programs participated in the Coach Smart online health and safety course.

Youth Fan Forums

The NFL launched a series of youth health and safety forums in 2011 to educate young fans and football players about safety precautions in sports. At the inaugural forum, Commissioner Goodell addressed a group of 200 high school football players, parents and coaches from the New York City area at Met Life Stadium, home of the New York Jets and New York Giants. Commissioner Goodell was joined by Jets owner Woody Johnson, league medical experts and several current and former players who spoke about the importance of safe and fair play. The event focused on concussion prevention and emphasized that players at all levels, including professionals, must put safety first.

Additional forums were held during Super Bowl week with a group of 50 Indianapolis-area youth football players. NFL players, medical experts and representatives from the Gatorade Sports Science Institute ran drills with the players and gave lessons on proper helmet fitting, basic football skills and concussion awareness. After the season, more than 100 parents of youth football players and 60 youth league coaches were hosted by the Atlanta Falcons. Participants discussed concussion prevention, identification, symptoms and best treatment practices with Falcons CEO and President Rich McKay, representatives from the CDC, and current and former players.

The league will continue to organize these events across the country, teaching young players and their parents and coaches that health and safety is a top priority for every athlete, at every level.

CDC and Youth Concussion Awareness

Since 2007, the NFL has worked closely with the CDC to produce materials promoting concussion awareness and management for young athletes and their coaches. The results of this partnership include multiple resources for parents, coaches, athletes and clinicians.

The NFL, USA Football and 25 medical organizations and other youth sports entities teamed up in 2007 on the **Heads Up** campaign. At the time, the NFL was the only sports league involved in this initiative, which aims to improve prevention, recognition, management of, and response to concussions across all youth sports. The league has worked with the CDC to create national television PSAs describing the importance of recognizing concussions and taking time to recover before returning to play. The PSAs have featured Commissioner Goodell, as well as former NFL player Kurt Warner. The TV PSAs and accompanying print materials received more than 60 million impressions.

The NFL has also supported the CDC Foundation's online training modules about concussion in sports. The NFL partnered with the CDC on a training module for youth sports coaches, released in 2010, which has been completed by nearly a half-million youth sports coaches across the country. This module educates coaches on how to identify concussions, supporting implementation of the Lystedt law across the country.

The CDC, with funding from the NFL, has developed another training module that supports Lystedt law implementation. **Heads Up to Clinicians** was designed to educate health care professionals about key steps to take prior to releasing a concussed athlete to return to play. Starting in 2012, the U.S. Olympic team medical director is requiring all medical staff to complete the course. New York is also requiring the course for school nurses and certified athletic trainers as part of state concussion law. Coaches and PE teachers in the state are also required to complete the course every two years. **Heads Up to Clinicians** won a 2012 Telly Award for groundbreaking online content. There were more than 12,000 Telly Award entries.

Additional modules are slated to be released in 2012, including an NFL-funded concussion module for teens and kids. The module will be supported with interactive games and videos featuring professional athletes on the kid-focused NFL RUSH website.

Building on the educational outreach of the **Heads Up** initiative, the NFL and CDC jointly designed a concussion awareness poster in 2010 about best treatment, prevention and detection methods. The NFL required the poster to be displayed in the locker rooms of all 32 teams, and collaborated with USA Football and 15 other national sport governing bodies to develop a version for youth sports. The poster and an accompanying fact sheet were distributed to approximately 300,000 coaches, parents, schools and sports leagues in 2011. In 2012, the NFL created new versions of the **Heads Up** fact sheets, posters and clipboard stickers customized with the logos of all 32 clubs. The materials will be distributed by the teams to youth athletes in their communities.

The locker room poster has been adopted by other sports leagues and organizations, including the US Soccer Federation and the Southeastern Conference.

Youth Helmet Replacement Program

As part of a joint commitment to player safety, the NFL and a group of sports entities and equipment manufacturers have entered into an unprecedented partnership to create a youth football safety and helmet replacement program, with an emphasis on underserved communities. The initiative removes helmets that are 10 years or older and replaces them with new ones at no cost to the beneficiary leagues and provides coaches with the latest educational materials.

"I am pleased to see the NFL, USA Football and manufacturers working together to make sure our young football players are not wearing 10-year-old helmets that no longer meet industry safety standards. Increasing awareness of equipment safety and sports concussion will help protect young players from injury."

– U.S. Senator Tom Udall

The NFL is joined in partnership with the NFLPA, USA Football, the CDC, National Athletic Equipment Reconditioners Association (NAERA), National Collegiate Athletic Association (NCAA), National Operating Committee on Standards for Athletic Equipment (NOCSAE), Sporting Goods Manufacturers Association (SGMA), Rawlings, Riddell, Schutt and Xenith, and supported by the U.S. Consumer Product Safety Commission (CPSC).

The NFL, NFLPA, NCAA and NOCSAE have committed approximately $1 million in the first year. The pilot program is designed to provide information on the state of youth football helmets, including the number of helmets 10 years old or older in use. As of 2012, NAERA members no longer recondition or recertify any helmet that is 10 years of age or older. NOCSAE collects the helmets when removed to use them for research programs.

The effort will educate youth football coaches on health and safety issues and has already provided 4,000 new helmets to football players in low-income communities in 2012.

While helmets are an important tool to protect players, helmets do not prevent concussions. Therefore, the program includes a strong campaign that features safety information from the CDC, the CPSC and USA Football, including materials on concussion awareness, proper helmet fitting, and football instruction from USA Football's Tackle Progression Model and Levels of Contact module. In addition, leagues that receive helmets are required to have their coaches complete USA Football's Level 1 coaching course.

Nutrition, Substance Abuse and General Fitness Education

NFL Play Safe!

The NFL Play Safe! Health and Safety Series is a unique youth football

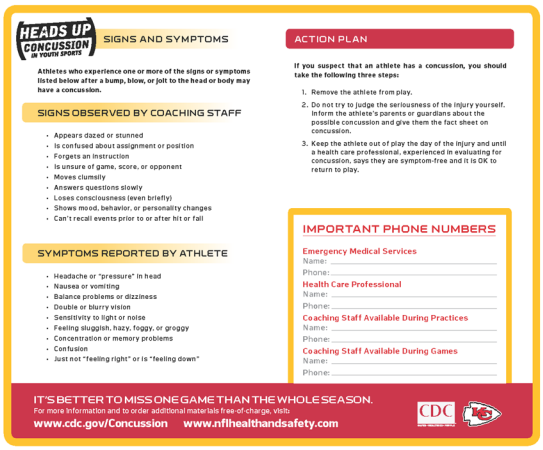
education module made of four books and 10 posters with comprehensive information about strength and conditioning, first aid, nutrition and psychological health. The NFL worked with the American Red Cross, Michigan State University's Center for the Study of Youth Sports, ACSM and the National Athletic Trainers' Association to develop the content. The kit was created with funding from the Youth Football Fund to provide youth and high school football coaches, their players and parents with user-friendly, football-specific information. The NFL distributed the module to more than 15,000 high school football programs and more than 10,000 youth football organizations across the country. The series is also available on the USA Football website.

ATLAS and ATHENA

The NFL Youth Football Fund has given more than $2.6 million to Oregon Health & Sciences University's **ATLAS** (Athletes Training & Learning to Avoid Steroids) and **ATHENA** (Athletes Targeting Healthy Exercise & Nutrition Alternatives) award-winning substance abuse prevention programs. The programs promote healthy living and the reduction of steroid, human growth hormone and other drug use among male and female high school athletes. The NFL **ATLAS** and **ATHENA** Schools program is used in 14 NFL markets and has reached more than 30,000 high school student athletes and 800 coaches. In 2012, Linn Goldberg, M.D., professor of medicine and chief of the Division of Health Promotion & Sports Medicine at Oregon Health & Science University, and head of the **ATLAS** and **ATHENA** programs, was awarded the President's Council on Fitness, Sports & Nutrition Lifetime Achievement Award for his groundbreaking work.

"The growth of the Korey Stringer Institute is due to our corporate partners like the NFL, and we are extremely proud of those affiliations. The support is altruistic, not everyone knows the NFL is backing the KSI, yet the NFL continues to do everything they can to impact sports at all levels."

– Douglas J. Casa, Ph.D., ATC, Chief Operating Officer, Korey Stringer Institute



Clipboard sticker for youth sports coaches, featuring the Kansas City Chiefs logo.

Gatorade and the Korey Stringer Institute

The NFL and Gatorade joined to establish the **Korey Stringer Institute** with the University of Connecticut in 2010 to further research, education and advocacy for the prevention of heat stroke and sudden death in sport. The NFL and Gatorade have also collaborated to run a "Beat the Heat" educational campaign for parents and coaches. The campaign involved NFL players and their wives leading hydration awareness and raising funds for the Kendrick Fincher Memorial Foundation. The NFL also supported Gatorade in developing the **Gatorade Heat Safety Kit**, a free educational resource for athletes, parents and coaches, to spread awareness.

Youth Fitness Programs

NFL PLAY 60 was launched in the fall of 2007 to tackle childhood obesity by encouraging kids to be physically active for at least 60 minutes a day. The NFL has committed more than $250 million to youth health and fitness through programming, grants, and media time for public service announcements since the program launched. The NFL has joined forces with partners such as the American Heart Association, KaBOOM!, National Dairy Council and United Way to build more than 125 NFL Youth Fitness Zones, organize more than 1,500 **NFL PLAY 60** youth events, and integrate programs into more

than 77,000 schools nationwide. In 2010, First Lady Michelle Obama's Let's Move! campaign began collaborating with **NFL PLAY 60** to fight childhood obesity and encourage the nation's youth to lead more active lifestyles. In addition, the NFL works with the Cooper Institute, a nonprofit dedicated worldwide to preventive medicine research and education, to fund its NFL PLAY 60 FITNESSGRAM program, which reaches more than 22 million children in all 50 states. The NFL's funding also supports the more than 1,100 schools across all NFL team markets taking part in a Cooper Institute-NFL PLAY 60 evaluation study.

Community Health Outreach

The NFL advocates for health and safety in communities, providing resources and programs to improve the health of everyone – from family members of players to fans in the stands.

A Crucial Catch

The NFL, its clubs and players are proud to support the fight against breast cancer. **A Crucial Catch**, in collaboration with the American Cancer Society (ACS), is focused on the importance of annual screenings, especially for women who are 40 years of age and older. Throughout October of each year, NFL games feature players, coaches and referees wearing pink game apparel and using special pink equipment to raise awareness of breast cancer. These items are then auctioned on the NFL Auction website, with 100 percent of the proceeds donated to ACS. Funds are also raised from the retail sale of pink NFL items. The NFL has created a community playbook to help high schools and youth sports leagues mobilize their communities in raising money for ACS. Since the NFL and ACS first joined forces in 2009, **A Crucial Catch** has raised nearly $3 million. In 2011, the campaign reached 151 million viewers, including 58 million females.

Proceeds from 2011 onward will fund a new community health worker program in 17 counties across the country that have the lowest screening numbers and highest rates of mortality from breast cancer. The program will provide educational outreach and events in these markets.

Driving Culture through Collaboration and Respect

The NFL has a deep respect for members of the Armed Forces, displayed annually through NFL Salute to Service events, which honor service members on Veterans Day and beyond. In recent years, the relationship between the NFL and Armed Forces has been harnessed to fuel a collaborative initiative to increase awareness of and address traumatic brain injury (TBI) in combat and sports. From openly discussing the effects of concussions to sharing safety equipment research and technology, this is a relationship that continues to develop and grow, benefiting both parties.

Collaboration between the Armed Forces and NFL was born out of supportive dialogue between NFL Commissioner Roger Goodell and former Vice Chief of Staff of the U.S. Army General Peter Chiarelli. In March 2012, a focus group of seven current and former NFL players and nine Armed Services members was convened to discuss head injuries. The meeting sparked a dynamic conversation. Both groups understood the importance of reporting concussions, but also admitted to failing to do so in the past. Above all, they shared strong bonds with their respective teammates, and felt that looking out for each other's health is always a priority. The NFL is utilizing these results to further improve the culture of the league through comprehensive education.

In August 2012, the NFL joined U.S. Army Chief of Staff General Ray Odierno at West Point to announce a long-term initiative to enhance the health of soldiers and players by sharing information, providing education and engaging in discussion on concussion and health-related issues that affect both organizations. They also announced the launch of NFL and Army websites that provide comprehensive TBI information

"If I try to address this with a soldier, they may understand what I'm saying. But if I put an NFL guy in there who says, 'Hey, I understand what you're going through, I had this issue, too,' boy, that resonates with our soldiers."

– Maj. Gen. Stephen R. Lanza

Photo: Tommy Gilligan, U.S. Army

On August 30, 2012, Army Chief of Staff Gen. Ray Odierno and NFL Commissioner Roger Goodell signed a letter formalizing the initiative between the Army and the NFL to help raise awareness about traumatic brain injury.

for players and service members. Other plans for the initiative include event-based forums to bring together players and soldiers to discuss their experiences with injuries, public service announcements and social media interactions to promote help-seeking behaviors in both organizations, a peer-to-peer program that matches retired NFL players with soldiers transitioning out of the Army, and the sharing of medical research and information between both organizations.

Upcoming activities include forums in which members of the military will visit NFL teams to speak with players about head injuries, integration of the NFL and Armed Services head injury awareness campaign into the NFL **Salute to Service,** and a series of educational health and safety posters for military bases and NFL facilities. Several NFL teams, including the Seattle Seahawks, have also promoted mental health programs for veterans.

Prostate Cancer Screening and Education

In addition to collaborating with the American Urological Association Foundation (AUAF) to offer free prostate screenings for retired NFL players through the NFL Player Care Foundation (PCF), the NFL supports the **Know Your Stats about Prostate Cancer** campaign. The campaign was developed by the AUAF to encourage men over 40 to talk with their doctors about prostate cancer, their PSA (prostate-specific antigen) score and getting regular physical exams. In just six weeks in 2010, more than 500 educational events were attended by 54,000 men in more than 300 cities nationwide. Prostate cancer screening offered at some of the event locations was completed by 33,000 men — just over the number of men who will die this year from the disease. In addition to supporting the campaign and AUAF with an annual grant from the PCF, the NFL assists the AUAF with media outreach and event support. The league also hosts screenings during events at the annual Pro Football Hall of Fame week and Super Bowl week to extend the reach of the program.

"As a cancer survivor, I'm lucky to be able to spread the message with the AUA Foundation and NFL encouraging other men to take charge of their prostate health and to stay in the game for life."

– Mike Haynes, Pro Football Hall of Fame player, Know Your Stats spokesman

Partnership for Clean Competition

In 2008, the NFL committed $3 million to The Partnership for Clean Competition (PCC), a nonprofit grant-making organization that funds high-quality and innovative anti-doping research. Founded by the NFL, United States Olympic Committee, United States Anti-Doping Agency and Major League Baseball, the PCC combines the resources and expertise of many of America's leading sports entities. The PCC has awarded $4.4 million in grants since 2008. The NFL has renewed its commitment to this partnership. In December of 2011, the NFL hosted a conference for PCC entitled, "The Doping Decision: Deterring Doping in Sport." The event brought together leaders and influencers in anti-doping to discuss new ways to detect drug use and to promote clean competition across all levels of sport.

NFL/NFLPA Research and Education Foundation, Inc.

The NFL/NFLPA Research and Education Foundation, Inc. (NNREF) is a 501(c)(3) not for profit organization founded by the NFL and the NFL Players Association. As a supporting charity of NFL Charities, NNREF is committed to supporting research and educational initiatives that focus on the health and safety of football players; particularly regarding the importance of clean competition and proper development of athletes at the youth and high school levels. In addition, the foundation issues grants to organizations that focus on youth steroid prevention efforts. In addition, the foundation issues grants to organizations that focus on youth steroid prevention efforts.

SAFETY RULES

As the game continues to evolve, so too do the rules that ensure fair competition and make the game safer.

Notable measures have included rules targeting unnecessary roughness, helmet to helmet contact and hits on defenseless receivers, as well as rules aimed at further protecting the quarterback.

In recent years, the NFL has modified its playing rules to sharply reduce contact to the head and neck of players. One driving force behind the NFL's continuous focus on safety rule improvements is the NFL Competition Committee, currently chaired by Rich McKay, President and CEO of the Atlanta Falcons.

Rich McKay
Chair, Competition Committee;
President and CEO, Atlanta Falcons

While the Committee examines rules and regulations covering all aspects of the game, it emphasizes those areas dealing with player safety. Each year, the NFL Competition Committee conducts a complete review of player injuries and discusses means by which the NFL can reduce them through the implementation of new rules, or by clarifying or strengthening enforcement of existing rules. The Committee solicits input from the clubs through an in-depth survey, and then thoroughly evaluates all suggested changes. In addition, on-field game officials, the NFL Players Association and player representatives offer input on the rules and state of the game.

The Competition Committee primarily bases its recommendations and priorities for each year on player safety insights and data provided to them by the following panels and committees. Rule changes are then voted on by team owners.

In March of 2012, the Competition Committee voted to expand the list of "defenseless players" to include defensive players on crackback blocks, making it illegal to hit them in the head or neck area. NFL owners then voted to make protective thigh and knee equipment mandatory for players beginning in 2013.

"We never are going to back up from player safety. We are always going to push the agenda as much as we can. We appreciate when teams push it, also."

– NFL Competition Committee Chair Rich McKay

Player Safety Advisory Panel

This Panel is charged with taking a long-term view toward making the game safer for all players at every level of the sport. The Panel is co-chaired by Pro Football Hall of Fame Coach and former broadcaster John Madden and Hall of Fame player Ronnie Lott, and comprised of former players, coaches and NFL executives.

John Madden
Co-Chair, Player Safety Advisory Panel;
Pro Football Hall of Fame Coach and
Former Broadcaster

Ronnie Lott
Co-Chair, Player Safety Advisory Panel;
Pro Football Hall of Fame player

The focus of the Panel is to review all aspects of the game — including playing rules, techniques, strategies, training methods, safety-related studies and equipment standards — with an eye toward improving player safety. The Panel also weighs considerations such as reducing the overall amount of offseason work, and/or limiting the use of helmets (and therefore contact) in practice, minicamps, Organized Team Activity, and training camps. Recommendations from the Panel are provided directly to the Competition Committee and NFL Commissioner Roger Goodell.

Injury and Safety Panel

In addition to the support the Injury and Safety Panel provides in the area of medical research, the data collected and analyzed by the Panel is also provided to the Competition Committee to inform the development of new player safety rules and regulations.

NFL Owners Health and Safety Advisory Committee

Founded in 2011, the Committee provides support for and oversees all areas of work the NFL is conducting in the area of health and safety. Chaired by John York, M.D., Co-Chairman of the San Francisco 49ers, the Committee is represented by:

- Jerry Jones, Dallas Cowboys Owner
- Rich McKay, Atlanta Falcons President and CEO
- John Mara, New York Giants Owner
- Mark Murphy, Green Bay Packers President and CEO

Rule Changes

In addition to the rule changes made prior to the 2012 season, the following rule changes focused on protecting player health and safety were recently enacted:

- The restraining line for the kicking team was moved from the 30- to the 35-yard line in an effort to increase touchbacks.
- All kicking team players other than the kicker must be lined up no more than five yards behind their restraining line, eliminating the 15-20 yard running "head start" that had become customary for many players.
- The list of "defenseless players" was expanded to include a kicker/punter during the kick or during the return, a quarterback at any time after a change of possession, and a player who receives a "blindside" block when the blocker is moving toward his own endline and approaches the opponent from behind or from the side. Previously, these players were protected against blows to the head, but not against blows delivered by an opponent with the top/crown or forehead/"hairline" parts of the helmet against other parts of the body.
- A receiver who has completed a catch is a "defenseless player" until he has had time to protect himself or has clearly become a runner. A receiver/runner is no longer defenseless if he is able to avoid or ward off the impending contact of an opponent. Previously, the receiver who had completed a catch was protected against an opponent who launched and delivered a blow to the receiver's head.

Evaluation and Impact of Rule Changes

Following the conclusion of the 2011 NFL season, the Competition Committee conducted a thorough evaluation of the impact that rule changes established prior to the season had on player safety.

At the Competition Committee's annual meeting held on March 26, 2012, significant and positive findings were reported in connection to the change in the restraining line for the kicking team being moved from the 30-to the 35-year line. This rule change achieved its intended effect to increase the number of touchbacks, with the number of kickoff returns reduced to 53 percent. More importantly, there was a 40 percent reduction in the number of concussions occurring on kickoffs compared to the 2010 season.

These initial findings provide further reinforcement of the critical importance for ongoing study and evaluation of the effectiveness of existing game rules and the continued pursuit of player safety improvements.

TOMORROW

Scientific advancements and a greater understanding of the issues that affect the health and safety of players are key to sustaining improvement. To that end, the NFL is dedicated to supporting the science and medical research communities. Throughout the past four decades, the league has provided grants to world-class research institutions investigating medical issues that can affect not only players, but also the general public. The results from these studies have helped shape playing techniques, safety equipment standards and development at all levels of the game, and will continue to improve the health and safety of players at all levels in the future.

RESEARCH

Continued progress on health and safety must come from rigorous, scientific research. In order to accelerate independent health and safety research of the highest caliber, the NFL supports health and safety research with unrestricted grants for medical institutions and through its non-profit arm, NFL Charities (NFLC).

The Commitment to Research

Looking Forward – Investing in Tomorrow

The NFL is providing $30 million in funding for medical research to the Foundation for the National Institutes of Health. The unrestricted gift is the NFL's single-largest donation to any organization in the league's 92-year history. The National Institutes of Health (NIH) will oversee the research, which will be designed to benefit athletes as well as the general population, including members of the military. The funding will support the most innovative and promising research on brain injuries and related topics, including: chronic traumatic encephalopathy; concussion detection, prevention, management and treatments; and the potential relationship between traumatic brain injury (TBI) and late-life neurodegenerative disorders, with a focus on Alzheimer's disease. In addition to brain research, funding will be dedicated to investigating: sudden cardiac death in young athletes; heat and hydration-related illness; chronic degenerative joint disease from athletic injuries; the transition from acute to chronic pain; and the detection and health effects of performance enhancing substances, including human growth hormone.

As part of the NFL and NFL Players Association's latest collective bargaining agreement, the two organizations agreed to commit $100 million to medical research over the next 10 years. Funds will be administered to research of the highest caliber, with the greatest potential impact on the future of football and those who play it.

"...not only is traumatic brain injury an issue in the military and in professional sports, but it also affects people of all different ages. It's the leading cause of death and disability in young children and has increasing impact in older adults. With this generous gift from the NFL..., NIH funded investigators will be able to determine what causes brain damage after traumatic brain injury."

- Story C. Landis, Ph.D., Director, National Institute of Neurological Disorders and Stroke, National Institutes of Health

In 2012, NFLC awarded a $75,000 grant to the National Foundation for the Centers for Disease Control and Prevention (CDC) to fund a study to be conducted by the Institute of Medicine Board of Children, Youth, and Families and the National Research Council on sports-related concussions in young athletes. A committee of statisticians, sports medicine experts, youth sports representatives, psychologists, bioengineers and neuroscientists will analyze literature about concussions in terms of their causes, relationship to hits to the head or body during sports, effectiveness of protective devices and equipment, screening and diagnosis, treatment and management, and long term consequences. The committee's consensus report will undergo peer review before being shared with research funding agencies, school districts, athletic personnel, parents and equipment manufacturers to be used as a guide for determining the concussive status of players and identifying the need for further research on sports-related concussions. The study is scheduled to take place from September 2012 until November 2013.

The NFL also supports leading researchers and institutions through NFLC medical research grants. Each year $1.5 million in medical research grants is allocated by NFLC to support these endeavors and help address risk factors that exist not only for football players but for all athletes and citizens with active lifestyles. The NFL and the NFLC have funded nearly $22 million in sports-related medical research throughout the past four decades.

In addition, the NFL has provided an unrestricted grant of $1 million to the Center for the Study of Traumatic Encephalopathy (CSTE) at Boston University School of Medicine for research into long-term effects of repetitive brain trauma in athletes and supported a successful CSTE application for NIH funding into the research of biomarkers. In 2012, the league gave more than $1.5 million to researchers and organizations to conduct studies on a range of player health and safety

issues, including: stem cells and nervous system injuries; MRI methods after concussions; the effect of temperature on the severity of potential brain injuries; the implications of helmet, facemask and shoulder pad designs on airway and cardiovascular care; and a sleep apnea program focused on NFL players.

Third-party Studies Look at Long-term Player Health

As part of the NFL's efforts to support the health and safety of both current and former players, close attention is paid to findings on long-term health. For example, the National Institute for Occupational Safety and Health (NIOSH) recently issued two important updates building on a study of retired NFL players commissioned by the NFL Players Association in the 1990s.

The first updated study, published in *The Journal of Cardiology* in January 2012, shows that former NFL players as a population live longer than the average male. Overall, NIOSH found the mortality rate of former players was nearly half the anticipated number, 334 observed deaths out of 3,439 former players versus 625 expected. NIOSH also found former players are significantly less likely to die from heart disease or cancer. The former players studied also had a suicide rate 59 percent lower than the general public.

The results from this study were shared with retired players in May 2012.

The second NIOSH study update examined neurodegenerative causes of death, and indicated that former players who played the game for at least five seasons between 1959 and 1988 were about three times more likely to die from a neurodegenerative disease such as Alzheimer's disease than the average person. Researchers were unable to establish a specific link to head injury because of a lack of data on concussions and other relevant injuries from that time period, or to speculate on how safety, policy and equipment and related changes since 1988 may affect current probabilities. However, the study clearly underscores the ongoing need to invest in research, education, advocacy, and advances in protection equipment and technology, as well as continued strengthening and enforcement of rules and policies to protect players – consistent with the NFL's actions outlined in this report.

The full NIOSH reports can be found via the following links: http://www.ajconline.org/article/S0002-9149(11)03387-X/fulltext and http://www.neurology.org/content/early/2012/09/05/WNL.0b013e31826daf50.full.pdf

"NIOSH tracked nearly 7,000 players and issued a report, in '94, concluding that NFL retirees were dying at about half the rate of their American male peers. In other words NFL players, in general, live longer."

- "Dead Wrong," Sports Illustrated, May 21, 2012, written by David Epstein

"We have to be very careful and note that we don't know if this is a result of concussions. Are these increased risks because of exposure to contact? In their words, there's an assumption that there is causality there."

- Jeffrey Kutcher, associate professor of neurology at the University of Michigan discussing the NIOSH study on neurodegenerative causes of death among former football players, CNN, September 5, 2012

***Dr. Mayland Chang**, a faculty member in the Department of Chemistry and Biochemistry at the University of Notre Dame, is applying an NFLC grant towards her work on developing therapeutics for the treatment of traumatic brain injury. Dr. Chang's research hopes to treat brain cells after an event to prevent damage that occurs. This is truly life-changing research that may one day lead to treatment for traumatic brain injuries.*

In 2009, the NFL Player Care Foundation (PCF) sponsored a study of the current health and well-being of retired players. A team of researchers at the University of Michigan conducted phone interviews with 1,063 retired players and asked questions across a range of health topics. Ultimately, the retired players reported being similar to or healthier than the general population with respect to most health issues, and showed lower rates of diabetes and cardiovascular disease. The retirees also reported higher rates of financial stability than the general population and satisfaction with their lives. The study also found that Alzheimer's disease or similar memory-related diseases were reported by the former NFL players at a rate higher than the general public. Lead study author David Weir noted the topic should be studied further, and that the results from the phone survey do not prove a link between playing football and later mental troubles.

Another study released in April 2012 conducted by Mayo Clinic reviewed a select group of males who played football in the 1940s and '50s and found they showed no increased risk of developing neurodegenerative diseases later in life when compared to non-football players from the same community.

Research Priorities in Action

NFL Charities Medical Research Criteria and Focus

Eligible applicants may apply for grants

Recipients of NFL Charities medical research grants include:

of up to $100,000, allowing for 10-15 projects to be funded annually. The NFLC medical grants run on an 18-month funding cycle. Grants cover direct research costs and target nonprofit educational and research institutions only. Grant awards are made based on scientific merit, clinical relevance and significance to the NFL community.

In 2010, NFLC revamped the application and review process. The updated process aligns with industry standards for medical research grants as outlined by the NIH. NFLC continues to review and enhance the process and structure to align with player health and safety research priorities, including:

- Concussion and TBI
- Cardiovascular health
- Orthopedic and musculoskeletal injury
- Methicillin-resistant Staphylococcus aureus (MRSA), an infection caused by a strain of Staph bacteria that has become resistant to the antibiotics commonly used to treat ordinary Staph infections

Grant applications submitted to NFLC are reviewed by committees of independent experts who sit on the Medical Grants Subcommittee of the NFL Injury and Safety Panel. After grants are reviewed, recommendations for awards are made by the subcommittees.

Research Results

Research funded by NFLC has resulted in studies published in peer-reviewed journals and presented at medical conferences. Recent notable studies include:

- Baylor College of Medicine discovered a specialized cholesterol test may predict carotid plaques better in individuals with metabolic syndrome. The study participants were retired NFL players and the study received funding from NFLC. Study results were presented at the American College of Cardiology 60th Annual Scientific Session & Expo and Innovation in Intervention: i2 Summit 2011.
- The University of Southern California received an NFLC grant for a first-of-its kind study of the heart rates of athletes in real-game situations. The grant team placed heart patches on USC football players, collecting data during a scrimmage in real time. The team plans to identify differences in heart rate by position, and to establish a baseline for normal and abnormal heart rates in order to improve athlete safety.
- Rush University Medical Center and the University of Iowa investigated recent advances in understanding structural damage and biological response following joint injury and identified directions that future researchers should take. The researchers concluded that further research should focus on understanding the health of joint tissue during the healing period after injury in order to develop more effective treatment options. The research findings were published in the *Journal of Orthopaedic Research*.

Previous studies have focused on improving the treatment of athletic hip disorders, improving stem cell-mediated healing in tendon overuse injuries, evaluating the biomechanics of ACL-reconstructed knees and more.

In 2010, grants were awarded for studies assessing the possible association between football exposure and dementia in retired football players; concussion surveillance among a large national sample of middle school football players; the role of the cervical spine in football-related concussion; examining how genetics may influence the outcome after repeated concussions; an integrated neuroimaging study for diagnosing and monitoring mild TBI in football players; the dynamic heart rate behavior of NFL athletes; and the prevalence, distribution and fate of MRSA on synthetic turf grass systems.

NFL Charities will continue to fund significant research that may lead to improvements in the health and safety of athletes at all levels.

Collaborating with Independent Experts

The NFL has convened committees of independent experts in a variety of medical fields to guide its medical research process. These experts play critical roles in advancing the NFL's agenda for the benefit of all athletes, from identifying priority areas, to analyzing injury data, to reviewing medical grants.

These committees include:

Head, Neck and Spine Committee

The NFL Head, Neck and Spine Committee advises the NFL on best practices for concussion prevention and management, as well as for avoidance or protection against other head, neck and spine injuries. The Committee is led by Dr. Hunt Batjer, Lois C.A. and Darwin Smith Distinguished Chair in Neurological Surgery at the University of Texas Southwestern Medical Center, and Dr. Richard G. Ellenbogen, Chairman of the Department of Neurological Surgery at the University of Washington School of Medicine.

Committee members are conducting independent research into a variety of subjects that play a role in player safety. For example, the Subcommittee on Safety Equipment and Playing Rules is analyzing different types of padding for football helmets that may reduce forces on the head from hits during play. This independent testing may potentially help manufacturers to consider or implement new or different materials. The Subcommittee is also studying the potential uses of accelerometer data, which include the number, location and magnitude of hits players receive.

There are six subcommittees that focus on specific issues related to head, neck and spine injuries and their prevention and treatment.

- **Subcommittee for the Development and Management of Prospective Database for NFL Players:** Developing a database to track player health. Led by Robert Harbaugh, M.D., FACS, Professor and Chair, Department of Neurosurgery, Penn State Hershey Medical Center.
- **Subcommittee on Former Players and Long-Term Effects of Brain and Spine Injury:** Developing a long-term study of former players' health. Led by Mitchel S. Berger, M.D., Professor and Chairman, Department of Neurological Surgery, University of California San Francisco.
- **Subcommittee on Brain and Spine Injury Research:** Contains scientist members of the Department of Defense, CDC and Massachusetts Institute of Technology. Evaluates new research avenues and grants. Research directions pursued range from TBI-related biomarkers, to novel imaging modalities and treatments of TBI. Led by Russell Lonser, M.D., Chief, Surgical Neurology Branch, National Institute of Neurological Disorders and Stroke.
- **Subcommittee on Advocacy and Education:** Develops educational material, advocates for safety issues of behalf of all youth and professional athletes. Led by Stanley A. Herring, M.D., Clinical Professor, Departments of Rehabilitation Medicine, Orthopaedics and Sports Medicine, and Neurological Surgery; Director, Spine, Sports and Orthopaedic Health, University of Washington School of Medicine; Co-Medical Director, Seattle Sports Concussion Program; and Team Physician, Seattle Seahawks and Seattle Mariners.
- **Subcommittee on Return-to-Play Issues:** Reviews and advises on return-to-play issues, including evaluation of sideline assessment tools and post-injury tools for concussion assessment in NFL players. The Subcommittee was designed to standardize on-field neurological assessment as well as return-to-play guidelines. Led by Margot Putukian, M.D., Director of Athletic Medicine Services, Head Team Physician, Princeton University, and Physician Representative, NCAA and American College of Sports Medicine.
- **Subcommittee on Safety Equipment and Playing Rules:** Evaluates performance of safety equipment for the protection of the head and neck. Led by Professor Kevin Guskiewicz, Ph.D., ATC, Kenan Distinguished Professor, Chairman, Department of Exercise and Sport Science, University of North Carolina at Chapel Hill.

H. Hunt Batjer, M.D., FACS
Co-Chair, Head, Neck and Spine Committee;
Lois C.A. and Darwin Smith Distinguished Chair in Neurological Surgery University of Texas Southwestern Medical Center

Richard G. Ellenbogen, M.D., FACS
Co-Chair, Head, Neck and Spine Committee;
Professor and Chairman
Residency Director, Department of Neurological Surgery
Theodore S. Roberts Endowed Chair
University of Washington School of Medicine;
Co-Director, Seattle Sports and Spine Concussion Program

Head, Neck and Spine Committee Focus:

- *Ensuring that NFL team medical staffs have ongoing access to information on the best technology and research on the prevention and treatment of head, neck and spine injuries.*
- *Studying injury data and equipment research to assist the NFL, its teams and its players in providing the safest environment for minimizing injuries to the head, neck and spine.*
- *Examining the latest treatment strategies and sharing information with medical staffs and players the best practices regarding treatment of injuries to the head, neck and spine.*

Injury and Safety Panel

The Injury and Safety Panel focuses on managing and overseeing the league's player injury surveillance system. Chaired by Elliott Hershman, M.D., Chairman, Department of Orthopaedic Surgery, Lenox Hill Hospital, and Team Orthopedist, New York Jets, the Panel provides yearly data compilation and analysis of the types and severity of injuries sustained by players. Data collected are utilized to support various player safety efforts, including the development of player safety rules by the NFL Competition Committee. The data are also used by team medical staffs to assist in injury prevention and treatment. The Panel meets quarterly, reporting to and making recommendations directly to Commissioner Goodell, and provides input and guidance on the league's medical research program.

Under the broader purview of the Injury and Safety Panel are three subcommittees:

Foot and Ankle Subcommittee

The Foot and Ankle Subcommittee focuses on collecting and analyzing data to aid in the development and effective use of protective equipment for players. The Subcommittee has funded pivotal studies at the University of Virginia, Michigan State University and Boise State University that analyze how shoe and turf factors relate to injuries. Data collected from these and other studies have been used by the Subcommittee in its work with shoe and equipment manufacturers, technology providers, and playing surface experts as well as equipment managers.

The Subcommittee is currently co-chaired by Michael Coughlin, M.D., Director, Coughlin Foot and Ankle Clinic, St. Alphonsus Regional Medical Center, and Former President, International Federation of Foot and Ankle Surgeons; and Robert Anderson, M.D., Team Physician, Carolina Panthers; Founding Member, OrthoCarolina Foot and Ankle Institute; and Past President, American Orthopaedic Foot and Ankle Society. The Subcommittee meets quarterly and reports its findings and makes recommendations to the Injury and Safety Panel.

Elliott Hershman, M.D.
Chair, Injury and Safety Panel;
Team Orthopaedist, New York Jets;
Chairman, Orthopaedic Surgery,
Lenox Hill Hospital

Cardiovascular Health Subcommittee

The Cardiovascular Health Subcommittee is charged with investigating the prevalence and risk factors for the development of premature cardiovascular disease, including diabetes, hypertension, sleep apnea and obesity in current and former NFL players. The Subcommittee oversees the cardiovascular and obesity health screenings for retired NFL players that are conducted by The Living Heart Foundation and The Boone Heart Institute and funded by the NFL PCF. Standards for screenings for cardiovascular risk factors, such as hypertension, among active players are established by the Subcommittee. Currently, the Subcommittee is conducting a three-year study analyzing the use of echocardiography at the Combine to identify cardiovascular risk factors among active players. Data from screenings of both active and former players are reviewed by the Subcommittee and used in their research, such as an ongoing study of the relationship between hypertension and race.

Research findings from the Subcommittee have been published in influential medical journals, including "Sleep-Disordered Breathing in the National Football League" in the journal *Sleep*, and "Prevalence of Cardiovascular Disease Risk Factors among National Football League Players" in the *Journal of the American Medical Association*.

The Subcommittee is co-chaired by Dr. Robert Vogel, Clinical Professor of Medicine, University of Colorado Health Sciences Center, and Dr. Andrew Tucker, Head Team Physician, Baltimore Ravens, and Medical Director of Sports Medicine, MedStar Union Memorial Hospital. Subcommittee members include experts in cardiology and cardiovascular medicine, endocrinology, obesity, sleep medicine, hypertension and cardiovascular disease epidemiology.

Sensors in football helmets are used to record impacts.

The Medical Grants Subcommittee

The Medical Grants Subcommittee is responsible for the quality assessment and grading of research grant proposals submitted annually to the NFL and NFL Charities for funding. The Subcommittee's process includes an external review board of independent specialists who identify proposals that address the most pressing issues related to football health and safety. Previous reviewers have included representatives from the NIH, CDC, Massachusetts Institute of Technology, Vanderbilt University School of Medicine, and Ohio State University College of Medicine, among others. To date, the Subcommittee has played a pivotal role in the funding of hundreds of research projects.

EQUIPMENT

An important component of protecting the health and safety of football players at all levels is the correct use of proper equipment. While equipment alone cannot prevent injury, by supporting and investing in the latest research and understanding of biomechanics, the league can play a key role in helping manufacturers develop the safest equipment available.

An Evolution in Safety Equipment

The NFL supports the efforts of equipment manufactures to provide equipment of the highest standard by investing in research. The application of new technology to game equipment includes more than just protective equipment; all game and player equipment is constantly evolving to protect the players of the NFL. The reach of advances made through NFL-supported research goes beyond the 32 teams of the league and onto the field of colleges, high schools and youth programs across the country, as well as other sports.

Advancing Playing Equipment through Research

The Subcommittee on Safety Equipment and Playing Rules, a subset of the Head, Neck and Spine Committee, focuses on studying injury data and equipment efficacy research to assist NFL teams and players in evaluating the performance of safety equipment for the protection of the head and neck with a goal of minimizing injuries. The NFL works to ensure that players are aware of the best options when choosing equipment. In 2010, with support of the NFL Players Association, the league commissioned an independent study at two laboratories to assess the performance of helmets worn by NFL players, and shared those results with team athletic trainers, physicians and equipment managers, and players. The league also shares research information with major helmet makers in order to develop better equipment. For the last two years, the NFL has offered manufacturers a video of every play that resulted in a concussion from the past season. Dr. Guskiewicz of the Head, Neck and Spine Committee led a recent laboratory assessment of helmets worn by NFL players in managing impact from field collisions. Through these types of work, the NFL is always improving its recommendations and requirements for on-field safety.

The Foot and Ankle Subcommittee of the Injury and Safety Panel oversees NFL-related biomechanical research conducted at the University of Virginia. Research results are shared with shoemakers and manufacturers of artificial turf. Following recommendations from the Subcommittee to standardize the characteristics of turf in order to decrease injuries, manufacturers have started to conduct tests on various aspects of the turf, including surface hardness and the depth of sand below the turf, prior to every game. Similar standards were developed for grass surfaces.

Additional research conducted by the Subcommittee identified the degree of stretch at which a "turf toe" injury occurs, finding that less movement of the toes within the shoe leads to a decreased chance of a turf toe injury. The Subcommittee has shared this information with the shoe makers to help build a shoe that will address the issue.

TOGETHER

Collaboration is a key part of the health and safety culture of the NFL. From research institutes to government organizations to independent researchers, doctors, surgeons and athletic trainers to equipment manufacturers, the NFL convenes experts across the spectrum of the sport to ensure comprehensive and collective discussions inform the decisions that impact health and safety.

The NFL thanks its partners, with special thanks to the members of committees and panels that volunteer their time and expertise to guide the NFL.

Competition Committee

- **Rich McKay, Chair, Competition Committee; Atlanta Falcons, President and CEO**
- **Jeff Fisher**, St. Louis Rams, Head Coach
- **Stephen Jones**, Dallas Cowboys, Executive Vice President, Chief Operating Officer, Director of Player Personnel
- **Marvin Lewis**, Cincinnati Bengals, Head Coach
- **John Mara**, New York Giants, President and CEO
- **Mark Murphy**, Green Bay Packers, President and CEO
- **Ozzie Newsome**, Baltimore Ravens, General Manager
- **Rick Smith**, Houston Texans, General Manager, Executive Vice President
- **Ken Whisenhunt**, Arizona Cardinals, Head Coach

Player Safety Advisory Panel

- **Ronnie Lott, Panel Co-Chair; Pro Football Hall of Fame Player**
- **John Madden, Panel Co-Chair; Pro Football Hall of Fame Coach and Former Broadcaster**
- **Ernie Accorsi**, Former General Manager
- **Antonio Freeman**, Former Player
- **Patrick Kerney**, Former Player
- **Willie Lanier**, Pro Football Hall of Fame Player
- **Oliver Luck**, Director of Intercollegiate Athletics, West Virginia University
- **Steve Mariucci**, Former Head Coach
- **Anthony Muñoz**, Pro Football Hall of Fame Player

Injury and Safety Panel

- **Elliott Hershman, M.D., Chair, Injury and Safety Panel; Chairman of the Department of Orthopaedic Surgery, Lenox Hill Hospital; Team Orthopedist, New York Jets**
- **Robert Anderson, M.D.**, Co-Chair, Foot and Ankle Subcommittee; Founding Member, OrthoCarolina Foot and Ankle Institute; Team Physician, Carolina Panthers; Past President, American Orthopaedic Foot and Ankle Society
- **John Bergfeld, M.D.**, Former Team Physician, Cleveland Browns; Former Chief of Sports Medicine, Cleveland Clinic
- **James Bradley, M.D.**, Team Orthopaedist, Pittsburgh Steelers; Clinical Professor of Orthopaedics, University of Pittsburgh School of Medicine
- **Lawrence Brown, M.D.**, NFL Advisor, Drugs of Abuse
- **Anthony Casolaro, M.D.**, Team Internist and Head Physician, Washington Redskins; Clinical Associate Professor of Medicine, Georgetown University School of Medicine
- **James Collins**, ATC, Head Athletic Trainer, San Diego Chargers
- **Michael Coughlin, M.D.**, Co-Chair, Foot and Ankle Subcommittee; Director, Coughlin Foot and Ankle Clinic, St. Alphonsus Regional Medical Center; Former President, International Federation of Foot and Ankle Surgeons
- **Robert Johnson, M.D.**, Professor Emeritus of Orthopaedic Surgery, University of Vermont School of Medicine
- **John Lombardo, M.D.**, NFL Advisor, Performance Enhancing Agents
- **Vandana Menon, M.D., Ph.D.**, MPH, Director of Clinical Epidemiology, Outcome Sciences
- **Jeff Silverstein, M.D.**, Associate Dean of Research, Executive Director, Internal Review Board, Professor of Anesthesiology, Surgery and Geriatrics and Palliative Medicine, Mount Sinai School of Medicine
- **Joseph Skiba**, Equipment Director, New York Giants
- **Kurt Spindler, M.D.**, Professor and Vice Chair, Department of Orthopaedics and Rehabilitation, Vanderbilt University School of Medicine
- **Andrew Tucker, M.D.**, Co-Chair, Cardiovascular Health Subcommittee; Head Team Physician, Baltimore Ravens; Medical Director of Sports Medicine, MedStar Union Memorial Hospital; Former President, NFL Physician's Society
- **Robert Vogel, M.D.**, Co-Chair, Cardiovascular Health Subcommittee; Clinical Professor of Medicine, University of Colorado Health Sciences Center
- **Edward Wojtys, M.D.**, Chief of Sports Medicine Service, Professor of Orthopaedic Surgery, University of Michigan School of Medicine
- **Anthony Yates, M.D.**, FACP, Team Physician, Pittsburgh Steelers; President, NFL Physicians Society; Clinical Assistant Professor of Medicine, University of Pittsburgh School of Medicine; Co-Director, Corporate Health Program, University of Pittsburgh Medical Center
- **John York, M.D.**, ex-officio member; Co-Chairman, San Francisco 49ers; Chairman, NFL Owners Committee on Health and Safety

Injury and Safety Panel Medical Grants Subcommittee

- **Russell Lonser, M.D.**, Head, Neck and Spine Research Grants
- **Robert Vogel, M.D.**, Cardiovascular Disease Research Grants
- **James Puffer, M.D.**, General Medical Grants; President and Chief Executive Office, American Board Of Family Medicine
- **Kurt Spindler, M.D.**, Orthopedic and Musculoskeletal Research Grants

Head, Neck and Spine Committee

- **H. Hunt Batjer, M.D., FACS, Co-Chair, Head, Neck and Spine Committee; Lois C.A. and Darwin Smith Distinguished Chair in Neurological Surgery, University of Texas Southwestern Medical Center**
- **Richard G. Ellenbogen, M.D., FACS, Co-Chair, Head, Neck and Spine Committee; Professor and Chairman, Residency Director, Department of Neurological Surgery, Theodore S. Roberts Endowed Chair, University of Washington School of Medicine;**

Co-Director, Seattle Sports and Spine Concussion Program

- **Ronald Barnes**, Senior Vice President of Medical Services, Head Athletic Trainer, New York Giants
- **Ernest Bates, M.D.**, Neurosurgeon; Chairman and CEO, American Shared Hospital Services
- **Mitchel Berger, M.D.**, Chair, Subcommittee on Former Players and Long-Term Effects of Brain and Spine Injury; Professor and Chairman, Department of Neurological Surgery, Director, Brain Tumor Surgery Program, Director, Neurosurgical Research Centers, Brain Tumor Research Center, University of California, San Francisco
- **Bradley F. Boeve, M.D.**, Professor and Chair, Department of Neurology, Mayo Clinic
- **Kathleen Welsh-Bohmer, Ph.D.**, Professor, Department of Psychiatry and Behavioral Sciences Director, Bryan Alzheimer's Disease Research Center, Duke University
- **T. Pepper Burruss**, Head Athletic Trainer, Green Bay Packers
- **John A. Butman, M.D.**, Ph.D., Staff Clinician, Radiology and Imaging Sciences, National Institutes of Health Clinical Center
- **Randal P. Ching, Ph.D.**, Research Associate Professor and Director Applied Biomechanics Laboratory, Department of Mechanical Engineering, University of Washington
- **Ron Courson**, ATC, PT, NREMT-I, CSCS, Director of Sports Medicine, University of Georgia Athletic Association
- **Henry Feuer, M.D.**, FACS, Associate Professor of Neurosurgery, Indiana University School of Medicine; Indiana Spinal Cord and Brain Injury Research Fund Board; Team Neurosurgeon, Indianapolis Colts; Co-Medical Director of the Indiana Sports Concussion Network
- **Richard Gliklich, M.D.**, President, Quintiles Outcome, Inc.
- **Kevin Guskiewicz, Ph.D.**, ATC, Chair, Subcommittee on Equipment and Playing Rules; Kenan Distinguished Professor, Chairman, Department of Exercise and Sport Science, University of North Carolina at Chapel Hill
- **Robert Harbaugh, M.D.**, FACS, Chair, Subcommittee for the Development and Management of Prospective Database for NFL Players; Director, Penn State Institute of the Neurosciences; University Distinguished Professor and Chair, Department of Neurosurgery, Professor, Department of Engineering Science and Mechanics, Penn State Hershey Medical Center
- **Andrew Hecht, M.D.**, Surgical Spine Consultant, New York Jets; Co-Chief, Orthopaedic Spine Surgery, Assistant Professor of Orthopaedics and Neurosurgery, Mount Sinai Medical Center and School of Medicine
- **Stanley Herring, M.D.**, Chair, Subcommittee on Advocacy and Education; Team Physician, Seattle Seahawks; Clinical Professor of Rehabilitation Medicine, Orthopaedics and Sports Medicine, Neurological Surgery, Director, Sports, Spine and Orthopaedic Health, University of Washington School of Medicine; Co-Medical Director, Seattle Sports Concussion Program
- **Merril Hoge**, Former Player; ESPN Analyst
- **Joel Kramer, Psy.D.**, Clinical Professor of Neuropsychology in Neurology, Director of the Memory and Aging Center Neuropsychology Program, University of California San Francisco
- **Geoff Ling, M.D., Ph.D.**, Professor and Vice-Chair, Department of Neurology, Uniformed Services University of Health Sciences; Colonel, U.S. Army (ret.); Program Manager, Defense Advanced Research Projects Agency (DARPA)
- **Russell Lonser, M.D.**, Chair, Subcommittee on Brain and Spine Injury Research; Chief, Surgical Neurology Branch, Program Director, Neurological Surgery Residency Training Program, National Institute of Neurological Disorders and Stroke (NINDS)
- **Thom Mayer, M.D.**, Medical Director, Studer Group; Medical Director, NFL Players Association; Founder and CEO, BestPractices, Inc.
- **Bruce Miller, M.D.**, Associate Professor, Department of Orthopaedic Surgery, University of Michigan Medical School; Head Orthopaedic Team Physician, University of Michigan Football; Team Physician, USA Ski Team; Team Physician, USA Rugby Team; Program Director, University of Michigan Orthopaedic Sports Medicine Fellowship
- **Frank A. Pintar, Ph.D.**, Chief of Research, Department of Neurosurgery, Medical College of Wisconsin
- **Margot Putukian, M.D.**, Chair, Subcommittee on Return-to-Play Issues; Director of Athletic Medicine Services, Head Team Physician, Princeton University; Associate Clinical Professor, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey
- **Raul Radovitzky, Ph.D.**, Associate Director, MIT Institute for Soldier Nanotechnologies, Associate Professor, Department of Aeronautics and Astronautics, MIT
- **Daniel Resnick, M.D.**, Professor and Vice Chair, Department of Neurological Surgery, University of Wisconsin School of Medicine and Public Health.
- **Joseph Skiba**, Equipment Director, New York Giants; Member, NFL Injury and Safety Panel, Foot and Ankle Subcommittee
- **Erik E. Swartz, Ph.D.**, ATC, FNATA, Associate Professor of Athletic Training, Kinesiology Department, University of New Hampshire
- **Joseph F. Waeckerle, M.D.**, Clinical Professor of Emergency Medicine, University of Missouri, Kansas City School of Medicine; Editor Emeritus, *Annals of Emergency Medicine*
- **Robert Watkins, III, M.D.**, Spine Surgeon; Co-Director of the Marina Spine Clinic; Founding Member, North American Spine Society
- **Anthony Yates, M.D.**, FACP, Clinical Assistant Professor of Medicine, University of Pittsburgh School of Medicine; Co-Director, Corporate Health Program, University of Pittsburgh Medical Center; President,

NFL Physician Society; Team Physician, Pittsburgh Steelers

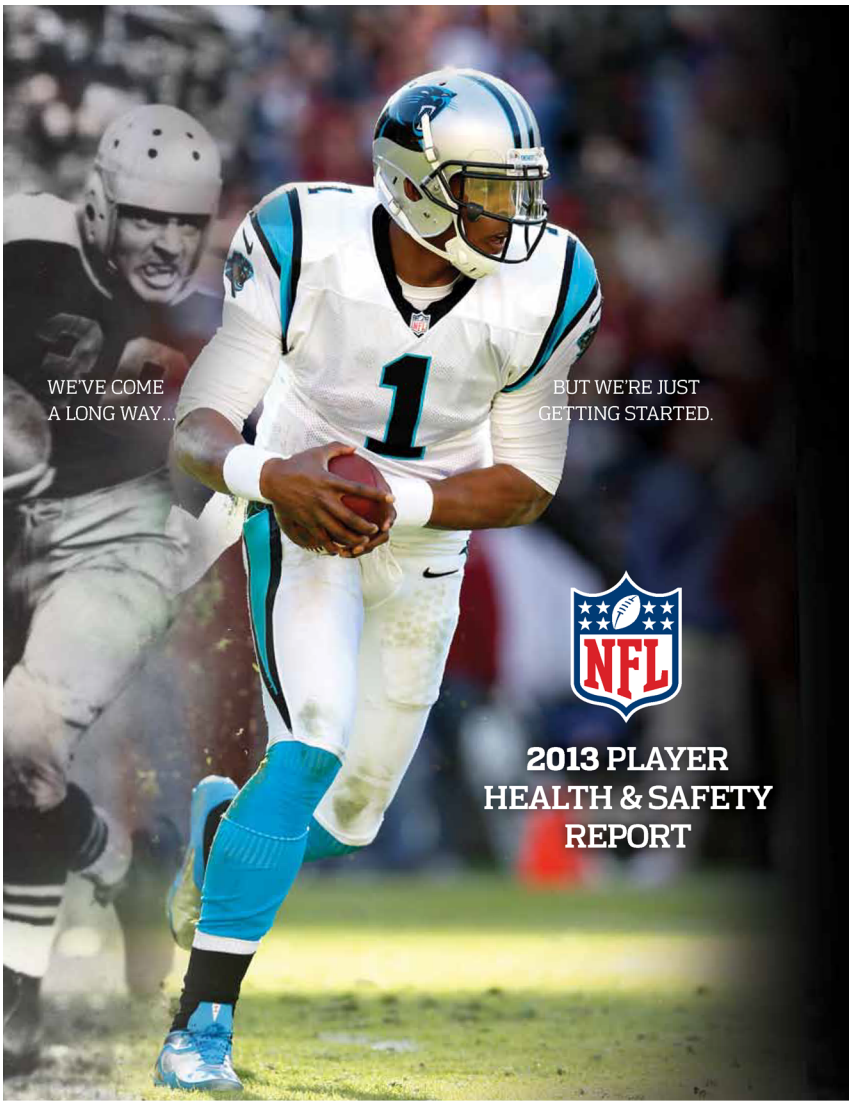
- **J. Christopher Zacko, M.D., M.S.**, Assistant Professor of Neurosurgery, Co-Director, Neurosciences ICU, Department of Neurosurgery, Penn State Hershey

The Head Neck and Spine Committee receives input from several independent consultants:

- **Robert C. Cantu**, M.A., M.D., FACS, FAANS, FACSM, Clinical Professor of Neurosurgery Boston University School of Medicine; Co-Director, Center for The Study of Traumatic Encephalopathy, Boston University Medical Center; Member/Co-Chair, Equipment and Rules Committee NFLPA Mackey/White TBI Committee; Co- Founder and Chairman, Medical Advisory Board, Sports Legacy Institute; Chairman, Department of Surgery, Chief, Neurosurgery Service, and Director, Service Sports Medicine; Emerson Hospital
- **Joseph Maroon**, M.D., FACS, Professor and Vice Chairman, Department of Neurological Surgery, University of Pittsburgh School of Medicine
- **David Meaney**, Ph.D., Professor and Chair, Department of Bioengineering; Associate Director, Penn Center for Brain Injury and Repair, University of Pennsylvania
- **Barry Myers**, M.D., Ph.D., MBA, Professor of Biomedical Engineering with appointments in Orthopaedic Surgery, Anatomy and Business, Duke University; Director, Emerging Programs, Duke Translational Research Institute; Executive-in-Residence, Pappas Ventures
- **Gunter Siegmund**, Ph.D., P.Eng, President, Senior Engineer, MEA Forensic Engineers and Scientists; Adjunct Professor, School of Kinesiology, University of British Columbia

Partners in Community Health

The following organizations have joined the NFL in educating athletes of all levels of play, and fans of all ages, on numerous public health and safety issues.


WE'VE COME
A LONG WAY...
BUT WE'RE JUST
GETTING STARTED.
NFL
2013 PLAYER
HEALTH & SAFETY
REPORT

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MESSAGE FROM COMMISSIONER GOODELL

Sports are an authentic part of American life and a cornerstone of many childhood experiences. Some of my fondest memories are of playing football and other sports as a child. Like many involved in sports growing up, I've carried the lessons of self-discipline, perseverance and teamwork with me and applied them to my life.

Today, as we consider the value of sports in society, and particularly in the lives of young people, safety must be a central part of the conversation. The more we learn about the impact of sports on health, the more we learn how to balance protection with enjoyment of the game.

We know that with virtually any sport there is the possibility of injury. The key question is: what can we all do to make the sports we play as safe as possible? This question is at the heart of an ongoing national dialogue about youth sports safety. It requires parents, coaches, educators, health professionals and sports professionals to work together. The responsibility for safe play is one that we share.

Studies repeatedly find that the rewards for sports participation, especially in children, are significant – and that broader youth participation in physical activities such as sports would be even more beneficial. The CDC reports that 12.5 million children and teens in the United States are obese. With this in mind, the physical benefits of building strength and managing weight through sports take on a greater importance. Beyond the physical, sports participation also leads to increased self-esteem, confidence, better performance in school, and enhanced social skills. According to the Women's Sports Foundation, girls who participate in sports are less likely to become pregnant or suffer from depression as teenagers, and are more likely to get better grades and to graduate from high school.

Football is a great game, America's favorite sport with unique rewards to those who play it – whether at the youth level, in the backyard or neighborhood field, in college, or, for the very best, in the NFL. In order to assure that it remains valued and cherished, we need to constantly strive to make it better and safer. We know that our game is safer than it was five years ago. As our efforts, detailed in this report, continue and deepen, as changes in culture occur, we are confident the game will be even safer 10 years from now.

This is at the core of our mission at the NFL, and we are proud to be working with organizations across the country to help educate communities on safety and fitness as our children head back to the playing fields this fall.

This report helps tell the story of how, together, we are creating a better, safer game for all.

Roger Goodell
NFL Commissioner

MESSAGE FROM DR. JOHN YORK

All of us in the NFL have an important function as the stewards of our sport. This is a role we take very seriously.

Since the release of the NFL Health & Safety Fall 2012 report in October, I am proud to report that substantial progress continues to be made in developing a culture of safety for NFL players, and advances in support of the health and safety of football players and athletes are progressing at all levels. Through key partnerships, commitments to research and continued advocacy the NFL is working to help ensure a safer experience for its players, athletes in all sports and the general population.

Highlights of recent advances include:

Deepening Partnerships and Collaborations. Our committees of independent experts, collaborations with organizations such as the Centers for Disease Control and Prevention, and joint programs with organizations such as the U.S. Army drive important scientific research, provide resources for our players and their families, and inform the policies and rules of our game. We thank the individuals and organizations who have joined us in promoting the health and safety of our players and who have made a positive impact across all sports.

Expanding Research, Accelerating Progress. Building on the $30 million grant the NFL committed to the Foundation for the National Institutes of Health, and the millions in medical research funded through our non-profit foundation, the NFL partnered with GE to dedicate $60 million to advance research and technology in preventing, diagnosing and treating head injuries. Every day work continues on new technologies in player health and safety. This research will accelerate new innovations, speeding the pace at which new technologies reach the marketplace and enhancing existing technology.

We are relentless in our pursuit of advancing science. The NFL will continue to fund research with premier institutes and partner with innovators to accelerate scientific progress.

We continue to evolve, improve and make the game better by working towards making it safer. We are not done. We remain committed to providing the resources, tools and support players deserve, and to leading the way to a safer and healthier game for players at all levels and for athletes in all sports.

Our passion for the sport cannot and will not distract our focus on the total health of athletes. It drives us to make even greater strides in advancing a culture of safety.

John York, M.D.
Co-Chairman, San Francisco 49ers
Chairman, NFL Owners' Committee on Health and Safety


ADVANCES
IN CULTURE

NFL PLAYER ENGAGEMENT: A 360° APPROACH TO PLAYER HEALTH AND WELLNESS

Fostering a strong culture of player health, wellness and safety – that extends across all aspects of a player's life, from his football career to his family and personal growth – is a focal point for the NFL. Players are provided resources, tools and support to assist them as they move through their careers and lives, from signing with their first NFL team to having their first child. An update on several programs enhancing the culture of health, safety and wellness in the NFL follows.

NFL players represent the pinnacle of physical fitness. However, more than physical fitness is necessary to ensure that players succeed, both on and off the field. The mission of NFL Player Engagement is to empower each player to reach his highest potential through guidance, support and resources for all phases and aspects of his career and personal life.

NFL Player Engagement programs are tailored for the period before, during and after a player's NFL experience; PREP, LIFE and NEXT assist in transitioning players through the athletic life cycle.

Troy Vincent at the Rookie Symposium

Q&A with Troy Vincent, NFL Senior Vice President of Player Engagement

Where did the NFL Total Wellness concept come from?

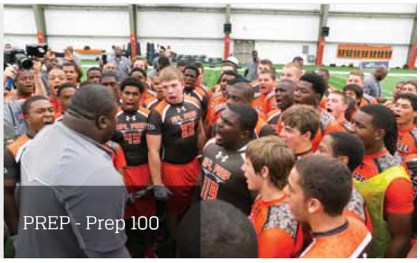
As we look at the athlete's life cycle and the evolution of the game, it is imperative that we approach the long-term wellness of the athlete holistically. The genesis of NFL Total Wellness was the need to foment cultural change emphasizing best practices in Family Safety, Lifestyle, Wellness and Transition.

What sets Total Wellness apart?

As part of our groundbreaking peer-to-peer counseling model under NFL Total Wellness, we have established the Transition Coach. NFL Transition Coaches are former NFL players who work at the club level to reach out to players, identify critical wellness needs and assist with possible solutions. They serve as peer counselors where one-on-one guidance is needed in areas such as: family, crisis, transition and career assistance, depression and finance.

This highly acclaimed Total Wellness initiative not only affords us the opportunity to assist our players, but also to engage in the national dialogue regarding mental health, domestic violence and general health and well-being.

NFL PREP provides high-school and college student athletes of all sports with tools to help them succeed in life. The program focuses on awareness, prevention and education in areas of player health and safety, on-field technique, off-field leadership, and academic and athletic experiences.


PREP - Prep 100

NFL LIFE provides current NFL players and their families with personal and professional development resources, while supporting and educating players' families to take full advantage of the opportunities afforded them by their NFL experience. Resources include social responsibility, professional development, community engagement and life-skills workshops.

LIFE - Rookie Symposium

NFL NEXT challenges former players through management and entrepreneurial programs and career "boot camps," which help former players to consider the next step in their lives and provide services and resources that foster a successful transition to life after football. These programs enhance their marketable employment skills and promote their search for post-NFL careers.


NEXT - Franchise Bootcamp

Participants in NFL **PREP**, **LIFE** and **NEXT** come together in the **NFL Engagement Zone**. The NFL Engagement Zone is a private social network, accessed by invitation only, created by NFL Player Engagement to provide a space for future, current and former NFL players and NFL Player Engagement staff to interact and share resources, ideas and feedback. The Engagement Zone features resources in the form of relevant articles, program information, calendar postings and career and professional development opportunities. Discussion boards enable members to interact with each other, and chat and webinar features allow NFL Player Engagement to provide continued, real-time educational opportunities to members.

Together, NFL PREP, LIFE and NEXT form the core of NFL Player Engagement, a 360° approach to the health and wellness of NFL players.

NFL TOTAL WELLNESS

NFL TOTAL WELLNESS

NFL Total Wellness (TW) is a comprehensive initiative that supports cultural change through an emphasis on family safety, lifestyle, wellness and transition. TW approaches the player with specific efforts to reduce various forms of stigma associated with behavioral health problems; measures to ensure better living through health and safety education; a strong social marketing campaign promoting cultural change; and development of life-skills critical for transition to "new normal conditions" of psychological, emotional, relational and spiritual fitness.

As a part of the TW program, and to provide the NFL family, including former players, NFL employees and their respective families, with a year-round support system that is needed once the fourth quarter ends, **Q5** was created. Created for players and by players, Q5 assists the NFL family in achieving total wellness through four core pillars: Physical Strength, Emotional Strength, Personal Strength and Financial Strength.

Physical Strength

Physical strength means more than just how much a player can bench press or how fast he can run a 40-yard dash. Physical Strength ensures that NFL players and their family members have resources to successfully manage their physical health.

Through Q5 and the Player Engagement website (NFLPlayerEngagement.com), NFL players have access to information on health topics and important links to resources, including the USDA's daily food plan and tracker, a men's health quiz from the U.S. Department of Health and Human Services, a BMI calculator and more.

NATIONAL FOOTBALL LEAGUE FOUNDATION

In December 2012, the newly formed NFL Foundation was announced following a restructuring of the NFL's previous non-profit organizations, NFL Charities and the Youth Football Fund. Efforts of the non-profit Foundation are reflective of the culture and priorities of the NFL, with an emphasis on improving the health and safety of sports, youth football and the broader community. In 2013, the NFL Foundation will provide more than $18 million to support health and safety efforts, such as the Heads Up Football initiative, youth and high school football programs, and community health initiatives, including NFL PLAY 60.

"I will not go through my life scared and I don't want my children to go through life scared. I started playing football when I was eight years old and I would never not want to give that opportunity to my children."

— **LaVar Arrington, former NFL player**

"The game is safer than it has ever been because we're being proactive with head trauma."

— **Merill Hoge, former NFL player**

HGH Testing: Protecting Player Health & Safety

Human growth hormone (HGH) is a naturally occurring hormone that stimulates cellular growth and regeneration in humans and animals. However, synthetic HGH can provide athletes with an unfair competitive advantage, allowing users to recover from injury more quickly while also boosting athletic performance on the field. HGH is believed by many doctors to increase the risk of health problems in its users, including diabetes, joint problems and cardiovascular issues.

HGH is a banned substance in the NFL, and both the league and the NFL Players Association (NFLPA) agreed to start testing for it in the 2011 collective bargaining agreement. However, testing has not been implemented yet due to disagreement on key points.

It is critical to implement HGH testing in order to maintain the integrity of the game. Together, the NFL and NFLPA have the opportunity to send a powerful message to young athletes across the country that performance enhancing substances dishonor the culture of the game and can endanger the well-being of those who use them.

NFL Personal Health Care Team: Chronic Health Management

Chronic health conditions can affect anyone. To aid in the often challenging management of chronic conditions, the NFL provides a dedicated NFL Personal Health Care Team of specialists for players and their family members. Once contacted through the NFL player's health plan hotline, a Personal Health Care Team specialist will serve as a "health coach," working alongside the NFL player and his family to create a personal care plan, help to understand medication or doctor's orders, identify health risks that affect his condition, aid in making educated decisions about treatment options, and explain what players should expect if hospital care is needed.

Personal assistance through this health coach is available for the following chronic conditions:

- Cardiovascular (e.g., acute myocardial infarction, angina, cardiovascular disease, congestive heart failure, coronary artery disease, peripheral arterial disease)
- Type I and Type II Diabetes
- Metabolic Syndrome
- Respiratory (e.g., asthma, COPD, emphysema, chronic bronchitis)
- Bone and Joint (e.g., osteoarthritis, lower back pain)
- Mental Health (e.g., anxiety, bipolar disorder, depression)

Close the Gap – Reversing Heart Disease Trends

NFL Total Wellness has teamed with Boston Scientific's health equity program Close the Gap to increase awareness of heart disease, which remains the most frequent cause of death in Americans, including NFL players. Close the Gap provides educational tools and risk assessments about heart disease to improve heart health for NFL players and their families.

The NFL Healthy Babies Program

Programs that support the four pillars of Q5 and NFL Total Wellness are intended for all members of the NFL family, including those that are "on their way." To provide NFL moms-to-be with assistance, the NFL created the NFL Healthy Babies Program. The program promotes good health for mothers and their babies, identifies and monitors high-risk pregnancies, and prevents premature births. NFL moms-to-be receive assistance that includes information on pregnancy and prenatal care, up to $600 for pregnancy-related expenses if they enroll within the first 14 weeks of pregnancy and specialty case management for high-risk pregnancies and neonatal care.

24-Hour Health Information Line

Because health issues can strike anytime and anywhere, NFL Total Wellness provides players and their families with a free 24-hour health information line staffed by registered nurses available to answer health-related questions and to provide referrals for services. Any member of the NFL family can call the NFL health plan line at 1-800-635-9671.

Emotional Strength

In order to support the emotional strength of NFL players and their families, the NFL provides resources through Q5 and the NFL Player Engagement website, with information from the Centers for Disease Control and Prevention (CDC), the National Institutes of Health and the Substance Abuse and Mental Health Services Administration. NFL Player Assistance and Counseling services has a wide range of resources for all members of the NFL family, including crisis counseling, up to eight face-to-face sessions with a counselor per issue per year, assistance in finding in-network counselors near the individual, and referrals to emotional health resources within their community.

AMERICAN FOUNDATION FOR Suicide Prevention

NFL Life Line was recently recognized by the American Foundation for Suicide Prevention (AFSP), the leading national non-profit organization exclusively dedicated to understanding and preventing suicide through research, education and advocacy. On May 8, 2013, the NFL received the Humanitarian Award from the AFSP for its work to "encourage help-seeking behavior among its players" through its establishment of NFL Life Line and its support of the advancement of neurological research that will help in understanding the impact of traumatic brain injuries on mental health.

"We know that one of the best ways to prevent suicide is by encouraging those who are struggling with a crisis or feeling depressed to seek help, but too often many people fear reaching out…this is why the NFL Life Line is so important. It provides a confidential support system specifically for the NFL family."

— **Robert Gebbia, Executive Director, American Foundation for Suicide Prevention**

AFSP Humanitarian Award Acceptance

NFL Life Line: A Resource for All Members of the NFL Family

NFL LIFE LINE (800) 506-0078 Independent Confidential Support

A recently expanded offering from Q5 and NFL Total Wellness is NFL Life Line. In 2012, recognizing the impact of personal and emotional crisis, the NFL established NFL Life Line as a free, independent and confidential phone consultation service (1-800-506-0078) and website (NFLLifeLine.org). All members of the NFL family, including current and former players, coaches, league staff and their families have complete access to the Life Line and its staff of trained mental health experts 24 hours a day, every day of the year.

The NFL Life Line is independently managed by Link2Health Solutions, a national leader in administering broad-scale crisis support programs, including the National Suicide Prevention Lifeline and Veterans Crisis Line.

Since its launch, the NFL has expanded NFLLifeLine.org to include new resources such as:

- **Education:** Information on the signs and symptoms of emotional distress, assisting users in determining if they or a friend, teammate or family member would benefit from mental health support.
- **A Self-Check Quiz:** Designed by the National Suicide Prevention Lifeline, this anonymous and confidential "self-check" quiz enables the individual to determine if stress or depression might be affecting them or someone they know. Crisis counselors are on call to personally respond to the quiz-taker through the website or in person.
- **Live Online Chat:** This function allows individuals to immediately and confidentially interact with professionals that are specifically trained in personal and emotional crises. Users can link the results from their "self-check" quiz to the chat request, providing the crisis counselor with a more detailed profile of their specific needs.
- **NFL Player Videos:** Several former NFL players, including Michael Strahan, Brett Favre, Cris Carter and Michael Irvin, recorded call-to-action video messages that appear on the Life Line website encouraging fellow players to seek help and recognize that, as a member of the NFL family, they are not alone in addressing emotional issues.

Personal Strength

Personal strength is more than following the rules, it's about keeping things in perspective and staying focused on what really matters — like family, friends and the future.

The NFL provides its family a number of resources to build their Personal Strength. For players with families, resources are available to assist in searching for the best child care services, creating a family's education plan, finding information on raising children, and providing assistance with adoption services. Q5 and the NFL Player Engagement website also provide resources on relationship management, including All Pro Dad (AllProDad.com), an innovative program available to NFL fathers that can assist them in their unique role in their family's life.

Women's Resource Initiative

NFL Player Engagement's Women's Resource Initiative provides research, resources, tools and inspiration for women in the football community. The Women's Resource Initiative was launched in May 2013 through NFL Player Engagement to connect women with their peers to share knowledge, experiences and opportunities in career, service, health and wellness, and lifestyle. Available on the Player Engagement website, the Women's Resource Initiative also provides information specifically tailored to women's health issues, including breast and gynecologic cancers.

Sharon Guillory-Reid, Eric Reid Jr.'s mother, spoke to NFLPE Women's Resource Initiative at the 2013 Draft about her son's transition into the NFL and the role she plays as the mother of an NFL player.

Financial Strength

Financial health is closely related to general wellness. NFL players and their families have financial services and tools through Q5's pillar of Financial Strength, including:

- **24/7 Confidential Financial Support** through Money Management International, the largest non-profit, full-service credit counseling agency in the U.S. It can assist in addressing and preventing a variety of financial challenges.
- **Investment Fraud Avoidance and Financial Tools** through the Financial Industry Regulatory Authority (FINRA), a non-profit organization dedicated to investor education, tools and education are provided to NFL players to outsmart scam artists that may target them.
- **Financial, Legal and Identify Theft Services** through NFL Player Assistance and Counseling Services equips NFL players with critical information to enhance their financial decision making.

Financial strength comprises more than sound financial education and tools. It's also about helping to provide former players with opportunities for rewarding employment after their NFL experiences end.

25 Years of Madden Football

Madden NFL games, named for legendary Hall of Fame coach John Madden, are a regular best seller, known for their realistic portrayal of professional football. Madden 25, released in August 2013, reflects the evolution of football and the dedication that John Madden has shown to improving player safety as co-chair of the NFL Player Safety Advisory Panel. The game includes a "Skills Trainer" to educate users about the game and open the door to educational modules on safer play, including heads-up tackling techniques.

"We have to look out for one another the way we did on the football field…we have to trust one another, we have to rely on one another, we have to share with one another, we can't isolate."

— **Michael Irvin, Pro Football Hall of Fame member**

"Has there been a culture change overall? I think the answer is, unquestionably, 'yes.' Could there be more done? Yes. Do all the players get it? No. Do they want to get it? No."

— **Robert Cantu, M.D., Co-Director of the Center for the Study of Traumatic Encephalopathy, Boston University School of Medicine**

POST-CAREER HEALTH AND SAFETY PROGRAMS

Former NFL players are supported through numerous health and career programs offered by NFL Player Engagement and the NFL Player Care Foundation (PCF), an independent organization dedicated to helping retired players with medical, emotional, financial, social and community needs.

The mission of the PCF is to help former NFL players improve the quality of their lives by providing education and information that will benefit all, as well as to provide financial assistance to former NFL players who are distressed and disadvantaged.

PCF carries out its mission through an individualized case management process that connects each former player with a PCF representative who listens to the player's concerns and provides a personalized, respectful and confidential care program for his needs.

PCF's customized approach and extensive knowledge of NFL benefits, programs and partnerships enables the former player to address his varied needs through one contact who can help him navigate the numerous programs that may be available.

NFL Legends

The league has tapped 19 former players to serve as ambassadors for the newly announced NFL Legends program. The players, who will serve a three-year term, will work to make other former players aware of the various programs and services the NFL has to offer after playing careers are over.

Transition Assistance Programs

The NFL Transition Assistance Program (TAP) is designed to provide the tools and peer-to-peer support for a successful transition. TAP was designed by and is administered by and for former players with academic partners. NFL TAP educates players and their families about essential components of transition including physical, psychological and social changes as they prepare for life beyond football. This interactive, four-day program seeks to provide connections and resources that will last a lifetime.

"With [TAP], I was looking for inspiration. Once I got here, I found exactly what I wanted: I found a path."

— **Obafemi Ayanbadejo, former NFL player**

"Football's a great game. Obviously it's a great game for NFL players, it's how we make a living, but most kids who play football aren't going to make it to the NFL. It's such a great game because it teaches you about life and lessons and there's so much to be gained by participating in football. It's served us all well and just to continue to have this conversation and continue to talk about it and just do whatever we can to make it safer whether it be through rule change or research."

— **Matt Birk, former NFL player**

"The league has done some great things — as best you can within a game of inherent dangers — in making the game as safe as possible."

— **Howie Long, Pro Football Hall of Fame member**

Jamar Nesbit at an NFL Player Care Foundation screening event

Since June 2010, more than 250 NFL players have participated in TAP, engaging in comprehensive business-oriented lectures, case studies and personality evaluations to aid in their post-NFL career transitions. The program also features voluntary and free health screenings.

Financial Grants

Former players who meet eligibility requirements may receive financial grants to help them pay certain outstanding expenses, or the PCF can authorize grants to be paid directly to creditors. PCF has prevented foreclosures on homes, repossessions of cars and helped pay for physical and mental health services. To date, PCF has administered 468 grants totaling more than $4.8 million.

New Benefit Announced for Former Players

In December 2012, eligible former players were notified about a new, collectively bargained benefit that provides monthly financial support as well as reimbursement for up to $10,000 per year in out-of-pocket medical expenses for those with neuro-cognitive impairment. Details for qualifying are set forth in the NFL-NFLPA Collective Bargaining Agreement.

Healthy Body and Mind Cardiovascular and Prostate Health Research Awareness Program

Since 2008, more than 1,500 retired players have had free, state-of-the-art cardiovascular and prostate cancer screenings. Screening events are conducted in 10 cities annually, including at the Super Bowl and Hall of Fame events. These screenings include a mental health component through a partnership with the Morehouse School of Medicine, operated under the leadership of former Surgeon General Dr. David Satcher. Mental health professionals are available to meet with former players to discuss the challenges and demands of their off-the-field lives and provide them with advice and resources to better cope with life's stresses.

Screening events feature:

- Cardiovascular health screenings, including EKGs, echocardiograms, coronary calcium scoring and carotid scans
- Prostate cancer testing
- Informational sessions about brain health, including the signs and symptoms of declining cognitive function, what to do if there are concerns, and where to get help
- Mental health forums offering retired players and their significant others opportunities to ask questions and meet privately with trained professionals
- Referrals to health care professionals
- Information about NFL-provided resources and services

"I wouldn't be here today if it wasn't for that screening. It doesn't matter how healthy you are – knowing your risk factors, educating yourself about heart disease and getting regular screenings can save your life."

— Dick Butkus, Pro Football Hall of Fame member

SALUTE TO SERVICE: A PARTNERSHIP FOR THE BENEFIT OF ALL

The NFL has a five-decade long history of supporting the armed forces. The league's Salute to Service campaign unifies this work under one national initiative. A major part of Salute to Service is joint work between the NFL and the military on head injuries.

Between 2000 and 2012, more than 244,000 service members were diagnosed with a traumatic brain injury (TBI), while an additional 1.7 million people, including athletes of all ages in every sport, sustain a TBI every year in the United States. To address this public health issue, on August 29, 2012, the U.S. Army and the NFL announced a long-term initiative to enhance the health of soldiers and players through a focus on shared culture change, information exchange, education, and increased awareness of concussion-related issues that affect athletes, men and women in the armed forces, and the broader public.

This public-private partnership brings together the resources to research and develop the technology and equipment needed to better protect against brain injury, and provides an opportunity for the NFL and members of the armed forces to collaborate on changing their cultures to improve reporting of concussion symptoms.

The launch of the joint initiative was celebrated with new interactive websites at NFLEvolution.com/military and army.mil/tbi. Since the launch, the U.S. Army and the NFL have co-hosted forums that bring players and soldiers together at NFL team facilities and Army bases across the country to share learnings and experiences, to promote culture change in both organizations, and to discuss TBI and concussion awareness for athletes and service members. These events feature members of the armed forces, NFL team medical staff, and current and former players. For example, on May 14 the Carolina Panthers, in partnership with Lenovo and USO of North Carolina, held a culture change forum for nearly 100 Army and Air Force service members, Department of Defense civilians, and their families at Fort Bragg, N.C., one of the largest military bases in the world. The group discussed the cultural responses of the military and football to injury, specifically focusing on concussion awareness and diagnosis, return-to-play and return-to-action protocols, and other health topics. Prior to the forum, 225 local fifth grade students participated in an NFL PLAY 60 event with Panthers players and cheerleaders and Fort Bragg service members. Similar forums have been hosted by the Kansas City Chiefs, Cleveland Browns, Chicago Bears and Seattle Seahawks.

"You don't want to let the rest of your team down, but you have to realize that because you have that concussion, you are letting your team down by staying in the fight."

— **Coy Estes, U.S. Army Specialist**

"Anybody that's played [football] knows what a great game it is and what it provides for young people. What it provides for people like me is an opportunity to grow as a person. It's challenging, it's tough, it's hard. There's no game like football. It's the type of sport that brings out the best in you. It kind of shows you who you are. I think it's a huge part of our educational system in this country and it's going to be around for a long time."

— **John Harbaugh, Head Coach, Baltimore Ravens**

To further the sharing of medical research and information between the NFL and armed forces, the NFL invited three military experts, retired four-star General and U.S. Army Vice Chief of Staff Peter Chiarelli; Colonel Dallas Hack, Director, Combat Casualty Care Research Program, Chair, Joint Program Committee 6 (Combat Casualty Care), and U.S. Army Medical Research and Material Command, Ft Detrick, Md.; and Lieutenant Colonel Gerry York, Defense and Veterans Brain Injury Center Site Co-Director, to participate in the research advisory board of the GE-NFL Head Health Initiative, a four-year research program aimed at improving diagnosis, prevention and treatment for TBIs (see page 18).

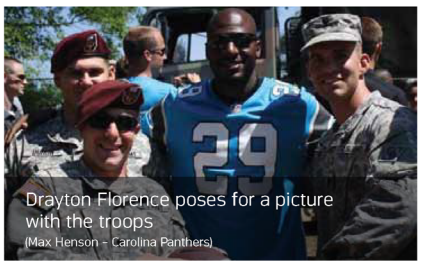
Together, the NFL and U.S. Army continue to work to improve education and awareness on the identification and treatment of head injuries among NFL players and service members for the benefit of all.

"I think the NFL and the Army have done an incredible job being at the forefront of this, and it's sort of helped kill the stigma that you're not tough if you don't carry on, if you don't continue."

— **Ryan Kalil, Carolina Panthers player**

The Panthers get set to attempt the leadership reaction courses
(Max Henson – Carolina Panthers)

Defensive tackle Frank Kearse leads a group of kids out of the tunnel
(Max Henson – Carolina Panthers)



Drayton Florence poses for a picture with the troops
(Max Henson – Carolina Panthers)

Former NFL player Herschel Walker has embarked on a tour of military bases to share his personal story of struggles with mental health, and encouraging 32,000 service members to share their struggles and ask for help. Walker has already completed more than 60 visits at home and abroad.

"To each his own I suppose but let me be real clear right from the start; if I had a son I would absolutely let him play the sport of football. In fact, I would highly encourage it if he were so inclined."

— **Ross Tucker, former NFL player**


ADVANCES
IN RESEARCH

THE GE-NFL HEAD HEALTH INITIATIVE

The NFL has focused on supporting efforts that accelerate progress and innovation. A new and exciting partnership was announced in March with the launch of the GE-NFL Head Health Initiative, a four-year, $60 million collaboration with GE and Under Armour to improve the health and safety of athletes, members of the military, and society overall through advances in concussion-related research. This joint initiative will accelerate the next generation of progress around brain injury diagnosis and treatment, aiding an estimated 1.7 million people in the United States who sustain a traumatic brain injury (TBI) each year.

The Head Health Initiative is comprised of two components:

- **A four-year, $40 million research and development program** between the NFL and GE, the world's leader in medical imaging, to evaluate and develop next-generation imaging technologies to improve diagnosis and allow for targeted therapy treatment for patients with TBI.
- **A two-year, $20 million open Head Health Challenge**, inviting scientists, researchers, entrepreneurs, academics and other experts to identify new and better ways to understand, diagnose and protect against brain injury.

In addition, the Army and the NCAA will join the NFL to help create game-changing solutions that transcend sports and reach across our society – from professional and recreational sports to the military. This work will benefit young athletes with next generation brain protection and assist our soldiers who will receive faster and more accurate diagnosis of their injuries.

Advancing Research to Map Brain Imaging Biomarkers

The four-year Head Health Initiative research program will take a whole-brain approach to determine the key magnetic resonance imaging (MRI) biomarkers for potential diagnosis, outcome prediction, and therapy management for patients with TBI. The research study will be guided by an independent advisory board consisting of a cross-disciplinary team of medical professionals from various academic, professional and military institutions.

"GE is a leader in developing sophisticated diagnostic imaging technology, but for all the advances in science our knowledge of the brain is far behind that of nearly every other organ in the body. With this initiative, we will advance our research and apply our learning to sports-related concussions, brain injuries suffered by members of the military and neurodegenerative diseases such as Alzheimer's and Parkinson's. Advancing brain science will help families everywhere."

— Jeff Immelt, GE Chairman and CEO

Chairman and CEO of General Electric Jeff Immelt, left, with NFL Commissioner Roger Goodell at the announcement of the GE-NFL Head Health Challenge (AP Photo/Seth Wenig)

Head Health Challenge: Two Challenges to Advance Science

From Charles Lindbergh's first non-stop flight across the Atlantic, to identifying a biomarker to measure the progression of Lou Gehrig's disease or ALS, prizes have been used as inspiration for great advancements in science and technology, answering critical needs of the time. The NFL, along with GE and Under Armour, is harnessing this approach to accelerate solutions for brain protection.

Through two innovation challenges over the course of two years, the organizations are pledging to find and fund ideas in critical areas:

- Challenge I: Methods for Diagnosis and Prognosis of Mild Traumatic Brain Injuries
- Challenge II: The Mechanics of Injury: Innovative Approaches For Preventing and Identifying Brain Injuries

Challenge I: Methods for Diagnosis and Prognosis of Mild Traumatic Brain Injuries

Challenge I focuses on technologies and imaging biomarkers to advance the detection and management of TBIs, addressing the current technical and scientific limitations in diagnosis of brain injuries, as well as assessment of long-term chronic impact.

This Challenge emphasizes a need for a better understanding of the molecular, physiological and behavioral/biomechanical changes that occur shortly after a traumatic event, and advancements needed in the ability to reliably diagnose brain injury. The ability to accurately diagnose should, in turn, lead to improvements in treatment. In addition to benefiting athletes who are dealing with brain injuries, this research will also aid members of the military and civilians with head trauma.

"We've never had a partnership that took a large issue in society and said we need faster advancement."

— Roger Goodell, NFL Commissioner

Focus areas for Challenge I include:

- Development and validation of imaging and/or sensor based biomarkers that can aid in the diagnosis and prognosis of mild traumatic brain injury events.
- Development of new technologies that are more sensitive to small contusions and injuries that are missed by current technologies; assessment of the long-term impact of these events.
- Improved algorithms for the quantification and visualization of markers of brain injury severity and longitudinal change.
- Algorithms and tools that link imaging data to clinical, cognitive and biomechanical data.
- Models of individual risk and long-term prognosis and clinical decision support tools using population studies.
- Robust methods for triaging acute-stage events and developing return-to-play guidelines using physiological, molecular, electrical or physical changes in brain or body functions.

Challenge I launched on March 13 and closed on July 15, with more than 400 submissions representing some of the top medical institutions from 27 countries around the world. Multiple cash awards with a cumulative total value of up to $10 million will be made, along with the possibility of future partnership and collaboration with GE.

Head Health Initiative Research Advisory Board

Dr. Thomas McAllister	Millennium Professor of Psychiatry and Neurology, Director of the Section of Neuropsychiatry and Vice Chair for Neuroscience Research for the Department of Psychiatry, Geisel School of Medicine at Dartmouth; Chair of the Department of Psychiatry and the Albert Eugene Sterne Professor of Clinical Psychiatry, Indiana University School of Medicine
Dr. Richard Ellenbogen	Theodore S. Roberts Endowed Professor, Chair of the Department of Neurological Surgery, University of Washington (UW); Co-Director of the Seattle Sports Concussion Program for Seattle Children's Hospital and UW; and Co-chair of the NFL Head, Neck and Spine Committee
Dr. Russell Lonser	Chair of The Ohio State University Wexner Medical Center Department of Neurological Surgery; Head of the Research Subcommittee of the NFLs Head, Neck and Spine Committee
Dr. Geoffrey Manley	Chief of Neurosurgery, San Francisco General Hospital; Professor and Vice Chairman, Neurosurgery, Co-Director Brain and Spinal Injury Center, University of California, San Francisco
Dr. Pratik Mukherjee	Attending Neuroradiologist and Associate Professor of Radiology and Biomedical Imaging, Bioengineering and Therapeutic, University of California, San Francisco
Lt. Col. Gerald York	Active Duty radiologist, Certificate of Added Qualification in Neuroradiology, Brooke Army Medical Center, Houston, Texas
Col. Jamie Grimes	National Director, Defense and Veterans Brain Injury Center
Dr. Larry Leverenz	Clinical Professor, Department of Health and Kinesiology, Director of Athletic Training Education, Purdue University
Dr. Teena Shetty	Neurologist, Hospital for Special Surgery
Dr. Brian Hainline	Chief Medical Officer, NCAA

THE GE-NFL HEAD HEALTH INITIATIVE

Proposals will be evaluated based on:

1. Potential to improve the diagnosis or prognosis of TBI.
2. Appropriate technologies, such as portable technology for proposals to aid in diagnosing brain injury on a playing field or sideline, or improvements in brain scanning technology for hospitals or doctors' offices.
3. Technologies that can demonstrate proof of concept within 1-2 years are preferred. However, game changing technologies will be strongly considered if good progress towards proof of concept and utility can be shown within 1-2 years.

Winning submissions will be announced in February 2014 after review by a panel of external judges that includes leading experts in brain health research, imaging technologies, and advocates for advances in brain research. Challenge I judges include:

Dr. William J Heetderks	Director of Extramural Science Programs, National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health
Dr. Walter Koroshetz	Deputy Director, National Institute of Neurological Disorders and Stroke, National Institutes of Health
General Peter Chiarelli	Chief Executive Officer, One Mind for Research; Retired four-star General with 40 years of experience with the U.S. Army and Department of Defense
Colonel Dallas Hack	Director, Combat Casualty Care Research Program; Chair, Joint Program Committee 6 (Combat Casualty Care), U.S. Army Medical Research and Material Command, Ft Detrick, Maryland
Dr. Geoff Manley	Chief of Neurosurgery, San Francisco General Hospital; Professor and Vice Chairman, Neurosurgery, Co-Director Brain and Spinal Injury Center, University of California, San Francisco

Challenge II: The Mechanics of Injury: Innovative Approaches for Preventing and Identifying Brain Injuries

Launching in the fall of 2013 and supported by the NFL, GE and Under Armour, Challenge II will invite proposals to advance the state-of-the-art for preventing and detecting TBIs, specifically new materials and technologies that can better protect the brain from injury, and innovative approaches for tracking head impacts in real time.

Challenge II features dual goals of preventing injuries by reducing impact forces transmitted to the brain, and providing a better understanding of the relationships between physiological biomarkers, mechanical factors responsible for brain injuries, and advanced brain imaging markers.

Focus areas for Challenge II include:

- **Protection Against Injury**
  - Materials or devices that can distribute the force of impact, including smart materials or active polymers that are comfortable but can adapt to sudden impacts are highly desirable.
  - Systems to predict and initiate protective responses to prevent injury, including systems that activate adaptive padding at the focus of impact.
- **Monitoring and Identifying Injury**
  - Systems that monitor and integrate directional and rotational impact forces with imaging/diagnostic equipment.
  - Sensors to provide biofeedback to modify behaviors that predispose athletes to injury.
  - Systems that monitor biomechanical and physiological responses to detect injury.
  - Systems to efficiently collect, interpret and organize large quantities of real-time data.

Regular updates for both Challenges are available through the Head Health Challenge website, NFLGEBrainChallenge.com, which features additional information and background on the challenge questions and criteria, how to submit a response, program updates, and resources for challenge participants including a forum to pose questions to a dedicated initiative support team. In addition, a webinar was hosted on May 22, dedicated to providing background information on Challenge I, answering potential participants' questions, and ensuring participants are aware of all resources, rules and guidelines for participation. Interested parties can also sign up for email updates to learn more about future opportunities to engage with the support team.

Through this unprecedented partnership, GE's cutting-edge technology and expertise in health care meets the NFL's visibility and drive to, above all, protect and improve player health, leading to advancements in neurological care that benefit all.

RESEARCH UPDATE

Study: Traumatic Brain Injury Does Not Increase Risk of Dementia

The *Journal of Neurology, Neurosurgery and Psychiatry* published a November 2012 study by the Icahn School of Medicine at Mount Sinai, which showed that a history of traumatic brain injuries with loss of consciousness is not associated with an increased risk for developing dementia or Alzheimer's Disease. First study author Kristen Dams-O'Connor, assistant professor of rehabilitation medicine at Icahn, noted there is conflicting information in current literature regarding the link between TBI and dementia, with this study challenging the belief that TBI leads to dementia.

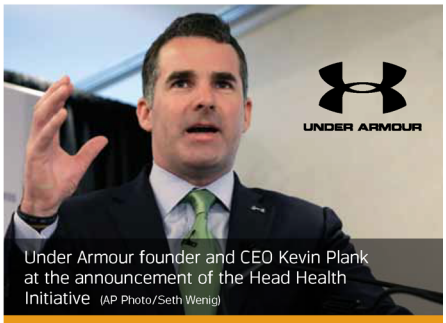
RESEARCH UPDATE

Study Reports Signs of CTE in Living Athletes

A study published in *The American Journal of Geriatric Psychiatry* by UCLA's Semel Institute for Neuroscience and Human Behavior and the NorthShore Neurological Institute reported signs of chronic traumatic encephalopathy (CTE) in five living former NFL players. Investigators noted that additional research with a larger sample size is needed in order to validate the study's findings. However, this research could provide a breakthrough in CTE, which is currently only diagnosed after death.

"Traumatic brain injury is one of the greatest unmet medical needs of our time. Every 20 seconds someone in the United States sustains a brain injury. A better understanding of the molecular, physiological, and behavioral/ biomechanical changes that occur shortly after a traumatic event is needed to reliably diagnose the types of changes that are difficult to identify using current technologies."

— **Dr. Geoff Manley, Chief of Neurosurgery, San Francisco General Hospital; Professor and Vice Chairman, Neurosurgery, Co-Director Brain and Spinal Injury Center, University of California, San Francisco**



Under Armour founder and CEO Kevin Plank at the announcement of the Head Health Initiative (AP Photo/Seth Wenig)

"As longstanding partners of the NFL, we recognize the magnitude of this initiative, and the impact it will have for athletes at all levels. Under Armour was founded upon the pillar of making all athletes better through the relentless pursuit of innovation. We take great pride in supporting this effort to reward new ideas and breakthrough concepts in this space, particularly as it applies to protecting athletes and influencing positive change in sports."

— **Kevin Plank, Founder and CEO of Under Armour**

NIH RESEARCH UPDATE

The NFL provides unrestricted grants to medical institutions in order to accelerate independent health and safety research. The single-largest donation in NFL history is a five-year, $30 million grant for the funding of medical research to the Foundation for the National Institutes of Health (FNIH), announced on September 20, 2012. The **Sports and Health Research Program (SHRP)** was formed through a public-private partnership of the National Institutes of Health (NIH), the FNIH and the NFL to administer the grant. Research supported through SHRP will focus initially on brain injury, especially in athletes and veterans, and will be conducted under the direction of the NIH, the nation's leading public medical research agency and one of the world's foremost medical research centers.

An initial focus of the SHRP research agenda was shaped through the Neuropathology of Chronic Traumatic Encephalopathy Workshop in December 2012, hosted by the NIH National Institute of Neurological Disorders and Stroke (NINDS). The Workshop focused on identifying what is known about the neuropathology of chronic traumatic encephalopathy (CTE), and what research strategies and resources are needed to fill critical gaps in knowledge.

The two-day workshop was attended by 60 experts in neurodegenerative disease, as well as representatives from military and sports organizations. The resulting NIH-published report laid the groundwork for the development of a five-year research plan by establishing what is currently known about CTE and its symptoms; identifying promising imaging tools and biomarkers; examining who is at risk for CTE; identifying how challenges to neuropathology research on the brain can be met; and developing key research questions to inform next steps.

Based on the workshop findings, SHRP has initiated the research funding process by issuing three funding opportunity announcements through NIH.

RESEARCH UPDATE

Neck Strength Linked to Concussion Risk

A pilot study conducted at the Colorado School of Public Health found that overall neck strength is a statistically significant predictor of concussion risk. The study found that for every one-pound increase in neck strength, concussion risk fell by 5 percent. Researcher Dawn Comstock has submitted this study for peer-review.

"We are encouraged by the momentum the SHRP team is building in such a short time with the announcement of these pioneering new research initiatives. Thanks to the generosity of the NFL, the program will provide us with invaluable data and ultimately ways to prevent and treat injuries in ways that will benefit athletes and non-athletes alike."

— **Maria Freire, Ph.D., President, Foundation for the National Institutes of Health**

Challenges and Key Questions:

- Brains studied to date have come from a narrow population of mostly professional athletes, resulting in a lack of data regarding the frequency of CTE. What are the population prevalence and incidence of CTE, and are there genetic susceptibilities to CTE?
- A large study of many persons who were exposed to repetitive head injury but have died for other reasons would expand knowledge of CTE. What is the best way to recruit brain donors with histories of repeated head injury while ensuring standard protocols for harvesting and preserving tissue samples are followed?
- What is the number of impacts to the head and the related magnitude that cause CTE?
- Current imaging technology is a major challenge in understanding CTE as the pathology can only be observed through post-mortem examination and cannot currently be detected through traditional MRI or PET scans. How can CTE be diagnosed in living people?
- What neuroimaging tools and biomarkers show promise in diagnosing CTE and providing information about the disease processes and progression?

Collaborative Research on Chronic Traumatic Encephalopathy and Delayed Effects of Traumatic Brain Injury: Neuropathology and Neuroimaging Correlation

Grants will be used to fund comprehensive studies of the effects of TBI in individuals exposed to repetitive head injury, as well as individuals who have died after repetitive TBI. One goal of this research will be to develop diagnostic tests that can be used in the general population.

This SHRP research initiative will investigate the neuropathology of CTE and the delayed effects of TBI. As part of this effort, grants will be used to support a multi-center team of neuropathologists, neurologists, neuroradiologists and other scientific experts to increase our understanding of CTE and other delayed effects of physical trauma to the brain, as well as the development of improved diagnostic tools that can be used in the general population. Comprehensive studies of the effects of TBI in individuals exposed to repetitive head injury, as well as individuals who have died after repetitive TBI, will be conducted.

Its main areas of research include:

- Developing a better understanding of how commonly CTE occurs in those exposed to a variety of head injuries.
- Development of neuroimaging or other tools that can diagnose the condition in living people, and can inform the relationship between clinical signs, symptoms and risk factors for post-traumatic neurodegeneration and CTE.
- Comparisons between repetitive traumatic events and single events.
- Characterizing the relationship of CTE with other neurodegenerative disorders such as Amyotrophic Lateral Sclerosis and Alzheimer's disease.

In addition, this research aims to establish a brain-donor program that will link high-quality behavioral information with neuropathology from an unbiased sample and distribute biospecimens and other relevant information to qualified investigators, thereby promoting data and tissue sharing to maximize the value of the brain donation.

Pilot Projects on Sports-Related Brain and Spinal Cord Injury

The second research initiative includes two funding opportunities – one for exploratory, novel studies and another funding opportunity for pilot or feasibility studies. This initiative will support pilot projects on sports-related TBI and spinal cord injury and explore new research directions to address the many gaps in knowledge that exist about these conditions. The program will provide support through small grants and larger exploratory/developmental grants for research on such topics as:

- Mechanical and biological mechanisms of injury and recovery.
- Genetic and environmental risk factors.
- Development of age-appropriate diagnostics and equipment for prevention.
- Ways that pain medications, psychiatric medications and other substances may interact with the effects of trauma.
- Preclinical therapy development for improving outcomes.

These announcements were available through the SHRP website on FNIH.org and widely advertised to the biomedical research community by NIH. More than 170 submissions were received during the open period of April-May 2013. NIH review of the applications for scientific merit began in August. The highest rated proposals will be presented to the Institute's advisory council in October with a goal of commencing research prior to the end of the year.

In the future, SHRP may expand to encompass other sports-related issues such as chronic degenerative joint disease, the transition from acute to chronic pain, sudden cardiac arrest in young athletes, and heat and hydration-related illness and injury.

"We are really excited about this partnership. I think [the NFL's] engagement and the potential future engagement of other sports organizations has the potential to produce great progress in our understanding of brain injuries in sports and outside of sports as well."

— **Story C. Landis, Director, National Institute of Neurological Disorders and Stroke**

CREATING A CONSENSUS IN SPORTS CONCUSSION MANAGEMENT

4th International Consensus Conference on Concussion in Sport

Collaboration among academic, medical and sports experts is key to advancing research and the management of concussions. In November 2012, various members of the NFL health and safety committees were invited to participate in the **4th International Consensus on Concussion in Sport (ICCS)** in Zurich, Switzerland. The conference, hosted by FIFA, is the preeminent international gathering of leaders in sports concussion, including medical experts and sports leagues from around the world.

Several of the experts in attendance who presented at the conference are members of the NFL's Head, Neck and Spine (HNS) Committee, including:

- **Dr. Richard Ellenbogen**, Co-Chair of the Committee
- **Dr. Margot Putkian**, Chair of the HNS Subcommittee on Return-to-Play Issues
- **Dr. Kevin Guskiewicz**, Chair of the HNS Subcommittee on Safety Equipment and Playing Rules
- **Dr. Stanley Herring**, Chair of the HNS Subcommittee on Advocacy and Education

Dr. John York, San Francisco 49ers Co-Chair and Chair of the NFL Owners' Committee on Health and Safety, represented the NFL. These participants shared updates on the NFL's commitment to player health and safety, including the impact of rule changes on head injuries, the NFL's approach to sideline evaluation, the role of procedures and policies in concussion diagnosis, and the NFL's efforts to help pass youth concussion legislation across the United States.

Dr. Herring moderated a panel discussion on whether youth athletes should participate in contact sports before a certain age, touching on key concepts from the **Heads Up Football** program, including the value of and need to teach proper fundamentals to parents, coaches and athletes, and educating coaches on effective concussion recognition and response.

RESEARCH UPDATE

AAN Concussion Guidelines Updates

In March 2013, the American Academy of Neurology (AAN) released an update to their 1997 guidelines for evaluating and managing athletes with concussion. Return-to-play guidelines were specifically cited among the important guidelines issued by AAN, with a recommendation that athletes with suspected concussion be immediately removed from play and not returned until they are evaluated by a licensed health care professional trained in concussions.

Recommendations and a consensus statement are developed in accordance with NIH standards following each ICCS. The consensus statement incorporates advances in understanding around concussion detection, prevention and treatment and provides guidance for athletes, coaches and physicians at all levels of sport on a number of topics, including the sideline evaluation of concussion, rule changes in sport, injury prevention through protective equipment, and chronic traumatic encephalopathy (CTE).

The consensus document is intended for use by physicians and health care professionals who care for athletes at the recreational and professional level, but has a much greater reach, impacting the policies of sports leagues around the globe and setting a standard for concussion management and care.

The full conference consensus statement and supporting materials, including a concussion recognition tool, sports concussion assessment tool and child concussion assessment card are available free online at: Concussion-In-Sport.com/2012.

"The Zurich panelists agreed that sports have made advancements in youth athlete player safety and that more work needs to be done. In football, it is essential to introduce proper tackling techniques early in a player's career and to avoid unnecessary head contact."

— **Dr. Stanley Herring, Chair, NFL HNS Subcommittee on Advocacy and Education**

ICCS Key Findings:

- The science of concussion is constantly evolving.
- Return-to-play (RTP) decisions remain in the realm of clinical judgment on an individual basis; there is no standard to follow beyond not allowing RTP on the day of the injury.
- Physical and cognitive rest is key to recovery.
- A progressive RTP protocol is recommended, with athletes advancing once they are asymptomatic at their current level.
- Children may take longer to recover than adults, and should not return to sports until they have successfully returned to school; in general, a conservative and cautious approach is recommended with concussion management for children.
- Pre-participation physicals allow for the collection of a detailed concussion history, which may help identify athletes who fit into a high-risk category and provide an opportunity to educate all athletes on concussion risk.
- A cause-and-effect relationship between CTE and concussions or exposure to contact sports has not yet been demonstrated, and the interpretation of causation in CTE case studies should proceed cautiously.
- Current science does not show current protective equipment will prevent concussion.
- Athletes, referees, administrators, parents, coaches and health care providers need to be educated about the serious nature of concussions, as well as concussion identification, management and return to play.

RESEARCH UPDATE

USA Football Studies Youth Player Health and Safety

In February 2012, USA Football commissioned Datalys Center for Sports Injury Research and Prevention to conduct an independent, scientific, two-year study of 10 youth football leagues in six states to examine player health and safety in organized youth tackle football. Preliminary results from the first year of the study found:

- More than 90 percent of the 1,913 youth players did not suffer an injury restricting participation.
- Fewer than 10 percent of players incurred an injury; of those, 64 percent were categorized as minor and athletes returned to play on the same day.
- Contusions were the most common injuries at 35 percent, followed by ligament sprains at 15 percent.
- Less than 4 percent of the youth players sustained a concussion.
- No catastrophic head, neck or heat-related injuries were reported.

The final study results will be released in 2014, with ongoing research planned for future years.

HEALTH AND SAFETY COMMITTEES: ADVANCING PLAYER SAFETY

NFL health and safety committees include independent experts from a variety of medical fields, as well as experts in the sport. The committees advance player health and safety by providing guidance to the NFL on its medical research process, including the review of medical grants; identifying priority areas for research, rules and more; analyzing injury data; and developing recommendations for new or updated safety rules, policies and procedures.

The committees provide feedback throughout the year to inform NFL practices. For example, with the increase in the number of Thursday night games in the 2012 season, there was a concern that players' recovery time would be limited, potentially increasing the risk of player injury. A review of the injury data showed no increase in risk of injury for games played on Thursday, with a rate of 5.2 injuries per game, as compared to Saturday, Sunday and Monday games with a rate of 5.3. The Competition Committee will continue to monitor this and other injury data relevant to NFL policies and safety rules.

Committee members also act as ambassadors for health and safety in sport through their participation in scientific meetings, conferences and other public events where they share updates on research, educating the public on best practices in sports safety, especially in the diagnosis and management of concussions, and addressing key questions regarding the risk and reward of sport. For example, in addition to participating in the 4th International Consensus on Concussion in Sport, Drs. Stanley Herring and Margot Putukian of the NFL Head, Neck and Spine Committee demonstrated the NFL's sideline concussion protocol to the media during the 2013 NFL Combine. The public demonstration of the protocol used to assist in the diagnosis of players who may have sustained head injuries allowed members of the media to see the protocol in action and ask questions about NFL sideline concussion management.

In 2013, there were several additions to the NFL Competition Committee, which studies all aspects of the game and recommends rules and policy changes to NFL clubs. Pittsburgh Steelers coach Mike Tomlin was named to the committee while four coaches were named to the Coaches' Subcommittee - Minnesota's Leslie Frazier, Miami's Joe Philbin, Carolina's Ron Rivera and Atlanta's Mike Smith.

Recent Additions to the NFL Competition Committee and Coaches' Subcommittee

Leslie Frazier
Vikings Head Coach

Joe Philbin
Dolphins Head Coach

Ron Rivera
Panthers Head Coach

Mike Smith
Falcons Head Coach

Mike Tomlin
Steelers Head Coach

Sports writer Peter King joins Seattle Seahawks' team physician Stanley Herring, M.D., and Princeton University team physician Margot Putukian, M.D., who are both members of the NFL Head, Neck and Spine Committee, for a discussion and demonstration at the 2013 NFL Scouting Combine in Indianapolis, on February 22, 2013 (AP Photo/Johnny Vy)

RESEARCH UPDATE

NFL Medical Research Grant Recipient Shares Progress

Dr. Mayland Chang, faculty member at the University of Notre Dame's Department of Chemistry and Biochemistry and recipient of a 2010 medical research grant from the NFL, is studying an enzyme inhibitor which she hopes can one day provide a treatment to those who suffer a severe traumatic brain injury (TBI).

Dr. Chang is studying the potential for an enzyme-inhibiting compound that can intervene and prevent secondary injury in which a cascade of biochemical events cause cell death in the hours and days following a TBI. Through her research, Dr. Chang hopes to find a way to prevent or decrease the secondary injury to the brain following a TBI.

While the complete results of the study are not yet available, Dr. Chang's preliminary data on animals show that the compound successfully delivers the enzyme inhibitor to the brain.

Dr. Chang's work was inspired by TBIs of two members of her family, including her son, who sustained a concussion while snowboarding.

YOUTH
EDUCATION
AND
OUTREACH

SHARING HEALTH AND SAFETY INFORMATION WITH PARENTS

The NFL has a tradition of leadership in sports to promote safe and fair play at all levels. Youth outreach and education continue to be a focal point for NFL health and safety efforts.

Since the Fall 2012 Health & Safety Report, the NFL has promoted health and safety in youth sports with parents, coaches and youth players across the United States. Ongoing Fan Forums have provided an opportunity for those involved in youth football to learn more about health and safety, culminating in the ultimate fan event, NFL Experience at Super Bowl XLVII in New Orleans. Fans participated in an interactive NFL Health and Safety exhibit that highlighted the league's work on advocacy, safety rules, research and equipment; got a first-hand look at examples of the protective knee and thigh pads that will be mandatory for all NFL players starting in the 2013 season; and learned about the importance of proper helmet fitting through demonstrations and fitting sessions from Riddell and Rawlings. Younger fans were invited to participate in NFL PLAY 60 clinics providing key health and safety information on heat and hydration, and concussion awareness and management.

"So we hope people have an accurate understanding of what we generally believe the risks to be, but certainly some people may be overly concerned and that may be because of some of the things that I have said. I'll accept that because I think people are dramatically safer playing football now than they were five years ago. I think Dr. Batjer and the other doctors of the NFL on the new committee are doing a great job and have moved the pendulum very far in terms of safety. I'll accept a little alarmism for safety."

— **Chris Nowinski, Co-Director, Center for the Study of Traumatic Encephalopathy, Boston University School of Medicine; Co-Founder and President, Sports Legacy Institute**

Children enjoy the interactive displays during the NFL Experience on Jan. 30, 2013, in New Orleans (AP Photo/Doug Benc)

NFL Blogger Event

The NFL has also connected with parents and coaches of youth sports through social media. During the last year, the NFL hosted three health and safety roundtable events at league headquarters, aimed at reaching parenting writers and bloggers with important information on many topics pertaining to youth sports safety. More than 40 writers attended each event, where they heard from speakers – including NFL Commissioner Roger Goodell, USA Football Executive Director Scott Hallenbeck, representatives from the Centers for Disease Control and Prevention (CDC), and neuropsychologists – on issues ranging from signs and symptoms of concussion to the proven value of sports participation.

Recent Events and Highlights

In support of **Brain Injury Awareness Month**, the NFL co-hosted a Twitter chat with the Centers for Disease Control and Prevention, USA Football, and the National Parent Teacher Association (PTA) on March 25. Parents, educators, coaches and medical professionals from across the country participated in the digital conversation, posing questions to experts representing the co-hosts. The conversation, tracked with the usage of #BrainInjury, was a trending topic on Twitter during the chat.

On June 11, nine national youth sports organizations – **US Soccer, USA Hockey, USA Football, USA Basketball, US Lacrosse, Little League Baseball, USA Gymnastics, USA Cheer and the National Federation of State High School Associations** – were invited to NFL's headquarters to participate in a roundtable discussion about youth sports safety. Bloggers from more than 30 outlets were also invited. Participants shared details about initiatives to enhance youth sports safety and discussed opportunities to improve communication across leagues to address youth sports health issues.

On June 21, the NFL participated in the **National Parent Teacher Association (PTA) annual convention** in Cincinnati, Ohio. During a panel discussion titled, "Health and Safety for a New Generation," NFL Commissioner Roger Goodell joined Betsy Landers, former National PTA President; Elizabeth Pieroth, Psy.D., ABPP, Head Injury Consultant, Chicago Bears and Neuropsychologist, NorthShore University HealthSystem and USA Football Heads Up Football Advisory Committee Member; and LaVar Arrington, former NFL linebacker and current USA Football Heads Up Football Ambassador and Advisory Committee Member. The panelists discussed the important role parents play in making decisions about their children's recreational activities, the rewards of sports participation, and the lessons of team sports participation.

As part of the event, the NFL and PTA announced a partnership on youth health and fitness, launching nationwide this fall. The **"Back to Sports"** initiative will help PTA leaders across the country educate their communities on youth wellness – from concussion education to NFL PLAY 60 tips to staying active. Local PTAs will plan **"Back to Sports Nights,"** engaging parents and community leaders on ways to help their kids stay safer and healthier as they head back to the sports field this fall.

The "Back to Sports" initiative marks the first time the National PTA has partnered with a sports organization, and Commissioner Goodell's appearance at the PTA Convention is the first time a sports commissioner has addressed PTA constituents at the event.

Commissioner Goodell and Ohio State Head Football Coach Urban Meyer hosted more than 500 Ohio mothers at the first-ever **OSU-NFL Moms Football Safety Clinic**. This free event emphasized player health and safety – including education on proper equipment fitting, concussion awareness, heat and hydration, and proper tackling technique. The three-hour clinic included a town hall, providing participants an opportunity to ask Commissioner Goodell and Coach Meyer questions.

This summer, Dallas Cowboys Executive Vice President and Chief Brand Officer Charlotte Jones Anderson, who also serves as chairman of the NFL Foundation, addressed bloggers on youth sports safety at the annual BlogHer convention, a large-scale gathering of bloggers, which draws more than 5,000 attendees annually. This year's **BlogHer** was held in Chicago and Anderson spoke with the group not only as a football executive and chairman of the foundation, but also as a parent whose children participate in sports. As part of the panel, Anderson was joined by Dr. Pieroth and bloggers who cover parenting issues.

Through events like these, and ongoing outreach, the NFL will continue to involve parents in the conversation about health and safety at all levels of the game and across all sports.

CONCUSSION LEGISLATION: PROTECTING YOUTH ATHLETES AROUND THE COUNTRY

The NFL has nearly achieved its goal of the passage of a Lystedt or similar law in all 50 states. An additional eight states have passed concussion legislation since the Fall 2012 Health & Safety Report, bringing the national total to 48. Zackery Lystedt is a young man from the state of Washington who suffered a significant brain injury when he returned to play in a middle school football game after sustaining a concussion. Zackery, his family and a broad range of medical, business and community partners lobbied the Washington state legislature for a law to protect young athletes in all sports from returning to play too soon.

"When we watch an NFL game, we see it so differently from others. The penalties you don't like or the score you aren't happy with are so insignificant. We know how impressionable the game is on our youth and are so proud of the NFL's push for safety and the concern for its players."

— Victor Lystedt, Zackery's father

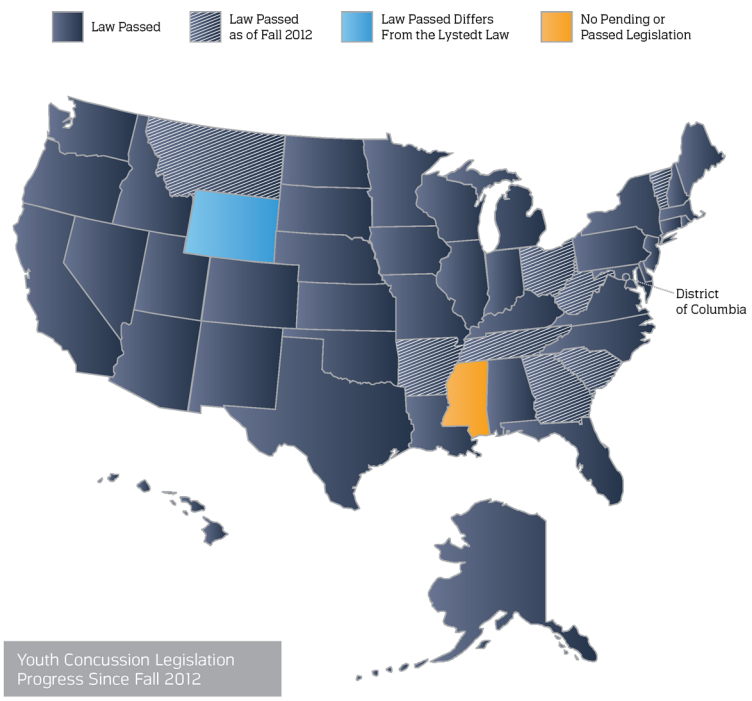
These laws protect young athletes from returning to play too soon through three essential elements:

- Athletes, parents and coaches must be educated about the dangers of concussions each year.
- If a young athlete is suspected of having a concussion, he/she must be removed from a game or practice and not be permitted to return to play. **When in doubt, sit them out.**
- A licensed health care professional must clear the young athlete to return to play in the subsequent days or weeks.

In March, the CDC published two reports looking at return to play laws. **Get a Heads Up on Concussion in Sports Policies** provides important information for parents, coaches and school and sports officials about taking concussions seriously, and on laws about concussion in sports. The report outlines the three essential elements of the Lystedt Law and summarizes some of the additional policies schools and sports leagues around the nation have included in their concussion management plans such as:

- Creating a concussion emergency medical action plan.
- Limiting contact during sports practices.
- Enacting rule changes including banning or limiting drills or techniques that may increase risk of injury.
- Checking sports equipment often to make sure it is in good condition and fits athletes properly.
- Focusing on education for parents, coaches and athletes through posted information and regular training sessions.

The NFL will continue to work to raise awareness about the importance of adopting return to play laws until all children in the United States are protected, and the pledge that Commissioner Goodell made after meeting the Lystedt family in October 2010 is fulfilled.



Implementing Return to Play: Learning from the Experiences of Early Adopters was also released in March 2013 by the CDC. The National Center for Injury Prevention and Control assesses the implementation of two of the earliest return to play laws, in Washington and Massachusetts, through a case study evaluation. The report provides an analysis of implementation challenges and successes, noting education and outreach as key components to execution, specifically when targeted to key groups including parents, referees, league coaches and health care professionals.

Both reports can be downloaded for free from: cdc.gov/concussion/policies.html.

HEADS UP FOOTBALL: TAKING THE HEAD OUT OF THE GAME

The NFL joined forces with USA Football, the sport's national governing body and the official youth football development partner of the NFL, to develop a comprehensive, national program designed to make football a better and safer experience for all youth, high school and other amateur players. **Heads Up Football** was officially launched on April 24, 2013, by NFL Commissioner Roger Goodell, NFL Foundation Chairman and Dallas Cowboys Executive Vice President Charlotte Jones Anderson, and USA Football Executive Director Scott Hallenbeck.

The educational outreach program, funded by a $1.5 million grant from the NFL Foundation, strives to improve player safety at the youth level by focusing on proper tackling technique and taking the head out of the game. Heads Up Football represents a key initiative between the NFL and USA Football that will improve the health and safety of sports and youth football through education.

"The culture of youth football is changing in a positive direction – as it must. There is greater awareness of the risks of brain injuries and greater attention to reducing those risks by teaching safer and smarter play. I applaud Commissioner Goodell, the NFL and USA Football for accelerating this effort, and I commend the coaches involved in teaching Heads Up Football to players across the country."

— **Inez Tenenbaum, Chairman, U.S. Consumer Product Safety Commission**

"What we expect long-term is to actually change the culture of the sport. Parents are coming to us already who have experienced Heads Up Football and they're saying, 'Thank you. You're making me feel more comfortable.'"

— **Scott Hallenbeck, Executive Director, USA Football**

Launch of Heads Up Football at the NFL Draft (Alix Drawec/NFL)

Heads Up Football is comprised of five primary elements:

Heads Up Tackling	USA Football's Heads Up Tackling Technique, endorsed by medical and football experts, teaches players to keep their heads up and out of the line of contact.
Coaching Certification	All participating coaches are trained to teach the game's fundamentals by completing USA Football's nationally accredited Level 1 Coaching Certification Course. *These are the highest national coaching standards for youth football.*
Concussion Recognition and Response	Coaches learn and are assessed on the Centers for Disease Control and Prevention (CDC) concussion recognition and response protocols through USA Football's Level 1 Coaching Certification Course. Coaches, parents and players are taught concussion-related protocols at the start of the season at a league-wide clinic. These protocols are reinforced throughout the season by the Player Safety Coach, who will monitor their league's practices and games in addition to using on-site clinics and mentoring.
Player Safety Coach	Appointed by each participating Heads Up Football youth organization, this individual is trained by USA Football to implement Heads Up Football's player safety protocols, including coaching certification. Player Safety Coaches also conduct safety clinics for coaches, parents and players.
Equipment Fitting	Coaches, parents and players are taught proper helmet and shoulder pad fitting.

In 2013, all Heads Up Football leagues in underserved communities will be eligible to participate in a helmet refurbishment program, which will recondition and provide new helmets for youth leagues at no cost. This initiative represents a continuation of the helmet replacement program launched in 2012 by the NFL and a host of partners, including the U.S. Consumer Product Safety Commission.

Heads Up Football Advisory Committee

Heads Up Football is guided by an advisory committee of 22 youth football experts, current and former coaches from all levels, retired NFL players, educators, medical professionals and parents of football players. The committee will provide feedback and direction on further development of the Heads Up Football program.

Members of the Heads Up Football Advisory Committee gathered with representatives from USA Football and the NFL at NFL headquarters in New York City on May 30. During the meeting, Advisory Committee members discussed how members of the football community – parents, coaches, commissioners, current and former NFL players and coaches, medical professionals, and others – can advance player health and safety in youth football. The committee provided feedback on the Heads Up Football initiative and discussed how to extend the program to all 10,000 youth tackle football leagues across the country. They also provided feedback on best practices for communicating to parents and players the importance of coaching certification, proper equipment fitting and using the appropriate techniques to take the head out of the game.

Members of the Advisory Committee, representing a diverse range of backgrounds and expertise, include:

- LaVar Arrington, Former NFL player
- Trish Arrington, Wife of former NFL player, mother of youth football players
- Dr. Mitchell Berger, President, American Association of Neurological Surgeons; Member, NFL Head, Neck and Spine Committee
- Cris Collinsworth, Former NFL player; NBC Sports football analyst
- Bill Cowher, Former NFL player and head coach; CBS Sports football analyst
- Brett Favre, Former NFL player; high school football coach
- Whoopi Goldberg, Actress, comedian, singer-songwriter, author, talk show host
- Christine Golic, Mother of two football players; wife of former NFL player

- Catherine Graves, Team Mom, Severna Park (Maryland) Green Hornets Football
- Merril Hoge, Former NFL player; former youth coach; ESPN football analyst
- Leroy Hollins, Youth football commissioner, Louisiana Youth Football League
- Chuck Kyle, Head football coach, Cleveland St. Ignatius High School
- Marvin Lewis, Head coach, Cincinnati Bengals
- Diane Long, Lawyer, author, wife of former NFL player, mother of two current NFL players
- Howie Long, Pro Football Hall of Fame member; father of two current NFL players
- Dr. Elizabeth Pieroth, Psy.D., ABPP, Head Injury Consultant, Chicago Bears; Neuropsychologist, NorthShore University HealthSystem
- Liz Raeburn, Teacher; wife of college football head coach
- Amanda Rodriguez, Blogger
- Erin Zammett Ruddy, Magazine writer and blogger
- Barry Sanders, Pro Football Hall of Fame member
- Deion Sanders, Pro Football Hall of Fame member; NFL Network analyst
- Michael Strahan, Former NFL player; co-host "Live with Kelly and Michael"
- Otha Thornton, President, National Parent Teacher Association

Master Trainers and Player Safety Coaches

An integral element of Heads Up Football is its network of coaches, starting with its **Master Trainers**, who instruct youth football league-appointed **Player Safety Coaches**, who in turn implement the Heads Up Football program. In addition to ensuring league-wide completion of the Level 1 Coach Certification Course, Player Safety Coaches conduct Heads Up Football Coaches Clinics and a Heads Up Safety Clinic for parents and players within each league. Throughout the season, Player Safety Coaches monitor their league's practices and games, and work alongside league commissioners, coaches, parents and players to implement the protocols of Heads Up Football.

USA Football conducted its first Master Trainer workshop in Indianapolis in March, instructing 21 of the top high school football coaches in the nation, as well as former NFL and college players, on the proper elements of the Heads Up Football program.

"You need to get the new [coaches] coming in to really focus on what's important. It's safety No.1. You have to talk to the older coaches and say, 'This is how it used to be done.' … We have to change, and we have to focus on safety."

— **Buddy Curry, Heads Up Football Master Trainer and former NFL player**

Charlotte Jones Anderson speaking at Heads Up Football launch
(AP Photo/Alix Drawec)

Q&A with Charlotte Jones Anderson, NFL Foundation Chairman

Why is the NFL Foundation supporting Heads Up Football?

The mission of the NFL Foundation states that we are dedicated to improving the health and safety of sports and youth football. Heads Up Football will help us to fulfill that mission. The NFL Foundation and USA Football are collaborating to educate parents and coaches on ways to keep our young players safe. Through Heads Up Football, coaches are required to complete a certification course which teaches proper fundamentals and tackling techniques. Parents and coaches also learn how to ensure players are wearing properly fitted equipment to keep our youth safe.

As a parent who also knows a lot about football, why do you think Heads Up Football is important?

As a parent, I believe it is important for children to learn the correct and safe way to play football. Parents of children who are participating in Heads Up Football will be encouraged knowing that their child will be taught by certified coaches who understand the proper fundamentals of the game and make safety their highest priority.

What benefits do you think children get from playing sports?

I have seen first-hand the benefits of my children participating in sports. They include leadership skills, the value of hard work, the importance of teamwork and being active while building self-confidence. Most importantly, though, they have fun building relationships with their teammates.

Heads Up Football Master Trainers include:

Chuck Kyle, head coach, Cleveland St. Ignatius High School; winner of 11 Ohio Division I state titles and three USA Today national championships

John Roderique, head coach, Webb City High School; winner of eight Missouri state high school championships; former assistant coach, NCAA Division II national champion Pittsburgh State University (1991)

Steve Specht, head coach, Cincinnati St. Xavier High School; winner of two Ohio Division I state titles; 2012 Don Shula NFL High School Coach of the Year Award winner

Buddy Curry, veteran youth football coach; former Atlanta Falcons linebacker and 1980 Co-NFL Defensive Rookie of the Year

Ambassadors to Safety

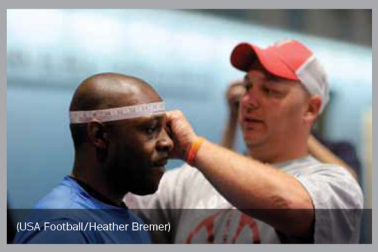
Heads Up Football has provided former NFL players an opportunity to enhance player safety in their own communities. One hundred former NFL players, including Randall Cunningham, LaVar Arrington, and Michael Strahan, will play an integral role in the success of the program as **Heads Up Football Ambassadors**. On May 16, more than 50 former NFL players convened in Indianapolis to kick off the ambassador initiative, participating in a Heads Up Football training session led by Dr. Patrick Kersey, USA Football's medical director, who demonstrated key elements of concussion recognition and response. The ambassadors also learned Heads Up Tackling techniques for better and safer tackling, and the proper way to fit protective equipment.

These ambassadors serve as the public face of Heads Up Football, working alongside leagues as mentors, attending practices and games, helping to implement the principles of Heads Up Football, and encouraging adoption of the program across the country. Ambassadors will use their unique perspective as former players and role as community leaders to advocate the goals of Heads Up Football.

"The National Football League understands the popularity of its sport and has accepted this as a social responsibility to take on the difficult topics of total health and safety…the bottom line is that in addition to all of the incredible work that the NFL and USA Football are doing with regards to youth health and safety, parent and player involvement is vital to the reduction of concussions."

— **Jessica Cohen, Blogger, FoundTheMarbles.com**

Helmet Measuring and Fitting Demonstration



(USA Football/Heather Bremer)

(USA Football/Heather Bremer)

Heads Up Football Partners

Pop Warner, the country's longest-running youth football organization, has endorsed the Heads Up Football program. Pop Warner leagues began voluntary adoption of Heads Up Football this season, with all 1,300 Pop Warner leagues participating in Heads Up Football in 2014.

In advance of the 2014 season, all Pop Warner coaches in 43 states and five foreign countries will be trained in Heads Up Football principles. All Pop Warner head coaches and assistant coaches will complete USA Football's Level 1 Coaching Certification Course, which includes Heads Up Tackling techniques, concussion recognition and response protocols, and proper helmet and shoulder pad fitting.

More than 590,000 youth football players nationwide will benefit from their leagues' Heads Up Football participation this season.

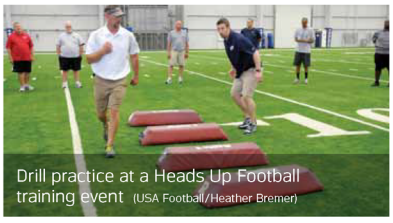
In addition to the NFL and NFL Foundation, organizations that support Heads Up Football include the NCAA, the Atlantic Coast Conference, the Big 12, Big Ten and Pac-12 Conferences, the National Federation of State High School Associations, the American Football Coaches Association and the Sports and Fitness Industry Association.

Spreading the Word about Heads Up Football

Engagement with media and the public represents a crucial piece to ensuring that Heads Up Football reaches youth players across the country. On January 16, the NFL and USA Football hosted more than 40 bloggers and writers focused on health and parenting issues at an open forum that allowed participants the opportunity to learn more about the program, its progress, and its plans for the future. Dr. Elizabeth Pieroth led the group in a discussion on youth sports safety, during which bloggers shared their feedback on implementing change in their communities; the need to have qualified medical personnel on the sidelines at youth sporting events; and the risk and reward of sports participation.

The NFL has further embraced the importance of expanding the reach of Heads Up Football through its official launch during the NFL Draft in April 2013. Using the high-profile media event of the NFL Draft as a vehicle to propel the Heads Up Football initiative to a new audience, the NFL Foundation and USA Football were able to successfully spread their message of ushering forth the evolution of the sport by protecting the youngest players. The goals of the program and information on how to get involved were also shared through a Facebook Q&A session with NFL Commissioner Roger Goodell, as well as in a recent appearance on "Live with Kelly and Michael" with NFL great Michael Strahan, where they discussed the national launch of Heads Up Football.

NFL clubs across the country have also hosted Youth Football forums in partnership with USA Football to support the implementation of Heads Up Football in their communities. The free events were open to youth football association presidents and commissioners, and provided an opportunity for attendees to share best practices, learn more about the latest in health and safety in sports including concussion legislation, and learn more about Heads Up Football.

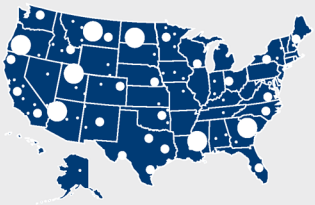


Drill practice at a Heads Up Football training event (USA Football/Heather Bremer)

Equipment fitting demonstration at a Heads Up Football training event (USA Football/Heather Bremer)

$1.5 million
grant from
NFL Foundation

2,700+ organizations



2013 Youth Summit Presentation
(Craig James Photography)

2013 Youth Summit Exercise
(USA Football/Heather Bremer)

2013 Youth Summit Meeting
(Craig James Photography)

At the 13th annual NFL Foundation-USA Football Youth Summit, attendees were trained in USA Football's Heads Up Football initiative, including 20 former NFL players serving as Heads Up Football Ambassadors and more than a dozen Player Safety Coaches from pilot Heads Up Football leagues around the country. In addition to Heads Up Football Ambassadors, a select group of coaches, including former NFL players now coaching high school and youth football, 30 delegates representing USA Football State Leadership Forums, and 92 other supporters of youth and high school football, including youth football commissioners and athletic directors from across the country attended the July event in Canton, Ohio.

NFL players will wear helmet stickers in support of the Heads Up Football program this preseason. Fans also will notice on-field stencils and banners in the end zones. NFL teams will hold youth football scrimmage games before kickoff or at halftime and will donate about 150,000 preseason tickets to players in leagues that use the program.

More than 2,700 youth football leagues across the United States, representing more than 590,000 players and 83,000 coaches, have adopted Heads Up Football. Heads Up Football will continue to work toward the goal of 10,000 youth leagues, improving the health and safety of youth players around the nation.

Following the 2013 season, USA Football will engage with youth league commissioners across the country at more than three dozen USA Football State Leadership Forums to discuss and evaluate the inaugural year of the Heads Up Football program and prepare to advance the health and safety of young football players through reaching even more youth leagues in 2014 and beyond.

More information, including how to join Heads Up Football, is available at USAFootball.com/HeadsUp.


2013
SAFETY
RULES
UPDATE

The rules of football evolve along with the game in an effort to promote better player safety. To this end, playing rules are reviewed annually by the Competition Committee, with guidance from the Player Safety Advisory Panel, the Owners' Committee on Health and Safety, the Head, Neck and Spine Committee, and other health and safety related NFL committees. Input is also solicited from the NFL Players Association, NFL players and coaches. This annual review by the Competition Committee identifies opportunities to further promote player health and safety through rule changes and special points of emphasis. For the 2013 season, several rule changes were approved that are expected to improve protection for both offensive and defensive players.

The following rule changes focusing on protecting player health and safety will be enacted for the 2013 season:

- The definition of "defenseless player" was expanded to include the offensive player who attempts a snap (long-snapper) during a field goal attempt or point after touchdown (PAT) and the player who receives a blindside block when the blocker is moving toward or parallel to his own end line and approaches the opponent from behind or from the side.
- During a punt, field-goal attempt, or a PAT kick, a defensive player who is within one yard of the line of scrimmage must have his entire body outside of the snapper's shoulder pads, in an effort to protect the defenseless long-snapper.
- During a field-goal attempt or a PAT kick, no more than six defensive players may be on the line of scrimmage on either side of the snapper at the snap.
- A player who is aligned in the tackle box when the ball is snapped cannot initiate contact on the side and below the waist against an opponent if: a) the blocker is moving towards his own end line; and b) he approaches the opponent from behind or from the side. This rule effectively makes a "peel back" block below the waist illegal in the tackle box (an area extending from tackle to tackle and from three yards beyond the line of scrimmage to the offensive team's end line).
- It is a foul if a runner or tackler initiates forcible contact by delivering a blow with the top/crown of his helmet against an opponent when both players are clearly outside the tackle box. Incidental contact by the helmet of a runner or tackler against an opponent would not be deemed a foul.

Mandatory Protective Equipment

Protective thigh and knee equipment usage will be mandatory for players beginning in 2013. The initiative was approved in 2012, and the league has coordinated with the NFL Players Association and equipment manufacturers to encourage the development of lighter, stronger and more comfortable thigh and knee pads. The use of protective thigh and knee equipment will be enforced just as the use of helmets or shoulder pads. Game day uniform inspectors evaluate each player and then work with designated team officials to ensure adjustments are made as needed. Players in violation during games are allowed an opportunity to make proper adjustments before penalties are assessed. Prior to the start of the 2013 season, each team's uniform inspector provided a presentation during training camp, league representatives toured the clubs to share information and players were provided details on approved protective equipment.

"All we're doing is re-introducing the core fundamentals that the game is built on. Now it's more important than ever to lead with your shoulder pads."

— Merril Hoge, former NFL player

A sample of the new thigh pads made mandatory equipment for the 2013 football season (AP Photo/David Goldman)

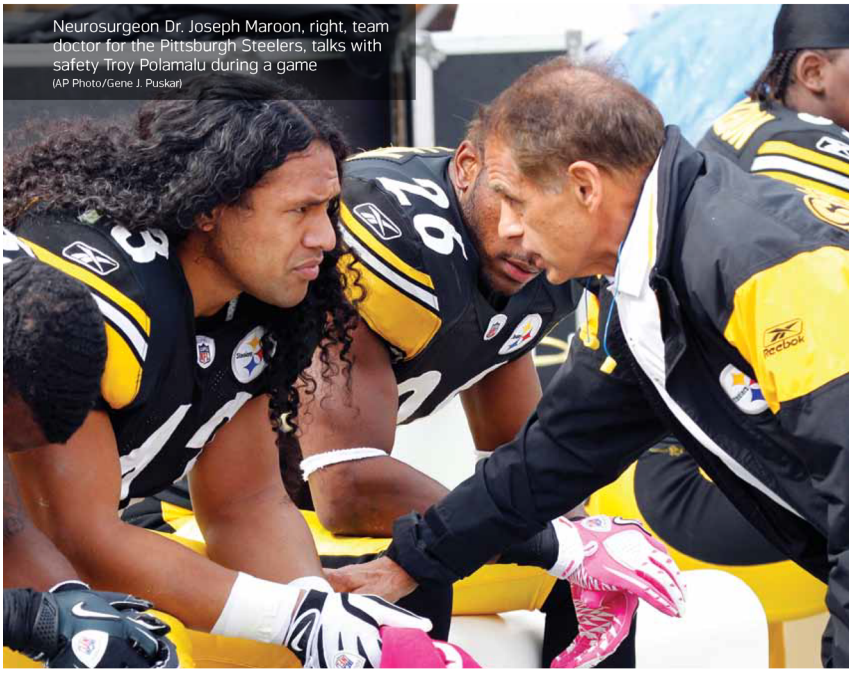
Sideline Evaluations

In addition to these new rules, the use of electronic tablets on the sidelines will be required by all clubs to assist team physicians with the diagnosis of concussions. During games, physicians will use an app to review a step-by-step checklist of protocols and the injured player's concussion baseline tests. The use of electronic tablets was made mandatory following a successful eight-team pilot program that was launched during the 2012 season. Throughout the 2013 season, the incorporation of player electronic medical records (EMRs) onto the electronic tablets will be piloted by eight teams — the Baltimore Ravens, Denver Broncos, Houston Texans, New England Patriots, New York Giants, New York Jets, Pittsburgh Steelers and San Francisco 49ers. This pilot test will allow team physicians to have a player's entire medical history, including X-rays, test results and exam notes, at quick reference if he is sidelined with an injury. EMRs on electronic tablets for sideline use could be rolled out league-wide based on the results of this pilot program.

Each team's medical staff this season will be augmented on the sidelines by an unaffiliated neuro-trauma consultant. These consultants will be available to assist team medical staffs in the diagnosis and management of suspected concussions or spine injuries during games.

"Rules make a difference. You can make a sport safer by making rules that make sense, make the game fun and interesting, and at the same time, lower the concussion rate."

— **Dr. Richard Ellenbogen, Co-Chair, NFL Head, Neck and Spine Committee**



Neurosurgeon Dr. Joseph Maroon, right, team doctor for the Pittsburgh Steelers, talks with safety Troy Polamalu during a game
(AP Photo/Gene J. Puskar)

TESTIMONY SUBMITTED BY THE

National Association of State Head Injury Administrators

to the

SENATE SPECIAL COMMITTEE ON AGING

"State of Play: Brain Injuries and Diseases of Aging"

June 25, 2014

On behalf of the National Association of State Head Injury Administrators (NASHIA), thank you for the opportunity to submit testimony regarding issues affecting individuals who are aging with a traumatic brain injury (TBI) as the result of a sports-related injury. We welcome the discussion on the long-term consequences of TBI that may affect an individual's ability to lead an independent, productive life, as well as the impact on the family who is usually the caregiver. NASHIA is a non-profit organization representing and assisting state governmental officials who administer an array of short-term and long-term rehabilitation and community services and supports for individuals with TBI and their families.

As sports- related injuries (concussions) are a contributing factor to TBI, all 50 states and the District of Columbia have enacted legislation calling for schools to develop "return to play" guidelines with regard to student athletes to prevent further injury. Most state laws include provisions for education and training for coaches and athletic trainers, as well as information for parents. Many states use materials (Heads Up) developed by the Centers for Disease Control and Prevention's National Injury Center, which has been a leader in developing resources for states and school districts. Two states this spring enacted additional legislation to address "return to learn" guidelines in recognition that sports-related concussions may impact a student's cognitive, emotional and behavioral functioning affecting academic performance.

There have been few prospective studies to ascertain the needs of individuals over a life time after a TBI. In some respects, the concerns of individuals with TBI may be similar to that of all individuals who age -- will they experience a decline in mental or cognitive abilities; encounter progressive health, physical, sensory or mobility problems; will they have opportunities to make choices as to how they wish to live, who to

socialize with, work or volunteer; and who will be there to provide assistance when needed.

While states tend to address prevention measures, it has been difficult to develop sufficient state capacity to address life long assistance after a TBI. Over the past thirty years, states have developed capacity for information and referral services, service coordination, rehabilitation, in-home support, personal care, counseling, transportation, housing, vocational rehabilitation services, respite care for families and other assistance. However, services vary in scope across the country and even within a state.

To pay for public services and supports, states use a variety of funding mechanisms. Some states have developed services using state appropriations for such purposes. Since 1985, twenty-four States have enacted legislation to assess fines or surcharges to traffic related offenses or other criminal offenses and/or assessed additional fees to motor vehicle registration or drivers license to generate funding for TBI programs and services, generally referred to as trust fund programs.

Twenty-one States have implemented TBI Home and Community-Based Medicaid Waiver Programs to provide community-based services to individuals with TBI who are Medicaid eligible and are at risk of institutionalization or nursing facility level of care. Several states provide services with funds from all of these sources – state, dedicated funding (trust fund), and Medicaid. Within a state, these services may be administered by the state public health, Vocational Rehabilitation, mental health, Medicaid, intellectual disabilities, education or social services agency. Direct care services are then carried out by community providers and professionals.

State TBI programs work with other state agencies to coordinate resources in order to develop capacity within programs which may not be housed in the same agency, such as Medicaid; Vocational Rehabilitation; and aging and disability resource centers funded by the U.S. Administration for Aging. The result is often a patchwork of programs and systems in order to provide the array of rehabilitative and long-term community and family services and supports.

In 1996, Congress passed the TBI Act which authorized funding to the Centers for Disease Control and Prevention to assist with obtaining data to determine the incidence and prevalence of TBI; prevention; public education and other activities. The federal law also authorized funding to the U.S. Department of Health and Human Services, Resources and Services Administration (HRSA) for grants to states to improve and expand access to rehabilitation and community services. (The program is due for reauthorization, and a bill is progressing in the U.S. House of Representatives.)

Since 1997, HRSA has awarded grants to 48 States, District of Columbia and one Territory, although not concurrently, to develop and improve services and systems to address the short-term and long-term needs. These grants have been time limited and are relatively small. Five years ago, HRSA increased the amount of the award from approximately $100,000 to $250,000 to make it more feasible for states to carry out

their grant goals and the legislative intent. While this increased amount is more attractive to states, this change reduced the number of grantees to 21 -- ***l****ess than half of the states and territories receive funding.*

Over the course of the grant program, states have developed state plans and implemented initiatives for improving service delivery; information & referral systems; service coordination systems; outreach and screening among unidentified populations such as children, victims of domestic violence, and veterans; and training programs for direct care workers and other staff. States have conducted public awareness and educational activities that have helped states to leverage and coordinate funding in order to maximize resources within states to the benefit of individuals with TBI. And, in some states, federal grant funds were used to assist in developing educational materials and training to implement their sports-concussion laws.

NASHIA has long advocated for the U.S. Department of Health and Human Services to develop a national plan to identify and coordinate federal resources, much like states do, in order to maximize resources and to streamline services for families and individuals with TBI who need an array of short-term and long-term supports. We have also recommended that a federal interagency entity be established to promote collaboration among federal agencies, state government, providers, consumers and other partners involved in TBI services over the lifespan and to take the lead for developing a plan. While HRSA has created an interagency TBI working group, this group has not involved or communicated with TBI stakeholders or solicited input from families and individuals with TBI. Furthermore, NASHIA recommends:

1) **Reauthorization of the TBI Act** – the *only* federal program providing assistance to states to improve services for individuals with TBI.

2) **Transferring the HRSA TBI State Grant Program to the <u>Administration for Community Living</u> to maximize resources to support the array of services and supports needed following a brain injury and to:**

   - Integrate TBI into the U.S. Department of Health and Human Services (HHS) long-term services initiatives, which also rely on Aging and Disability Resource Centers (ADRCs) as the entry point into these systems;

   - Promote collaboration with the Administration on Aging (AoA) on falls-related TBIs among older adults;

   - Include TBI in the Office of Disability and Aging Policy's Office of Integrated Policy initiatives (i.e. Lifespan Respite Care Program, Participant Direction Program, Evidenced-Based Care Transitions, and Transportation Research and Demonstration Program); and.

   - Coordinate with the Independent Living program and the National Institute of Disability and Rehabilitation Research (NIDRR), which funds the TBI Model

Systems, should those programs move to the ACL as called for in the Workforce Innovation and Opportunity Act (WIOA) moving through Congress.

3) Fund research to study community living service needs over the long-term for both individuals with TBI and their families or other caregivers.

4) Provide funding for coordinated education and training among professionals and providers to better identify TBI as an underlying condition as people age who may access medical, aging or other health care systems to prevent misdiagnosis and to better address an individual's needs.

5) Provide funding for respite services and training for family caregivers.

Thank you again for this opportunity. Should you wish additional information, please do not hesitate to contact Rebeccah Wolfkiel, Governmental Consultant, at 202-480-8901 (office) or 717-250-6796 (cell) or email: rwolfkiel@ridgepolicygroup.com. You may also contact Susan L. Vaughn, Director of Public Policy, at 573-636-6946 or publicpolicy@nashia.org or William A.B. Ditto, Chair of the Public Policy Committee, at williamabditto@aol.com.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

State of Play: Brain Injuries and Diseases of Aging

Testimony before the

U.S. Senate

Special Committee on Aging

Walter J. Koroshetz, M.D., Deputy Director

National Institute of Neurological Disorders and Stroke

National Institutes of Health

June 25, 2014

Mr. Chairman and Members of the Committee, I am pleased to testify at today's hearing on brain injury and diseases of aging. I will present my perspective as a neurologist, scientist, and Deputy Director of the National Institute of Neurological Disorders and Stroke (NINDS) on what we know, where there is uncertainty, and how the NIH is working with other agencies, the private sector, the scientific community, and patients to address the gaps in our knowledge.

TRAUMATIC BRAIN INJURY

I begin with a reminder that Traumatic Brain Injury (TBI) is remarkably common, especially among the elderly. The U.S. Centers for Disease Control and Prevention (CDC) estimates that in 2010 there were 2.5 million emergency-department visits, hospitalizations, or deaths associated with TBI in the United States, with TBI contributing to the deaths of more than 50,000 people.[1] As CDC notes, this estimate does not include people who experience TBI but do not seek emergency care. Adults aged 65 years and older have the highest rates among all age groups of TBI-related hospitalization and death. Older people also recover more slowly and die more often from these injuries than do younger people. The most common cause of TBI in this age group is falling. This month, NIH and the Patient Centered Outcomes Research Institute (PCORI) announced a five-year $30 million national study that will test a uniquely patient-centered approach to reducing rates of fall-related injuries among non-institutionalized older adults. The National Institute on Aging (NIA), which leads this study for the NIH, also supports research on age differences in TBI, as well as research on dementia.

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[1] http://www.cdc.gov/traumaticbraininjury/get_the_facts.html

Although I will focus today on consequences of TBI that may not become apparent for decades after trauma, bear in mind that TBI can immediately affect many aspects of brain function. Problems with attention, memory, and thinking, especially "executive function," are common and persistent after moderate and severe TBI, as are social and emotional problems. Most people with mild TBI appear to recover completely, but perhaps ten percent report lingering problems months after injury, classified as the post-concussive syndrome. Why some people have persistent problems is an important, but poorly understood, public health issue. This May, at the White House "Healthy Kids and Safe Sports Concussion Summit," the National Collegiate Athletic Association (NCAA) and the Department of Defense (DOD) announced that they will jointly initiate the largest study to date of concussion and head impact exposure in sports to better understand the features that predict long-term problems.

CHRONIC TRAUMATIC ENCEPHALOPATHY

Simply put, there is compelling evidence that repeated blows to the head can lead to a specific form of dementia. This phenomenon was recognized in boxers as early as the 1920's and was thus labeled *dementia pugilistica.* Now called *chronic traumatic encephalopathy,* or *CTE,* this disorder has been identified in the autopsied brains of athletes from other sports, including football, hockey, and soccer, and in brains from a few military Veterans who were exposed to blast injury as well as other forms of TBI.[2] In addition to other signs of degeneration, including loss of brain cells in advanced disease, the brains of deceased people with CTE exhibit characteristic abnormal clusters

[2] Brain 136:43-64 2013

of a protein called *tau* inside neurons. Tau aggregates are also one of the two key findings in the brains of people with Alzheimer's disease, although it is important to note that the locations in the brain where tau aggregates are different in CTE than in Alzheimer's disease. The other key finding is deposition of a protein called *amyloid* outside the cells. Multiple studies have demonstrated that tau is altered and amyloid precursor protein is increased after head injury in animals, and a recent human study using amyloid-PET (positron emission tomography) scans demonstrated transient increases in amyloid in the brain after moderate to severe head injury.[3] Amyloid-PET scans use small tracer doses of radioactive markers tailored to bind to amyloid to create an image of amyloid deposition in brain. Tau-PET scans, now in late stage development, will provide the ability to scan for tau deposits as well. The anticipated introduction of Tau-PET scanning could revolutionize the study of CTE by providing the ability to diagnose the condition during life. Abnormal tau deposition inside brain cells is the pathological signature of CTE and Alzheimer's and is also implicated in other forms of neurodegeneration, including frontotemporal dementia (FTD) in which mutations in the tau gene cause neurodegeneration. Surprisingly, recent evidence suggests that tau and other abnormally aggregating proteins can spread from cell to cell in the brain, which may represent a key insight leading to new strategies to treat Alzheimer's, CTE, Parkinson's, and other neurodegenerative diseases. Because CTE may be the purest form of an acquired neurodegeneration, studying CTE may provide clues on cell to cell tau propagation for other neurodegenerative disorders.

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[3] JAMA Neurology 71:23-31. 2014

Although we know that repeated TBI can cause CTE, there is much we do not know about this disease. The most critical roadblock is the lack of diagnostics that can definitively identify CTE in living people. Consequently, CTE can only be confirmed or refuted upon examination of the brain at autopsy. Without such a diagnostic, we cannot estimate how frequently CTE occurs or how the number, timing between concussions, severity, and direction of blows to the head affect the likelihood of CTE. We do not know how age, gender, lifestyle, genetics, or other individual differences affect susceptibility. We do not have a good understanding of the clinical features that are specific for CTE, especially in the early stages. The latter is especially concerning given that varying degrees of tau pathology have been repeatedly found on brain examination in men without dementia who had a history of concussions and died from suicide. Likewise, we do not know whether blast injury or repetitive TBI might lead to CTE in our exposed service members or whether there is any connection to suicide. In all such cases, brains should be autopsied and carefully assessed for signs of CTE. Finally, we do not understand how trauma triggers later neurodegeneration, although recent findings that injury can affect tau, and that abnormal tau aggregation can propagate throughout the brain, provides a tantalizing clue. Most importantly, no interventions are proven to prevent the occurrence of CTE.

NIH is actively addressing these gaps in our knowledge. In September 2012, the Foundation for NIH established the Sports and Health Research Program with a generous donation from the National Football League. Scientific workshops in December 2012 and July 2013 convened experts in CTE, Alzheimer's disease, and other dementias to discuss the best pathways forward. Based on that guidance, two

large, cooperative projects, led by investigators at Boston University and at Mount Sinai Hospital in New York City, have been funded that will define the scope of long-term changes that occur in the brain years after a single TBI or after multiple concussions. Through these projects ten neuropathologists from eight universities are coordinating research to describe the chronic effects of TBI in brain tissue from hundreds of individuals in order to develop standards for diagnosis and staging. The Mount Sinai team will examine brain tissue for signs of CTE from elderly participants of the NIA-funded Adult Changes in Thought study who had a history of TBI at some time prior to death. Both teams will examine brain tissues collected by the NIH NeuroBioBank from individuals who died years after a variety of TBI exposures. These studies will provide a foundation for understanding how commonly CTE occurs and, more generally, whether TBI contributes to development of dementia.

In these two CTE cooperative projects, neuropathologists will work with advanced brain imaging teams to identify a signature of CTE on brain scans that will allow clinicians to diagnose CTE in living individuals. The second major effort of the Sports Health Research Program will be a longitudinal study that will define the clinical characteristics of CTE over time and evaluate advanced neuroimaging techniques to detect changes in brain structure and function, including use of tau-PET imaging to diagnose and monitor progression of CTE. NIH also supports research to develop brain imaging that can detect mild TBI and post concussive syndrome, which are usually not evident in conventional brain scans. For example, *diffusion tensor imaging* is a variant of the more-familiar magnetic resonance imaging (MRI) that better tracks nerve fiber pathways. This method has shown promise for studying the relationship between head

impact exposure and cognition in college athletes over a single season, and joint NIH-DOD research using this technique has also identified brain damage in soldiers diagnosed with mild TBI whose conventional brain scans appeared normal.[4] Ongoing studies are also developing behavioral and laboratory tests that can be used on the sidelines to detect concussions or help determine in the days following when an athlete is ready to return to play.

TBI and DEMENTIA

In addition to CTE from frequent brain trauma, there are compelling reasons to investigate whether multiple TBIs, or even a single TBI, increase the likelihood that a person will develop Alzheimer's disease or other types of dementia. TBI, especially moderate and severe, can certainly cause immediate, long lasting cognitive problems. This may affect persons' "cognitive reserve" and would diminish their ability to compensate for brain changes due to aging or neurodegeneration, increasing the likelihood that functional problems become apparent. In addition, the underlying mechanisms of damage to the brain from TBI and from neurodegenerative disorders are closely intertwined. Chronic inflammation, as well as tau and amyloid changes, are associated with both conditions, raising the concern that changes due to TBI might accelerate age-related neurodegeneration such as Alzheimer's disease. Some large epidemiological studies have found an association between later dementia and a prior history of TBI, especially moderate and severe TBI. This includes, for example, a prospective study of World War II Veterans and a recent very large nationwide

[4] Neurology 82:1-7 2014; New England Journal of Medicine 364:2091-100, 2011

population study in Taiwan.[5] However, other large epidemiological studies have not found an association, especially for mild TBI.[6] It is also unclear whether the dementias that are detected in these studies arise from Alzheimer's disease, CTE, or other types of dementia.

Research is continuing to address these questions. In addition to the studies already described on long term consequences of TBI, an NIH supported study is following a cohort of former National Football League players to determine, among other questions, whether genes affect susceptibility to later problems. DOD is funding a parallel study to the Alzheimer's Disease Neuroimaging Initiative (ADNI) to investigate the link between TBI and subsequent dementia among Vietnam War Veterans who suffered TBI, using the same scientists and protocols as the main ADNI project, which is jointly funded by NIH and private sources through the Foundation for NIH. DOD and the Department of Veterans Affairs (VA) have jointly launched a new Chronic Effects of Neurotrauma Consortium to investigate potential links between TBI in the military and cognitive decline in Veterans. VA supports ongoing and comprehensive surveillance of TBI among Veterans who served in Iraq and Afghanistan and includes data from multiple sources. Such information is critical for increasing understanding of the prevalence and characteristics of TBI and associated health outcomes.

More generally, researchers are increasingly attending to overlap among causes of dementia, whether TBI and Alzheimer's, Alzheimer's and vascular dementia, or neurodegeneration from other causes. We now know, for example, that there is a

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[5] Neurology 55:1158-66 2000; PLOS ONE 8:e62422

[6] Neurology 53:1959-62 1999; J Neurology Neurosurgical Psychiatry 84:177-82 2013; reviews in J. Alzheimer's Disease & Parkinsonism 4:137 2014 & Lancet Neurology 11:1103-12 2012

spectrum from Alzheimer's disease to vascular dementia, the second most common dementia, which is due to abnormalities in brain blood vessels. Most patients have neither isolated Alzheimer's nor pure vascular dementia, but rather contributions from both. There is also suggestive evidence that TBI may contribute to other neurodegenerative disorders, including FTD, amyotrophic lateral sclerosis (Lou Gehrig's Disease), and Parkinson's disease. The 2012 NINDS Stroke Research Priorities Meeting and the 2013 Conference on Alzheimer's Disease Related Dementias both stressed the importance of understanding the overlap among types of dementia. The latter meeting was part of National Alzheimer's Project Act (NAPA) activities, and the NAPA Council has incorporated those recommendations into the National Alzheimer's Plan.

DEVELOPING TBI INTERVENTIONS

NIH supports research to develop interventions that prevent immediate and delayed problems from TBI, from laboratory studies in animals through large, multi-site clinical trials. NIH research has contributed to better critical care that has dramatically improved survival from severe TBI. NINDS and partners in Europe and Canada recently launched the International TBI Research Initiative. This prospective, observational study of 3,000 adults and children with TBI in the United States, coordinated with large studies by the European Union and the Canadian Institute of Health Research, will inform TBI classification and identify those therapies associated with the best outcome. NIH laid the foundation for meaningful comparison across these and other future studies by working with the research community and other federal agencies through the NINDS Common Data Elements program to harmonize the data

that are collected and the way data are categorized. The DOD- and NIH-led Federal Interagency TBI Informatics System (FITBIR) provides a database for sharing information from these and other TBI studies among qualified investigators.

BASIC RESEARCH

Progress in basic neuroscience has yielded advances in understanding the biology of the brain in health and disease, and an impressive array of tools to study the brain that will drive progress against TBI, dementia, and other brain disorders. The Human Connectome Project, for example, is applying advances in computer science, math, and diffusion tensor MRI brain imaging to develop a complete picture of the brain's functional architecture in more than 1000 people, that is, a map of how different brain areas are connected and work together in the living brain. Pathologic studies demonstrate that damage, called "shear injury," in the brain's connections or "white matter" is common in moderate and severe TBI. Shear injury, which may occur diffusely throughout the brain, is relatively invisible with conventional imaging techniques. The Connectome will greatly enhance the ability to recognize and quantify the disruption in communication pathways between brain regions, and why some people's brains compensate better than others. Complementing this project at a more fine grained level of analysis, the President's Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative is developing tools with the spatial and temporal resolution to yield a dynamic, real time picture of how circuits formed by millions of interconnected nerve cells and synapses work. The BRAIN Initiative may ultimately yield insights about how TBI, Alzheimer's, and other disorders affect the

functioning of important brain circuits and how the brain attempts to recover or compensate for these changes.

This January, an NINDS intramural research team showed the power of applying emerging methods from basic neuroscience to TBI.[7] These researchers developed a novel mouse model of mild TBI and used advanced microscopy and cell labeling techniques to watch in real time in living animals how particular types of cells responded to mild TBI from the start. The investigators saw the swarming of immune cells and leakage of dye out of blood vessels on the surface of the brain during the initial inflammatory response and the recruitment of brain supporting cells that reconstituted damaged protective barriers. Using MRI brain imaging, the team was also able to detect similar dye leakage from surface blood vessels in humans after concussion, underlining the likely relevance of the animal studies. Because researchers could watch the cells' responses to pharmacological agents, they could analyze how chemical signals orchestrate damage and repair responses and test potential interventions that target these mechanisms. Methods like these promise to greatly increase our understanding of how the brain reacts to TBI and why there may be long term consequences.

CONCLUDING REMARKS

To answer the key challenges discussed today, NIH supports a full spectrum of research and works closely with others, including DOD, CDC, and the international scientific community. With great anticipation we await the introduction of new MRI

[7] Nature 505:223-228 2014

and PET brain imaging methods that will enable us to identify and quantify important brain changes in living TBI survivors for the first time. Longitudinal studies can then determine what occurs in the brain that leads to delayed cognitive decline, and whether Alzheimer's disease is more likely to occur. New structural and molecular imaging techniques may also enable scientists to identify and track markers of the neurodegenerative process over time, which can provide targets against which to test new therapies. Progress is imperative because of the enormous impact of TBI and dementia on individuals and their families, on the public health, and on the economy of the United States and the world. Thank you.

Parkinson's Action Network

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Statement for the Record of the Parkinson's Action Network
"State of Play: Brain Injuries and Diseases of the Aging"
Special Committee on Aging
United States Senate

July 1, 2014

Dear Chairman Nelson and Ranking Member Collins,

The Parkinson's Action Network (PAN) appreciates the opportunity to submit a statement for the record as part of the Senate Special Committee on Aging's hearing, "State of Play: Brain Injuries and Diseases of the Aging." Studies have identified strong links between the development of Parkinson's disease and other neurological conditions and disorders and traumatic brain injury (TBI). It is critical that new and ongoing brain injury-related research initiatives focus on the long-term effects of TBI and its contributions to the development of neurological disease later in life. Our comments will focus on current and developing TBI-related Parkinson's research at the Department of Defense and the National Institutes of Health.

PAN is the unified voice of the Parkinson's community advocating for better treatments and a cure. In partnership with other Parkinson's organizations and our powerful grassroots network, we educate the public and government leaders on better policies for research and improved quality of life for people living with Parkinson's and their families.

About Parkinson's
Parkinson's disease, the second most common neurodegenerative condition after Alzheimer's disease, is a complicated, chronic progressive disorder that impacts between 500,000 and 1.5 million Americans. It is believed that nearly 60,000 people are diagnosed each year in the United States with Parkinson's, and currently there is no cure, therapy, or drug to slow or halt its progression. The economic burden of Parkinson's disease is estimated to cost the United States at least $14.4 billion a year, and that number will only grow as the prevalence of Parkinson's is expected to more than double by the year 2040.

Today , we are seeing more cases of retired professional athletes developing progressive, degenerative neurological conditions following incidents of mild or severe TBI during their active playing careers. Certainly, improving safety and identifying risk factors associated with TBI is critical to better understanding how neurological diseases, like Parkinson's, develop and may be prevented. Studies have even compared the pathological changes found in the human

brain in young athletes exposed to sports-related impact injuries to those found in blast-injured military service members.[1]

Department of Defense Parkinson's Research

In fact, medical research supported by the Department of Defense (DoD) has funded some of the most cutting edge initiatives identifying linkages between incidents of TBI and resulting neurological impairments. The Neurotoxin Exposure Treatment Parkinson's Research (NETPR) program at the U.S. Army Telemedicine & Advanced Technology Research Center is a forward-looking, peer-reviewed national grant program that provides DoD with innovations in materiel design, protocols for harmful exposures, pathways to develop neuroprotective drugs, and has set the foundation for the current DoD program in TBI. This congressionally directed program, funded annually at $16 million, has also advanced understanding on the biomarkers of head injury and the biochemical basis of depression. The program is supporting research to determine the genetic basis for neurodegenerative disease risk to the aging veteran as a consequence of risk factors, such as TBI and neurotoxic chemical exposure. NETPR research contributed heavily to the Veterans Health Administration's recent decision[2] to recognize the relationship between TBI and the onset of Parkinson's by making parkinsonism a secondary service-connected disease when a veteran has suffered moderate to severe TBI. The NETPR program continues to address fundamental gaps in understanding how Parkinson's disease develops through the specific lens of military service, leveraging its resources to discover new ways to diagnose, prevent, and treat the disease for not only our current service members and the 80,000 veterans living with Parkinson's, but all Americans facing the hard realities of this disease, including those most at risk for developing Parkinson's in the future.

National Institutes of Health

There are also encouraging signs at the National Institutes of Health (NIH) that the development of clinical tools, such as biomarkers, may include TBI. In January 2014, the National Institute of Neurological Disorders and Stroke (NINDS) approved a list of 31 priority research recommendations specific to Parkinson's that highlight areas in which NINDS and the broader field should direct its resources to achieve the greatest impact in addressing treatments and the underlying causes of the disease. Among these recommendations is a greater, more expansive focus on biomarker identification in the clinical and translational research spaces. The National Institute for Environmental Health Science (NIEHS) is also conducting a Parkinson's-specific planning meeting this fall to build upon the work of NINDS. NIEHS has already included TBI as part of its general research portfolio for environmental exposure, and we are encouraging them to more clearly define TBI as an external environmental contributor to Parkinson's disease in their ongoing and future research initiatives. We believe it is critical for NIH more broadly, as well as the NINDS and NIEHS

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[1] McKee AC, Robinson, Meghan E. "Military-related traumatic brain injury and neurodegeneration," *Alzheimer's & Dementia.* Vol. 10 (2014) S242-S253

[2] "Secondary Service Connection for Diagnosable Illnesses Associated with Traumatic Brain Injury; Final Rule," 78 *Federal Register* 242 (17 December 2013), pp. 76196-76209.

research communities, to view biomarkers and external environmental factors like TBI in a more integrative perspective.

Funding for Medical Research
Unfortunately, due to ongoing fiscal constraints, funding for medical research across the board has not kept pace with inflation or the growing needs of aging Americans and the overall public health. While funding for DoD Parkinson's research has remained relatively steady over the past few years, it has been cut by 36 percent, down from $25 million to $16 million, since 2010. NIH, the largest funder of Parkinson's research in the world, has also been forced to reduce its Parkinson's-related research from a high of $154 million in FY 2012 to $135 million in FY 2013, a 12 percent decrease. Continued TBI research at DoD and NIH could be instrumental in unlocking many of the mysteries of progressive neurological conditions and instructive in developing tools to protect young and professional athletes, members of the military, and the broader civilian population – and these initiatives must be met with a commitment to prioritize medical research spending.

We appreciate the Committee's examination of this critical issue and look forward to opportunities to work with you and serve as a resource in the future. If you have any questions, please contact Jamie Tucker, senior government relations manager, at jtucker@parkinsonsaction.org.

Sincerely,

Amy Comstock Rick, CEO

TALKING POINTS

AMERICAN ACADEMY OF NEUROLOGY

The American Academy of Neurology, an association of more than 27,000 neurologists and neuroscience professionals, is dedicated to promoting the highest quality patient-centered neurologic care. For more information about the American Academy of Neurology, visit www.AAN.com or find us on Facebook, Twitter, Google+ and YouTube.

A neurologist is a doctor with specialized training in diagnosing, treating and managing disorders of the brain and nervous system such as Alzheimer's disease, stroke, migraine, multiple sclerosis, brain injury, Parkinson's disease and epilepsy.

With more than one million athletes now experiencing a concussion each year in the United States, in March 2013 the AAN released an evidence-based guideline for evaluating and managing athletes with concussion.

Key Message:

The updated AAN guideline recommends athletes with suspected concussion be immediately taken out of the game and not returned until assessed by a licensed health care professional trained in concussion, return to play slowly and only after all acute symptoms are gone.

According to the guideline:

- Among the sports in the studies evaluated, risk of concussion is greatest in football and rugby, followed by hockey and soccer.
- The risk of concussion for young women and girls is greatest in soccer and basketball.
- An athlete who has a history of one or more concussions is at greater risk for being diagnosed with another concussion. The first 10 days after a concussion appears to be the period of greatest risk for being diagnosed with another concussion.
- There is no clear evidence that one type of football helmet can better protect against concussion over another kind of helmet. Helmets should fit properly and be well maintained

Signs and symptoms of a concussion include:

- Headache and sensitivity to light and sound
- Changes to reaction time, balance and coordination
- Changes in memory, judgment, speech and sleep Loss of consciousness or a "blackout" (happens in less than 10 percent of cases)

"If in doubt, sit it out"

The guideline is endorsed by the National Football League Players Association, the American Football Coaches Association, the Child Neurology Society, the National Association of Emergency Medical Service Physicians, the National Academy of Neuropsychology, the National Association of School Psychologists, the National Athletic Trainers Association and the Neurocritical Care Society.

To learn more about concussion, please visit www.aan.com/concussion.

TALKING POINTS

AMERICAN BRAIN FOUNDATION

Elevator Speech: The American Brain Foundation funds the most crucial research to cure brain diseases, such as traumatic brain injury, Alzheimer's disease, stroke, and epilepsy. One in six people are affected by brain disease. We want to reduce the prevalence of brain disease by supporting research into prevention, treatment, and cures. Give to research now at AmericanBrainFoundation.org.

Key Messages:

- Brain disease is in the news every day, yet research funding is flat. Help us fund research to cure brain disease. Donate now at AmericanBrainFoundation.org.
- Whether you are a patient, caregiver, neurologist, researcher, or someone who cares deeply about our cause, we are counting on you to join us in this fight now to cure brain disease once and for all by making a donation now at AmericanBrainFoundation.org.
- The American Brain Foundation is the foundation of the American Academy of Neurology, the world's largest association of neurologists committed to the highest quality patient-centered neurologic care.
- [Spokesperson] Brain disease affects one in six people in the world. I am one of them [insert personal story].

Mission: The American Brain Foundation supports vital research and education to discover causes, improved treatments, and cures for the brain and other nervous system diseases.

Vision: Cure Brain Disease

For more information about the American Brain Foundation and how you can support research, visit www.AmericanBrainFoundation.org or visit them on Facebook, Twitter, Google+, and YouTube.

Press Release

AMERICAN ACADEMY OF NEUROLOGY

FOR IMMEDIATE RELEASE

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Super Bowl Champion Ben Utecht Receives Public Leadership in Neurology Award

PHILADELPHIA – The American Academy of Neurology (AAN) and the American Brain Foundation have announced that Ben Utecht, former NFL tight end and Super Bowl champion, is the recipient of the 2014 Public Leadership in Neurology Award. Utecht is being recognized for his outstanding commitment to raising awareness for traumatic brain injury.

The Public Leadership in Neurology Award honors an individual or group outside of the medical profession. Honorees are known for advancing public understanding and awareness of neurologic disease, being effective advocates for neuroscience research and making significant contributions to improve patient care.

Utecht will receive the award during the AAN and American Brain Foundation Awards Luncheon held on Wednesday, April 30, 2014, at the Philadelphia Convention Center as part of the AAN's Annual Meeting, the world's largest gathering of neurologists with more than 10,000 attendees.

A Super Bowl champion with the Indianapolis Colts, Utecht experienced a career-ending traumatic brain injury (TBI) in 2009 while playing for the Cincinnati Bengals. Utecht is now embarking on a career as a recording artist and motivational speaker, as well as working with the American Brain Foundation to help raise awareness for TBI.

"I am incredibly humbled to be honored with the 2014 Public Leadership in Neurology Award, and for my name to be placed alongside of such an esteemed group of former recipients," Utecht said. "My life has been impacted by traumatic brain injury and brain disease, challenging me and my family constantly. Brain disease threatens to steal from us what makes us human, and I will fight relentlessly to see that through research we can in fact find the origins of healing through the cures that are waiting to be discovered."

Utecht will be at the American Brain Foundation's Brain Health Fair in Philadelphia on Saturday, April 26, to talk about his efforts in building TBI awareness. He lives in Minnesota with his wife, Karyn, and their three daughters.

For more information about traumatic brain injury, visit www.aan.com/patients.

To learn more about concussion, please visit www.aan.com/concussion or download the AAN's new app, Concussion Quick Check, to help coaches and athletic trainers quickly recognize the signs of concussion.

AAN 2014 Annual Meeting

Press Release

-more-

The American Academy of Neurology, an association of more than 27,000 neurologists and neuroscience professionals, is dedicated to promoting the highest quality patient-centered neurologic care. A neurologist is a doctor with specialized training in diagnosing, treating and managing disorders of the brain and nervous system such as Alzheimer's disease, stroke, migraine, multiple sclerosis, brain injury, Parkinson's disease and epilepsy.

For more information about the American Academy of Neurology, visit http://www.aan.com or find us on Facebook, Twitter, Google+ and YouTube.

The American Brain Foundation, the foundation of the American Academy of Neurology, supports crucial research and education to discover causes, improved treatments, and cures for brain and other nervous system diseases. Learn more at http://www.americanbrainfoundation.org/ or find the Foundation on Facebook, Twitter, Google+ and YouTube.

ELSEVIER

Alzheimer's & Dementia 10 (2014) S242-S253

Alzheimer's & Dementia

Military-related traumatic brain injury and neurodegeneration☆

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Abstract Mild traumatic brain injury (mTBI) includes concussion, subconcussion, and most exposures to explosive blast from improvised explosive devices. mTBI is the most common traumatic brain injury affecting military personnel; however, it is the most difficult to diagnose and the least well understood. It is also recognized that some mTBIs have persistent, and sometimes progressive, long-term debilitating effects. Increasing evidence suggests that a single traumatic brain injury can produce long-term gray and white matter atrophy, precipitate or accelerate age-related neurodegeneration, and increase the risk of developing Alzheimer's disease, Parkinson's disease, and motor neuron disease. In addition, repetitive mTBIs can provoke the development of a tauopathy, chronic traumatic encephalopathy. We found early changes of chronic traumatic encephalopathy in four young veterans of the Iraq and Afghanistan conflict who were exposed to explosive blast and in another young veteran who was repetitively concussed. Four of the five veterans with early-stage chronic traumatic encephalopathy were also diagnosed with posttraumatic stress disorder. Advanced chronic traumatic encephalopathy has been found in veterans who experienced repetitive neurotrauma while in service and in others who were accomplished athletes. Clinically, chronic traumatic encephalopathy is associated with behavioral changes, executive dysfunction, memory loss, and cognitive impairments that begin insidiously and progress slowly over decades. Pathologically, chronic traumatic encephalopathy produces atrophy of the frontal and temporal lobes, thalamus, and hypothalamus; septal abnormalities; and abnormal deposits of hyperphosphorylated tau as neurofibrillary tangles and disordered neurites throughout the brain. The incidence and prevalence of chronic traumatic encephalopathy and the genetic risk factors critical to its development are currently unknown. Chronic traumatic encephalopathy has clinical and pathological features that overlap with postconcussion syndrome and posttraumatic stress disorder, suggesting that the three disorders might share some biological underpinnings.

Keywords: Chronic traumatic encephalopathy; Veterans; Neurodegeneration; Traumatic brain injury; Tauopathy; TDP-43; Alzheimer's disease

1. Introduction

In military settings, most traumatic brain injuries (TBIs) are mild TBIs (mTBIs). For U.S. forces deployed to Afghanistan and Iraq in Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND), blast exposure is the leading cause of mTBI, although service members are also susceptible to concussions [1]. Estimates of the prevalence of mTBI among returning service members range from 15.2% to 22.8%, affecting as many as 320,000 troops [1–4]. Despite their frequency, the acute and long-term effects of mTBI have been a relatively unexplored area of medical inquiry until very recently. Undoubtedly, the "invisible" nature of mTBI, notably the lack of any external physical evidence of damage to the head or brain, has been a major factor contributing to the impression of inconsequentiality.

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However, there is accumulating evidence that some individuals develop persistent cognitive and behavioral changes after mild neurotrauma. In addition, the relative contributions of physical injury or psychic stress to chronic sequelae after mTBI remain a matter of debate–a discussion that began during World War I regarding the basis for "shell shock," and that continues today concerning the relative contributions of posttraumatic stress disorder (PTSD) and physical brain injury to persistent symptoms after mTBI.

The first large-scale evidence of military-related mTBI occurred in World War I (1914–1918) in association with the frequent use of high explosives in trench warfare. Service members who experienced high doses of explosive artillery fire sometimes developed shell shock or "commotio cerebri," a mysterious condition characterized by headache, amnesia, inability to concentrate, difficulty sleeping, depression, and suicidality [5–7]. At the time, it was unclear whether shell shock was a maladaptive, psychiatric condition related to the stresses of combat or whether the condition was caused by physical injury to the brain. Despite the lack of any pathological studies on the brains of individuals diagnosed with shell shock, wartime committees entreated with the responsibility to inquire into the entity declared the disorder to have psychiatric origins [7].

Shortly thereafter, Harrison Martland, a New Jersey pathologist, drew attention to a symptom complex that affected professional boxers, "Punch Drunk," a condition well known to boxing enthusiasts that appeared to result from repeated sublethal blows to the head [8]. Martland described unsteadiness of gait, mental confusion, and slowing of muscular movements occasionally combined with hesitancy in speech, tremors of the hands, and nodding of the head. Later, Winterstein summarized the psychiatric manifestations of approximately 50 professional boxers and noted impairment of intelligence, mental dullness, difficulty concentrating, paranoia, and garrulousness [9]. Johnson later added memory loss, dementia, rage reactions, and morbid jealousy to the clinical syndrome [10]. In the scattered, small case series of "dementia pugilistica" reported over the next half century, the condition was variously referred to as "traumatic progressive encephalopathy" and later as "chronic traumatic encephalopathy" (CTE) to highlight the chronic and progressive nature of the disorder [11,12]. In 1973, Corsellis, Bruton, and Freeman-Browne detailed the neuropathological findings found in the brains of 15 retired boxers and correlated the pathological findings with retrospective clinical symptoms [13]. The authors noted gross neuropathological changes of cerebral atrophy, enlargement of the lateral and third ventricles, thinning of the corpus callosum, cavum septum pellucidum with fenestrations, and cerebellar scarring. General cell stains and Von Braunmühl's silver stain were used to demonstrate neuronal loss in the cerebellar tonsils and substantia nigra, neurofibrillary degeneration of the substantia nigra and cerebral cortex, and senile plaques in approximately one quarter of the cases. The authors speculated that pathology in the limbic structures (such as the hippocampus, medial temporal lobe, and fornix) was responsible for impairments in learning and memory, that pathology in the substantia nigra accounted for the Parkinsonian features, and that pathology in the septal cortex for the abnormal rage reactions.

Studies of CTE in boxers were followed by reports of CTE in civilians exposed to repetitive brain trauma as a consequence of head-banging behaviors, physical abuse, and poorly controlled epilepsy (reviewed in [14]); other sports, including Omalu's seminal observations in American football players [15,16]; and in ice hockey, baseball, soccer, rugby, and professional wrestling [14,17,18]. CTE was also reported in a few Iraq and Afghanistan veterans whom experienced military-related blast TBI [17,19,20]. In addition, CTE has been reported in military veterans, many of who were also athletes, including former National Football League (NFL) players [17]. CTE has been reported in military veterans who saw combat in the Gulf War, Vietnam, World War II, and Iraq and Afghanistan. In this review, we summarize the acute and long-term effects of mTBI that have been reported in veterans and describe the experience over the past 6 years at the VA Boston Brain Bank with military service-related mTBI.

Understanding the effects of military-related mTBI presents additional challenges not encountered in studies of neurotrauma associated with play of sports. Unlike the relatively stereotyped features of brain trauma that occur during athletic participation, in which injury is dependent on the rules of engagement specific to the sport, military-related mTBI is acquired in widely heterogeneous ways, including athletics, recreational activities, physical training practices (e.g., combatives, boxing competitions, and ropes courses), falls, motor-vehicle accidents, and exposure to explosive blasts. Injury from explosive blasts varies depending on the strength of the explosive; whether the injury occurs in an open field, in, or near buildings; or in a motor vehicle. Military mTBI is also random and unpredictable, ranging from a single injury to many thousands of traumatic injuries over similar time periods depending on an individual's chance exposure to blasts and impacts.

1.1. Acute injury

1.1.1. Concussion, subconcussion

A concussion is a mTBI induced by an impulsive force transmitted to the head resulting from a direct or indirect impact to the head, face, neck, or elsewhere [21,22]. In the combat setting, most concussions occur as a result of blunt trauma associated with blasts from explosive devices, such

as hitting the head against the interior of a vehicle [23]. Symptoms from concussion and other forms of mTBI are usually self-limited and resolve spontaneously over a period of a few weeks, although 10–15% of individuals develop prolonged symptoms or postconcussive syndrome (PCS). Signs and symptoms of concussion and PCS include irritability, sleep disturbance, forgetfulness, anxiety, headaches, poor concentration, pain, and psychological distress [24]. Neuropsychological testing in PCS may reveal persistent, yet subtle, cognitive deficits, often in the executive domain [24]. Less severe impact injuries that do not produce overt neurological symptoms but are associated with subtle neuropsychiatric deficits or changes in functional magnetic resonance imaging (fMRI) are referred to as "subconcussion" [25,26]. Concussion and subconcussion are produced by acceleration and deceleration forces on the brain that may be linear or rotational [27]. Rapid acceleration, deceleration, or rotational forces cause the brain to elongate and deform, stretching individual cells and blood vessels and altering membrane permeability. Although all cell compartments are affected by the injury, axons are especially vulnerable to shear injury given their relatively long length and high membrane-to-cytoplasma ratio. In addition to axonal damage, the integrity of the microvasculature is compromised, with disruption of the blood-brain barrier and focal cortical hypoperfusion [28]. Moreover, acceleration-deceleration forces produce rapid release of neurotransmitters, including glutamate, and alterations in sodium channels with subsequent ionic dysregulation [29], producing an influx of calcium and an efflux of potassium, acceleration of the cellular sodium-potassium (Na^+-K^+) pump to maintain membrane homeostasis, and large increases in glucose metabolism [30].

Pathological studies of concussion and PCS demonstrate microscopic evidence of multifocal traumatic axonal injury (TAI) [18,31] that is best visualized by amyloid precursor protein (APP) immunohistochemistry [32], often located around small blood vessels in the corpus callosum, fornix, subcortical U-fibers, and cerebellum [18]. In general, the severity of the multifocal axonal injury is parallel to the severity of the TBI. However, APP immunohistochemical identification of traumatic axonal swellings may significantly underestimate the overall magnitude of the axonal damage [33]. TAI affects multiple axonal populations, including large caliber myelinated and non-neuropathologically detected fine-caliber myelinated and unmyelinated fibers. There is evidence that fine-fiber unmyelinated axons are disproportionately vulnerable to traumatic injury and, as such, may be significant contributors to the morbidity associated with mTBI. There are currently no reliable neuropathological markers for unmyelinated fine-fiber damage; accordingly, it is likely that the total axonal damage associated with TAI is considerably more than what is detectable with conventional neuropathological methods [33]. In addition, concomitant with the breakdown of the axon and myelin sheath, axon terminals also undergo neurodegenerative change and deafferentation. This axonal degeneration and deafferentation likely contribute significantly to the morbidity associated with TAI. Furthermore, deafferentation sets the stage for subsequent neuroplastic changes that may be adaptive or maladaptive. These neuroplastic responses to mild neurotrauma have not been well studied in the human brain [34,35].

After concussion, there is pathological evidence of blood-brain barrier damage with microhemorrhage, astrocytosis, and perivascular clusters of activated microglia [18]. In addition, some cases of recent concussion and PCS show isolated focal perivascular accumulations of hyperphosphorylated tau (p-tau) as neurofibrillary tangles (NFTs) and neurites as well as hemosiderin-laden macrophages. The finding of focal p-tau abnormalities in the brains of individuals with PCS in close proximity to focal axonal injury, microhemorrhage, astrocytosis, and perivascular microgliosis suggests that the development of p-tau pathology may be mechanistically linked to axonal injury, breach of the blood-brain barrier, and neuroinflammation [18]. Whether these acute pathologies are reversible and resolve over time is unknown. Because most patients with mTBI recover fully, it suggests that intrinsic mechanisms are generally able to repair low-level injury [33]. However, repetitive TAI superimposed on continuing, perhaps broadening, breach of the blood-brain barrier; disruption of sodium channels; ionic dysregulation; and metabolic irregularities might trigger a self-perpetuating, progressive neurodegenerative cascade in some individuals.

Concussion and subconcussive injury are associated with microstructural changes in the white matter and alterations in fiber tract integrity that are detectable with diffusion tensor imaging (DTI) and susceptibility weighted imaging but are not evident on conventional structural imaging studies such as computed tomography (CT) scan and magnetic resonance imaging (MRI). The significance of these asymptomatic subconcussive injuries is increasingly recognized in sports such as football, ice hockey, and soccer, in which accumulating evidence demonstrates microstructural changes in the white matter on DTI as well as abnormalities in functional MRI (fMRI) [26,36–40]. Similar changes recently have been demonstrated in asymptomatic military-related blast injury [37,41]. Bazarian and colleagues found a strong association between exposure to blast and reduced first percentile fractional anisotropy (FA) on DTI that was independent of symptoms of mTBI at the time of blast exposure. Because these asymptomatic mTBIs are difficult to assess, it is likely that DTI and fMRI will become useful tools to guide the prognosis and management of these injuries moving forward.

Our experience with repetitive concussive injury includes a 28-year-old male U.S. Marine veteran with two combat deployments. Similar to many other military personnel, his history was notable for multiple concussions

that occurred as a civilian and in combat. His first concussion occurred at age 12 in a bicycle accident with temporary loss-of-consciousness (LOC) and posttraumatic amnesia (PTA). At age 17, he experienced a second concussion without LOC during football practice. At age 25, during his second military deployment, he experienced a third concussion with temporary alteration in mental status but no LOC, after which he was diagnosed with PTSD. Four months later at age 26, he sustained a fourth concussion with temporary LOC and PTA resulting from a motor vehicle-bicycle collision. He subsequently developed persistent anxiety, difficulty concentrating, word-finding difficulties, learning and memory impairment, reduced psychomotor speed, and exacerbation of PTSD symptoms. He died from a self-inflicted gunshot wound 2 years after his last concussion. Neuropathological analysis revealed multiple areas of p-tau immunoreactivity surrounding small blood vessels in the temporal cortex, consistent with the diagnosis of early-stage CTE, although the limited availability of tissue precluded any further histological analysis.

1.1.2. Blast injury

Most military-related TBI comes from exposure to explosive blast; blast TBI accounts for approximately 60% of military-related TBI, of which 80% is mTBI [3]. The physical effects of the blast depend on many factors, including the characteristics of the improvised explosive device (IED); the relationship of the individual with respect to the source of the blast, including the distance from the blast; whether the exposure occurred in an open environment or in an enclosed space such as a building or vehicle; and whether a solid structure is located between the individual and the device, because the reflection of blast pressure waves off of various surfaces can lead to multiple pressure waves impacting an individual from various directions for a prolonged period [42]. Blast injury is often further complicated by an accompanying concussive mTBI.

Blast injury is the result of the rapid transmission of an acoustic wave through the brain tissue and accompanying blast winds [20]. Many animal models of blast-induced injury exist, although the precise biomechanics of blast-related traumatic injury and its neuropathological consequences are the subject of debate [43,44]. In our experience with experimental single-blast injury in wild-type C57BL/6 mice [20], detailed kinematic analysis demonstrated that blast winds produce forces similar to multiple, severe concussive impacts occurring over microseconds. In addition, simultaneous intracerebral pressure recordings demonstrated that blast waves traversed the brain with minimal change. The blast wavefront transmissions were not associated with thoracovascular or hydrodynamic contributions; indeed, separation of the mouse head from the thorax did not significantly change the blast-induced intracerebral pressure amplitudes. Furthermore, head immobilization during blast prevented neurological sequelae, confirming that the effect was not triggered by blast waves but rather by inertial forces from blast wind (the "bobblehead effect").

Pathologically, blast injuries produce hemorrhage and edema as blood vessels and brain tissue rapidly contract and expand several times within a fraction of a second after a blast wind, damaging cerebral vasculature [45]. In the acute phases, blast injury may produce large intraparenchymal and subarachnoid hemorrhages [46–48]. Blast injury is also associated with pseudoaneurysm formation and the development of vasospasm. When severe, vasospasm can lead to cerebral ischemia and clinical deterioration that can be delayed as long as 30 days after initial blast exposure [49–51]. Lu and colleagues investigated the effects of relatively low-level single and repetitive primary blast injury in nonhuman primates [52]. Ultrastructural analysis and histopathology at 3 days and 1 month postinjury revealed microvascular degeneration and collapse with obliterated capillary lumens, hypertrophic astrocytic endfeet, vacuolated endothelial cytoplasm, and increased perivascular reticuloendothelial cells. Other changes included chromatolysis of cortical neurons, hippocampal pyramidal neurons, and Purkinje cells in the cerebellum; white matter damage; and increased astrocytic aquaporin-4, suggesting cerebral edema.

The number of neuropathological analyses of acute blast injury in humans are few. In the instances reported by Mott, there was mild brain edema, severe vascular congestion, variable amounts of extravasation of blood around small vessels, intraparenchymal and subarachnoid hemorrhage, and generalized chromatolysis of neurons [5,6]. Warden and colleagues described the neuroimaging findings in a service member exposed to a series of large explosions. Three months after exposure, the service member still experienced headache, occasional nausea, and eye twitching, but she was found to have a normal neurological examination. Her MRI showed a resolving hematoma in the internal auditory canal and an area of hyperintensity in the cerebellum. In addition, there was abnormal FA in the cerebellar white matter on DTI [53]. Other investigators using DTI have demonstrated lower FA and higher radial diffusivity after blast injury [41,54], although the white matter abnormalities found in various studies tend to be heterogeneous and spatially diverse. Using [18 F]-fluorodeoxyglucose positron emission tomography imaging of cerebral glucose metabolism, Peskind and colleagues demonstrated regional brain hypometabolism in veterans with repetitive blast injury [55]. A recent study of Iraq and Afghanistan veterans with one or more blast/impact mTBIs found reduced FA in the corpus callosum; reduced macromolecular proton fraction values in white matter tracts and gray matter/white matter border regions; reduced glucose metabolism in the cerebral cortex; and higher scores on measures of PCS, PTSD, combat

exposure, depression, sleep disturbance, and alcohol use. The neuroimaging metrics did not differ between participants with versus those without PTSD [56].

We examined the postmortem brains of four young military veterans (n = 4 males; ages 22–45 years; mean 32.0 years) with histories of known blast exposure ranging from 1 to several years before death and found evidence of myelinated fiber loss, axonal degeneration, microvascular degeneration, neuroinflammation, and early changes of CTE.

A 28-year-old male U.S. military Marine veteran who experienced several blast exposures during multiple tours in Iraq and Afghanistan subsequently developed severe behavioral abnormalities including poorly controlled anger, debilitating social isolation issues, difficulty with attention and concentration, aggressive tendencies, paranoia, difficulty sleeping, and depression. At age 25, he "snapped" and attempted suicide in Afghanistan. He was diagnosed with combat-related PTSD. At age 27, he was honorably discharged from the Marines. At age 28, during an early-morning incident in which he allegedly fired on police and other civilians, he was shot and killed. At autopsy, his brain weighed 1410 g and was remarkable for slight thinning of the posterior body of the corpus callosum and discoloration of frontal tracts in the cerebral peduncle. Microscopically, there was evidence of severe axonal loss with widespread axonal swellings and axon retraction bulbs, myelinopathy, astrocytosis, and foci of dystrophic calcification in the cerebral subcortical white matter, internal capsule, and cerebellar white matter. Myelinated fiber loss was particularly prominent in the frontal lobes and frontal tracts of the cerebral peduncle. A single focus of perivascular p-tau NFTs and neurites was found at the sulcal depths of the inferior parietal cortex consistent with Stage I/IV CTE (Fig. 1, case 1).

A 45-year-old male U.S. Army veteran with a single close-range IED blast exposure experienced a state of disorientation without LOC that persisted for 30 minutes after blast exposure. He subsequently developed headaches, irritability, difficulty sleeping and concentrating, and depression that continued until his death 2 years later from a ruptured giant basilar aneurysm. His medical history was notable for a concussion associated with a motor-vehicle accident at age 8 years. At autopsy, neuropathological analysis showed acute intrapontine hemorrhage and bilateral infarction in the posterior cerebral artery territories. Microscopic examination also revealed multiple areas of perivascular p-tau NFTs in the frontal, parietal, and temporal cortices with a predilection for sulcal depths and superficial cortical layers diagnostic of CTE Stage II/IV. Myelinated fiber degeneration with axon retraction bulbs and axonal dystrophy was found, most prominently perivascularly, in areas well away from the areas of infarction. There were also perivascular clusters of activated microglia in the subcortical white matter [20] (Fig. 1, case 2).

A 34-year-old male U.S. Marine veteran without a history of previous concussive injury sustained two separate IED blast exposures 1 and 6 years before death. Both episodes resulted in LOC of indeterminate duration. He subsequently developed depression, short-term memory loss, word-finding difficulties, decreased concentration and attention, sleep disturbances, and executive function impairments. His neuropsychiatric symptoms persisted until death from aspiration pneumonia after ingestion of prescription analgesics. At postmortem examination, there was evidence of CTE Stage II/IV and widespread hypoxic-ischemic injury [20] (Fig. 1, case 3).

A 22-year-old male U.S. Marine veteran was exposed to a single close-range IED blast exposure 2 years before death. There was no LOC, but he reported headache, dizziness, and fatigue that persisted for 24 hours after the blast. He subsequently developed daily headaches, memory loss, depression, and decreased attention and concentration. In the year before his death, he became increasingly violent and verbally abusive with frequent outbursts of anger and aggression. He was diagnosed with PTSD 3 months before death from an intracerebral hemorrhage. His past history included 2 years of high school football and multiple concussions from altercations. At autopsy, there was an acute intraventricular hemorrhage with tonsillar herniation. There was also evidence of multifocal axonal injury and p-tau neuritic immunoreactivity consistent with CTE Stage I/IV. In the thalamus, multiple small- to medium-sized blood vessels showed prominent perivascular lymphocytic cuffing as well as foci of lymphocytes and hemosiderin-laden macrophages within the vascular walls. Focal dystrophic calcification was also found in the walls of scattered small blood vessels in the thalamus and subcortical white matter (Fig. 1, case 4).

A similar case involving a 27-year-old veteran who had been exposed to multiple mortar blasts and IEDs was reported by Omalu and colleagues [19]. The veteran had developed progressive cognitive impairment, impaired memory, behavioral and mood disorders, and alcohol abuse, and he was diagnosed with PTSD. He committed suicide approximately 8 months after his discharge. His brain at autopsy showed changes of CTE consisting of multifocal NFTs that were most prominent at the depths of sulci in the frontal cortex.

Of interest, two of the five veterans died from spontaneous intracerebral hemorrhage several years after exposure to explosive blast, one died secondary to rupture of a giant basilar aneurysm, and the other died of intraventricular hemorrhage. The unusual locations of the hemorrhages might be interpreted to suggest that vascular integrity was initially compromised by the blast exposure and that subsequent vascular degeneration led to basilar artery aneurysm formation in one individual and to focal vasculitis and small vessel rupture in the other. The findings of focal dystrophic calcification and lymphocytic and hemosiderin-laden macrophage infiltration in the walls of small thalamic vessels in one individual support the concept of trauma-associated vasculitis and vascular degeneration (Fig. 1, case 4).

The changes of CTE, axonal injury, and microvasculopathy found in the postmortem brains of blast-injured veterans are

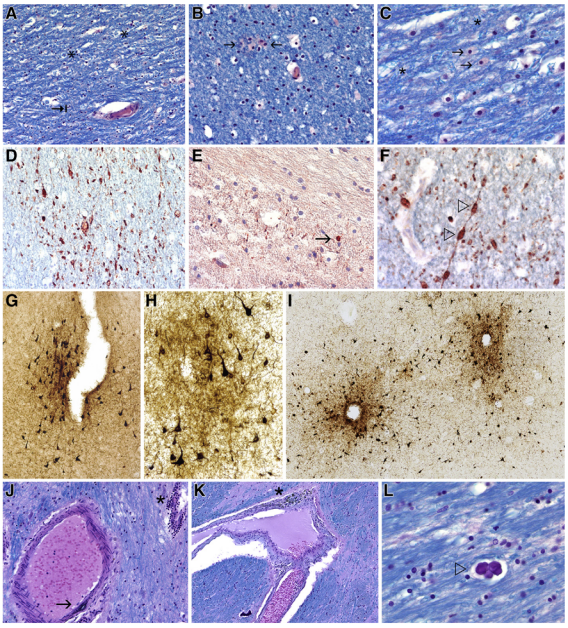

Fig. 1. Neuropathological changes associated with blast injury. (A–C). Subcortical frontal white matter shows loss of myelinated fibers, abnormal myelin clumps (asterisks), and astrocytosis (arrows), case 1, luxol fast blue-hematoxylin and eosin stain, original magnification (A) ×200, (B) ×400, and (C) ×600. (D) Axons in the frontal white matter are severely depleted with many irregular axonal swellings, case 1, SMI-34 immunostaining, original magnification ×400. (E) APP immunostaining shows axon retraction bulbs and other axonal irregularities (arrow), APP immunostaining, case 1, original magnification ×400. (F) Axonal swellings, case 1, SMI-34 immunostaining, original magnification ×600. (G) A single focus of perivascular NFTs and neurites at the depth of sulcus in inferior parietal cortex consistent with Stage I/IV CTE, case 1, AT8 immunostaining for hyperphosphorylated tau (p-tau), original magnification ×100. (H) Perivascular NFTs at the sulcal depths of frontal cortex, case 3, AT8 immunostaining, original magnification ×200. (I) Multiple areas of perivascular NFTs, case 2, AT8 immunostaining, original magnification ×100. (J) Small blood vessels in the thalamus show prominent perivascular lymphocytic cuffing (asterisk) whereas a neighboring medium-sized artery shows focal degenerative calcification of the blood vessel wall (arrow), case 4, luxol fast blue-hematoxylin and eosin stain, original magnification ×200. (K) A medium-sized vessel in the thalamus shows lymphocytic infiltration of the vascular wall with hemosiderin-laden macrophages (asterisk), case 4, luxol fast blue-hematoxylin and eosin stain, original magnification ×200. (L) Focus of dystrophic calcification in the white matter (open triangles), case 4, luxol fast blue-hematoxylin and eosin stain, original magnification ×400. APP, amyloid precursor protein; NFTs, neurofibrillary tangles; CTE, chronic traumatic encephalopathy.

consistent with neuroimaging studies of blast-injured service members showing white matter abnormalities and cerebral glucose hypometabolism [52–56]. The pathological changes found after blast are also strikingly similar to the pathological findings found in young athletes exposed to sports-related impact injuries [20]. The histological parallels suggest that similar biomechanical mechanisms underlie concussion and blast-related neurotrauma [20]. Experimental blast neurotrauma mouse models using wild-type C57BL/6 mice provide additional evidence linking the two types of trauma [20,41]. Two weeks after wild-type mice were exposed to a single blast, neuropathological analysis demonstrated hyperphosphorylated tauopathy, myelinated axonopathy, microvasculopathy, astrocytosis, and microgliosis that in several ways recapitulated human CTE pathology. These neuropathological changes were associated with hippocampal-dependent learning and memory deficits that persisted for at least 1 month and correlated with impaired axonal conduction, which also mirrors some of the clinical aspects of human blast mTBI [20]. Moreover, a recent study in C57BL/6 mice demonstrated acute elevations of p-tau and cleaved tau species after a single blast exposure; these elevations were significantly higher than levels in similarly anesthetized, sham-treated mice and persisted for at least 30 days after blast exposure [57].

1.2. Chronic effects of TBI

1.2.1. Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis

Moderate-to-severe TBI is associated with progressive atrophy of gray and white matter structures that may persist months to years after injury [58,59]. In addition, multiple studies support a link between single moderate-severe TBI and Alzheimer's disease (AD) [60,61], Parkinson's disease (PD) [62], and amyotrophic lateral sclerosis (ALS) [63,64]. In a meta-analysis of 15 case-control studies, males who had a single head injury associated with LOC had a 50% increased risk of AD dementia [60]. A longitudinal study involving World War II Navy veterans also demonstrated increased risk for AD in late life with increasing TBI severity [61]. Veterans with severe TBI were 4 times more likely to have AD, whereas veterans with moderate TBI were twice as likely to have AD in late life compared with controls [61]. No increased risk was found for veterans who had a mild TBI. Some studies have also suggested that TBI is associated with an earlier onset of AD [65]. An analysis of 1283 TBI survivors found that the time to onset of AD was significantly reduced in those who sustained a TBI compared to a control population [66]. Moreover, an autopsy study of long-term survivors of single moderate-severe TBI found significantly increased p-tau and neuritic Aß plaque pathology compared to uninjured controls suggesting that a single TBI may accelerate the development of AD-type neurodegeneration [67]. In addition to AD, a link has been suggested between TBI and PD. In a case-control study, data from the Rochester Epidemiology Project were used to identify 196 subjects who developed PD and to compare to controls matched for age and gender. The frequency of head trauma was significantly higher in PD cases compared with controls (odds ratio [OR] 4.3). The OR for PD was also substantially increased (11.0) in subjects who experienced mTBI with LOC or more severe TBI [62]. Because Parkinsonian symptoms may result from neuronal loss in the substantia nigra associated with either accumulation of α-synuclein in Lewy bodies, as occurs in PD, or p-tau inclusions in the form of NFTs, as occurs in CTE and AD, it is possible that multiple pathologies contribute to the increased frequency of Parkinsonism after TBI. Trauma has been considered as a possible trigger of ALS neurodegeneration as well [63,64,68]. Literature points toward a trend not only between CNS trauma and the development of ALS, but also between a smaller number of years between the last injury and ALS diagnosis and older age at the last injury and the development of ALS [64]. In a case-control study of 109 cases of ALS and 255 controls, Chen and colleagues [63] found that having experienced repeated head injuries or having been injured within the 10 years before diagnosis was associated with a more than 3-fold higher risk of ALS (OR 3.1; 95% confidence interval [CI], 1.2–8.1; and OR 3.2; 95% CI, 1.0–10.2, respectively), with a slightly elevated risk for the interval 11–30 years. The authors further performed a meta-analysis of eight previous ALS studies and estimated a pooled OR of 1.7 (95% CI, 1.3–2.2) for at least one previous head injury.

1.2.2. Chronic traumatic encephalopathy

Repetitive mTBI is associated with CTE [8–20]. CTE is clinically characterized by mood and behavioral disturbances, progressive decline of memory and executive functioning, and cognitive deficits that eventually progress to dementia over the course of several decades [14,17,69,70]. Mood and behavioral disturbances typically include depression, apathy, impulsivity, anger, aggression, irritability, and suicidal behavior [14,17,69]. At the present time, there are no validated clinical criteria to aid the clinician in differentiating CTE from AD or any other neurodegeneration associated with aging; however, in CTE, mood and behavioral symptoms often appear in an individual's 20s, 30s, and 40s, ages far younger than the typical age at onset of neurodegenerations such as AD. Similar to many neurodegenerative diseases, CTE can only be diagnosed definitively at postmortem neuropathological examination [14,17,69]. The most commonly observed gross pathologic features of CTE are generalized cerebral atrophy with a predilection for the frontal, temporal, and medial temporal lobes; thalamic and hypothalamic atrophy; shrinkage of the mammillary bodies; enlargement of the lateral and third ventricles; thinning of the corpus callosum; cavum septum pellucidum often with fenestrations; and pallor of the substantia nigra and locus coeruleus [17].

CTE is a tauopathy, and microscopically there are widespread deposits of p-tau protein as NFTs and disordered neurites throughout the brain [14,17]. Two hallmark microscopic features of CTE, features not found in other tauopathies, are that the p-tau pathology in CTE is (1) perivascular and (2) irregularly distributed in clusters at the depths of cortical sulci. P-tau is also commonly found in the subpial astrocytes at the sulcal depths, as astrocytic tangles, and as axonal varicosities and neuropil threads in the white matter.

Studies in athletes suggest that there is a stereotyped progressive increase in p-tau pathology in CTE that increases with time [17]. P-tau pathology begins focally as perivascular clusters of NFTs, usually at the sulcal depths of the frontal, septal, insular, temporal, or parietal cortices (Stage I). As the disease progresses, multiple discrete clusters of perivascular p-tau NFTs are found in the sulcal depths as well as NFTs in the superficial layers of adjacent cortex (Stage II). In Stage II CTE, the nucleus basalis of Meynert and locus coeruleus usually show neurofibrillary degeneration, but the medial temporal lobe structures (entorhinal cortex, amygdala, hippocampus) are generally spared. In Stage III CTE, NFTs are frequent in the medial temporal lobe, and there is spreading involvement of the frontal, temporal, parietal, insular, and septal cortices. NFTs are usually also found in olfactory bulbs,

hypothalamus, thalamus, mammillary bodies, substantia nigra, and raphe nuclei as well as the nucleus basalis and locus coeruleus. In Stage IV CTE, NFTs are distributed widely throughout the brain, with increasing myelinated fiber and axonal loss in the white matter. Axonal loss and myelin pathology is present at all stages of CTE and progresses with CTE severity. Most CTE cases also demonstrate TDP-43 immunoreactive intraneuronal and intraglial inclusions and neurites. Neuroinflammation is another consistent feature of CTE, and activated microglia are found throughout the subcortical white matter accompanied by a robust astrocytosis. β-amyloid (Aβ) deposits are only found in 40–50% of CTE cases, are significantly associated with age at death, and are not a characteristic of early CTE. In CTE, Aβ is found predominantly as diffuse plaques in low densities. α-Synuclein-positive Lewy bodies are found in approximately 20% of CTE cases and are significantly associated with the age of the subject at death [17].

Of the 110 cases neuropathologically diagnosed with CTE at the Boston VA TBI Brain Bank, CTE has been diagnosed in 23 veterans (Table 1, Fig. 2). Sixteen veterans with CTE were accomplished athletes, including nine former NFL players, one former semiprofessional football player, three former professional boxers, one former Army rugby player, one former Army boxer, and an amateur hockey player. Of those, three were also diagnosed with AD, three with PD, and one with motor neuron disease. Two nonathlete veterans who experienced a moderate to severe TBI from an assault or motor-vehicle accident while in service (one intraparenchymal TBI with persistent, poorly controlled posttraumatic epilepsy, one spinal cord injury) were also diagnosed with CTE (Fig. 2).

1.3. Relationship between postconcussive syndrome, chronic traumatic encephalopathy, and posttraumatic stress disorder

It has been increasingly recognized that there is a frequent association of mTBI and PTSD in modern warfare [2]. Of 2525 U.S. Army infantry soldiers surveyed after deployment to Iraq for 1 year, 44% of the soldiers with mTBI and subsequent LOC met criteria for PTSD [2]. However, it is often difficult to distinguish PTSD from PCS [72], and there is considerable overlap between PTSD and CTE, especially in the early stages. Combining our experience at VA Boston with that of Omalu [19], 80% (4 of 5) of OIF/OEF/OND veterans exposed to blast injury with neuropathologically verified early CTE were also diagnosed with PTSD. PCS, CTE, and PTSD are all characterized by neuropsychiatric symptoms indicative of frontal lobe dysfunction, including alterations in working memory, planning, multitasking, complex decision-making, judgment, empathy, executive function, impulsivity, emotional lability, and disinhibition, as well as changes in personality, social behavior, and sleep [72,73]. Recently, using a model of blast overpressure injury in rats, Elder and colleagues demonstrated that blast injury induced under anesthesia produced PTSD-related

Table 1
Subject demographic information

Subject	Age, years	Race/ethnicity	Sex	Exposure to TBI	CTE stage	Other pathology	Cause of death	PTSD
1	60–69	C	Male	NFL	IV	AD	FTT	
2	70–79	C	Male	NFL	IV	AD	FTT	
3	80–89	C	Male	Amateur hockey	IV	AD, PD	FTT	
4	70–79	C	Male	NFL	IV	PD	Cardiac	
5	70–79	C	Male	NFL	IV		FTT	
6	80–89	AA	Male	NFL	IV		FTT	
7	80–89	AA	Male	NFL	IV		Respiratory failure	
8	70–79	C	Male	NFL	IV		Respiratory failure	
9	80–89	C	Male	NFL	II		Cardiac	
10	90–99	C	Male	NFL	IV		FTT	
11	80–89	C	Male	Semiprofessional football	IV		FTT	
12	60–69	C	Male	Army rugby	IV	PD	FTT	
13	70–79	C	Male	Professional boxing	IV		FTT	
14	70–79	AA	Male	Professional boxing	IV		Pneumonia	
15	90–99	C	Male	Professional boxing	IV		FTT	
16	40–49	C	Male	Army boxing	III	MND	Respiratory failure	
17	80–89	C	Male	Assault, posttraumatic epilepsy	III		Pneumonia	
18	70–79	C	Male	MVA, assaults	III		Pneumonia	
19	20–29	C	Male	IED blast	I		GSW	PTSD
20	20–29	H	Male	IED blast, HS football	I		Hemorrhage	PTSD
21	40–49	C	Male	IED blast	II		Aneurysm	
22	30–39	C	Male	IED blast, HS football	II		Overdose	PTSD
23	20–29	C	Male	Military concussion, HS football	I		Suicide	PTSD

Abbreviations: AA, African American; AD, Alzheimer's disease; C, Caucasian; CTE, chronic traumatic encephalopathy; FTT, failure to thrive; GSW, gunshot wound; H, Hispanic; HS, high school; IED, improvised explosive device; NFL, National Football League professional football; PD, Parkinson's disease; PTSD, posttraumatic stress disorder; MND, motor neuron disease.

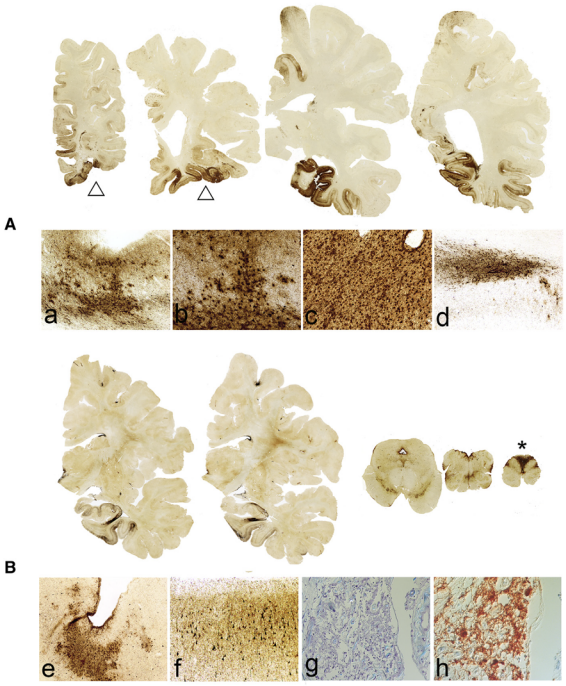

Fig. 2. CTE in two nonathlete veterans. (A) A 77-year-old veteran experienced a severe TBI with LOC during an assault while in service, resulting in intraparenchymal cystic cavities with calcification in the left inferior frontal cortex, left hippocampus, and left calcarine cortex (open triangles). Afterward, he developed poorly controlled posttraumatic grand mal epilepsy that resulted in multiple visits to the emergency department for mTBI. At autopsy, he was found to have a marked tauopathy, most severe in the areas surrounding the traumatic lesions, which was strikingly perivascular, most severe at the depths of the sulci, and affected the white matter and subpial regions. (A) Whole-mount, AT8-immunostained, free-floating coronal sections, original magnifications (a) ×100, (b) ×200, (c) × 200, and (d) ×100. (B) An 82-year-old veteran suffered a TBI and cervical spinal injury in a motor-vehicle accident while in service. Upon discharge, he was involved in multiple assaults as a police officer that eventually resulted in permanent disability and quadriplegia. At autopsy, his brain showed p-tau-immunoreactive NFTs and neurites in an irregular, multifocal distribution in the frontal and temporal cortices, with a predilection for sulcal depths and perivascular, periventricular, and subpial regions diagnostic of Stage III/IV CTE. The posterior columns in the medulla showed intense p-tau immunoreactivity (asterisk). In addition, his cervical spinal cord from C2 and below was replaced by loose neuroglial tissue that showed intense immunoreactivity for p-tau. (B) Whole mount, AT8-immunostained, free-floating coronal sections: (e) irregular clusters of p-tau NFTs at depths of sulcus, original magnification ×40; (f) p-tau NFTs in the superficial frontal cortex, original magnification ×100; (g) loose neuroglial tissue at C2 level of the spinal cord, luxol fast blue-hematoxylin and eosin stain, original magnification ×200; (h) neuroglial tissue at C2 level of the spinal cord, AT8 immunostaining, original magnification ×200. CTE, chronic traumatic encephalopathy; TBI, traumatic brain injury; LOC, loss of consciousness; p-tau, hyperphosphorylated tau.

behavioral traits, suggesting that the biological aspects of blast injury could evoke PTSD behaviors in the absence of psychological stressors [74].

The co-occurrence of symptoms of mTBI, PCS, PTSD, and CTE; the symptom overlap among the disorders; and accumulating evidence that the neuropathological foundations of each may be more convergent than previously recognized have fueled controversies regarding how to best to provide care for veterans and military service members. Clearly, understanding the importance of microstructural physical brain injury to persistent symptoms after mTBI and the role of physical injury in producing or augmenting psychological stress is a focus of investigation that will help guide proper diagnosis, therapy, and management for veterans.

2. Conclusion

Understanding the effects of military-related mTBI presents numerous challenges. Military mTBI is diverse and difficult to assess, and no validated, objective biomarkers of the acute injury exist. Acute mTBI, whether from concussion or blast, is characterized by physical changes in the brain, including multifocal axonal injury, microvascular damage, neuroinflammation, and elevations in p-tau. Although these changes are generally considered to be reversible and to improve or resolve with time and rest, no well-established methods to monitor status or judge prognosis have yet been identified. Understanding rehabilitative strategies or treatments that will facilitate more rapid and complete recovery from acute mTBI are obviously needed; these restorative practices might well focus on mechanisms that promote innate neuroplasticity, such as graded exercise, restorative sleep, and nutritional support. Repetitive mTBI can sometimes provoke the development of CTE, as has been demonstrated in veterans of the Iraq and Afghanistan conflict exposed to explosive blast and in other veterans who were exposed to repetitive concussive injury often in conjunction with the play of sports. The contribution of genetic, environmental, and other exposure factors to the risk of CTE after mTBI remains to be determined. In addition, some individuals with CTE are also diagnosed with PTSD, illustrating the symptom commonalities between the two disorders and possibly signifying shared pathogenetic foundations. The development of a new national PTSD brain bank, under the auspices of the National Center for PTSD, in conjunction with continued neuropathological analysis of mTBI, will promote better understanding of the neuropathological, biochemical, and molecular underpinnings of PTSD, mTBI, and CTE and the interrelationship among the disorders.

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In vivo tau imaging: Obstacles and progress☆

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Abstract The military conflicts of the last decade have highlighted the growing problem of traumatic brain injury in combatants returning from the battlefield. The considerable evidence pointing at the accumulation of tau aggregates and its recognition as a risk factor in neurodegenerative conditions such as Alzheimer's disease have led to a major effort to develop selective tau ligands that would allow research into the physiopathologic underpinnings of traumatic brain injury and chronic traumatic encephalopathy in military personnel and the civilian population. These tracers will allow new insights into tau pathology in the human brain, facilitating research into causes, diagnosis, and treatment of traumatic encephalopathy and major neurodegenerative dementias, such as Alzheimer's disease and some variants of frontotemporal lobar degeneration, in which tau plays a role. The field of selective tau imaging has to overcome several obstacles, some of them associated with the idiosyncrasies of tau aggregation and others related to radiotracer design. A worldwide effort has focused on the development of imaging agents that will allow selective tau imaging in vivo. Recent progress in the development of these tracers is enabling the noninvasive assessment of the extent of tau pathology in the brain, eventually allowing the quantification of changes in tau pathology over time and its relation to cognitive performance, brain volumetrics, and other biomarkers, as well as assessment of efficacy and patient recruitment for antitau therapeutic trials.

Keywords: Alzheimer's disease; Chronic traumatic encephalopathy; Tau; Tauopathies; Molecular neuroimaging; Neurodegeneration; Radiotracer design

1. Introduction

Tauopathies is the term used to describe a group of neurodegenerative conditions characterized by the pathologic accumulation of tau aggregates in the brain. Along with Alzheimer's disease (AD) and some variants of frontotemporal lobe degeneration (FTLD), other tauopathies include Down's syndrome, Guam Parkinsonism-dementia complex, frontotemporal dementia with parkinsonism linked to chromosome-17 (FTDP-17), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), and chronic traumatic encephalopathy (CTE) [1–5]. Although all these conditions share tau immunoreactivity in postmortem analysis, they can be composed of different tau isoforms and show distinct histopathologic and ultrastructural differences [2,6].

AD is the leading cause of dementia in the elderly, accounting for 50% to 70% of dementia cases [7], whereas FTLD is responsible for 10% to 20% of cases [8,9]. In AD, the typical macroscopic picture is gross cortical atrophy. Microscopically, there are widespread cellular degeneration and diffuse synaptic and neuronal loss, accompanied by reactive gliosis and the presence of the pathologic hallmarks of the disease: extracellular β-amyloid (Aβ) plaques and intraneuronal bundles of hyperphosphorylated tau aggregates [10–12]. In AD, these tau deposits can be

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recognized histologically as neurofibrillary tangles (NFTs) and neuropil threads, as well as dystrophic neurites in senile plaques, whereas ultrastructurally, they aggregate in paired helical filaments (PHFs) [2,5,13].

CTE is considered to be a slowly progressive tauopathy associated with repetitive (concussive and subconcussive) brain trauma, prevalent among contact sports athletes, physical abuse victims, and military personnel victim to blasts and other injuries in the battlefield [4,14,15]. CTE is clinically characterized by progressive cognitive decline affecting memory and executive function, as well as depression, higher impulsivity and aggressiveness, speech and gait abnormalities, suicidal ideation, parkinsonism, and dementia [16]. Neuropathologically, CTE is distinguished by cerebral atrophy, a fenestrated cavum septum pellucidum, atrophy of the hippocampus, brainstem, and mammillary bodies, and tau inclusions [4]. In CTE, in contrast with other tauopathies, NFTs are observed mainly in superficial cortical layers with a tendency to cluster around deep sulci and involvement of astrocytes [16]. In several cases, transactive response DNA-binding protein 43 (TDP-43) inclusions and Aβ plaques are also present [17].

Tau is found bound to tubulin to stabilize microtubules, which are critical for the axonal support of neurons. Based on the number of tubulin-binding repeats found on the tau protein, six isoforms have been identified [18]. Although the underlying mechanisms leading to tau hyperphosphorylation, misfolding, and aggregation remain unclear, tau aggregation and deposition follows a stereotyped spatiotemporal pathway both at the intraneuronal level [19,20] and in its topographic and neuroanatomic distribution in the brain [5,21–24]. Furthermore, mutations within the tau gene (*MAPT*) have been shown to lead to FTDP-17 [25], providing solid evidence that tau malfunction triggers neurodegeneration and dementia.

Although the prevalent etiologic hypothesis for AD postulates that either misprocessing of the amyloid precursor protein or disruption of its clearance leads to the accumulation of Aβ in the brain in the form of plaques [26], human postmortem studies have shown that it is the density of NFTs and not of Aβ insoluble plaques that strongly correlates with neurodegeneration and cognitive deficits [27–32]. Concurring with the postmortem studies, Aβ burden as assessed by positron emission tomography (PET) does not strongly correlate with cognitive impairment in AD patients [33,34]. Moreover, although age-related limbic NFTs are frequently present in cognitively unimpaired individuals, neocortical NFTs are much less prevalent, in contrast with neocortical Aβ plaques, which appear abundantly in some nondemented individuals [33,35–39]. The lack of a strong association between Aβ deposition and measures of cognition, synaptic activity, and neurodegeneration in AD, in addition to the evidence of Aβ deposition in a high percentage of asymptomatic healthy controls, points to the involvement of other downstream mechanisms, such as tau aggregation and NFT formation, leading to synaptic failure and eventually neuronal loss, indicating that Aβ is an early and necessary, though not sufficient, cause for cognitive impairment in AD [40]. The fact that tau plays a key role in neurodegeneration [25,41–43] has led to the development of disease-specific therapeutic strategies aimed at either inhibiting tau hyperphosphorylation or aggregation or seeking direct stabilization of microtubules [44–52].

In this context, there is a need to develop reliable diagnostic and prognostic biomarkers that can identify incipient focal or diffuse pathology that will allow, when available, early therapeutic interventions. Definitive diagnosis of these neurodegenerative diseases can only be established by examination of the human brain at autopsy. Molecular imaging procedures are suited to overcome the need for a neuropathologic examination to identify the underlying pathology of these diseases. The last two decades have been focused on developing novel Aβ ligands for the noninvasive detection of Aβ deposition in the brain [33,53]. Among these tracers, 2-(1-{6-[(2-[18F]fluoroethyl)(methyl)amino]-2-naphthyl}ethylidene)malononitrile (^{18}F-FDDNP) was the only one reported to bind to not only Aβ deposits but also NFTs [54]. Therefore, a selective and specific tau imaging agent will be necessary to achieve a more profound understanding of the pathophysiology of AD, CTE, FTLD, and other neurodegenerative conditions in which tau plays a role. The development of a selective tau imaging agent will also lead to improvements in differential diagnostic accuracy while accelerating treatment discovery and monitoring of therapeutics.

2. The idiosyncrasies of tau deposition

Tau is normally phosphorylated, and the degree of phosphorylation determines its binding to microtubules. The hyperphosphorylation of tau leads to weaker microtubule binding [55] and an increase of unbound phospho-tau concentration in the cytosol. Hyperphosphorylated tau migrates from the axonal compartment to the somatodendritic compartment [56] where its accumulation leads to the formation of the pathologic tau aggregates in the form of filamentous inclusions [57], found in neurons, astrocytes, and oligodendroglia [58].

There are several obstacles to be surmounted to be able to image tau deposits [59]. In contrast to Aβ, most tau aggregates are intracellular. Furthermore, there are six isoforms of tau, and different combinations of these isoforms are manifested as different clinical phenotypes [60,61]. To complicate matters, tau aggregates are subjected to a wide spectrum of posttranslation modifications such as phosphorylation, nitration, acetylation, glycosylation, truncation, prolyl-isomerization, glycation, ubiquitination, and so forth [62] that, in addition to the combination of different isoforms, lead to diverse ultrastructural conformations and typical pathologic lesions [2,6,63,64]. Another obstacle to be overcome by selective tau tracers is the coexistence of other misfolded

proteins sharing the same β sheet secondary structure, as is in the case of AD in which tau and Aβ are both colocalized in gray matter areas. This issue is further complicated by the much lower brain concentrations of tau than Aβ and aggregates in AD, where the concentrations of tau are, depending on the brain region, ~5 to 20 times lower than those of Aβ [65,66], requiring a radiotracer with high selectivity for tau over Aβ to be successful in AD.

These particular characteristics of tau deposition affect the design of selective tau tracers. For example, the intracellular location of tau aggregates means that a neuroimaging radiotracer has to be able to cross not only the blood-brain barrier (BBB) but also the cell membrane to reach its target, imposing certain constraints in tracer design in terms of lipophilicity and molecular size.

3. Radiotracer design

Useful neuroimaging probes are required to fulfill a number of key general properties: they should be nontoxic lipophilic molecules of low molecular weight (<450) that readily cross the BBB, with rapid clearance from blood and preferably not metabolized, and with low nonspecific binding while reversibly binding to its target in a selective and specific fashion [67–70]. It is also desirable that these novel tau tracers are labeled with isotopes with longer half-lives, such as fluorine 18 (^{18}F; half-life of ~2 hours), that allow centralized production and regional distribution, as is practiced worldwide in the fluorodeoxyglucose (^{18}FDG) supply. Among the aforementioned properties, binding affinity and lipophilicity are the most crucial for in vivo radioligands. Most successful neuroimaging radiotracers show an initial brain uptake above 5% of the injected dose at 2 to 5 minutes after intravenous injection [69]. This brain initial tracer uptake depends on several factors such as cerebral regional blood flow, plasma radiotracer concentration, BBB permeability, free fractions of the radiotracer in plasma and brain, and so forth [69]. Ideally, tracers with $\text{Log}P_{\text{OCT}}$ values between 0.9 and 3.0 are sufficiently lipophilic to adequately cross the BBB [71]. Within this ideal range, although more lipophilic radioligands will display faster accumulation of radioactivity in the brain than less lipophilic ones, they will also be bound by plasma proteins and usually undergo fast metabolism, leading to lower central nervous system uptake.

Exquisite selectivity is required for a tau radioligand. The selectivity required for a particular neuroimaging radiotracer depends on the concentration of available binding sites [68]. As mentioned before, in AD, there are higher cortical concentrations of Aβ than PHF tau. Although in vitro reports have already shown that based on affinity alone, a 3- to 30-fold selectivity for PHF tau is attainable [72–77], simulation studies estimate that a 20- to 50-fold selectivity for PHF tau over Aβ will be required to image PHF tau in vivo [78]. In addition to the initial assessment of safety, brain kinetics, and tracer metabolism, the evaluation of tau tracer selectivity in vivo poses some challenges. In the evaluation of novel neuroreceptor radiotracers, competition and/or displacement studies are used to ascertain selectivity and specificity of the binding. The relatively high density of aggregated tau in the brain requires micromolar concentrations of an unlabeled competitor to effectively compete or displace the tau radioligand, and untoward toxic effects are likely at those high doses. Therefore, validation of tau tracer selectivity relies on comparison of the regional distribution of the tracer in both controls and pathologic cases in parallel with other tracers that while sharing the property of binding to β sheet conformation have been shown to have selective binding to a different aggregated protein such as Aβ or α-synuclein, as well as comparison to the known regional brain distribution of tau aggregates amassed from neuropathologic studies of individuals with the same pathology. Further validation requires relating the binding of the tracer to clinical measures of cognitive impairment or to biomarkers such as gray matter atrophy, cerebrospinal fluid or plasma analytes, or cerebral glucose metabolism known to be directly affected by or correlated to tau deposition. The ultimate validation is attained by direct comparison of the regional distribution of tau as assessed antemortem by PET and the tau regional distribution assessed postmortem at autopsy.

4. Tau imaging tracers

The achievement of Aβ imaging with Pittsburgh compound B (PiB) [79] led to a renewed international effort to develop selective tau radiotracers. Given that the ultrastructural form that tau aggregates adopt in AD is PHF, most of the efforts for developing selective tau imaging radiotracers are focused on PHF tau. It is not clear at this stage if or how well these tracers recognize the other conformations of tau aggregates present in non-AD tauopathies. Although most of the proposed novel PHF tau imaging tracers in recent years originated from research groups working on therapeutic tau antiaggregation or defibrillization agents [72,80–82], the most successful attempts come from research groups concentrated on screening available or novel chemical libraries to identify potential high-affinity selective PHF tau compounds that might be amenable to radiolabeling [83–85].

Several strategies for developing tau imaging agents have been proposed. Based on the structure-activity relationship (SAR) of *N'*-benzylidene-benzohydrazides and their fluorescent staining profile and antiaggregating activity, it has been proposed that higher PHF tau selectivity can be attained by incorporating bulky hydrophilic groups, which prevent binding to Aβ fibrils, into these amphiphilic ligands [80]. Another group, also using SAR and tracer docking simulation studies as a way to address differences in protein composition and structural polymorphism, is proposing to achieve PHF tau selectivity of 2-aryl benzothiazole derivatives by altering the side chain composition of the compounds [72,86]. A group focused on PHF tau therapeutics [50,87] assessed different imidazothiazole, benzothiazole, and pyrimidazole derivatives in primuline displacement

studies and fluorescent studies in both human and tau transgenic mouse brains [81]. One of these derivatives, SKT04-137, was radiolabeled with ^{18}F for biodistribution studies in mice, in which it showed sufficient brain uptake but slow clearance from the brain (2 minute-to-60 minute ratio of 2.9) [81]. A series of thiohydantoin [88], oxindole [89], and styrylbenzimidazole [90] derivatives were designed and synthesized for the detection of tau pathology. Preclinical evaluation of these compounds showed that although all of them displayed somewhat high affinity for NFT in autoradiographic studies, only one of the styrylbenzimidazole derivatives presented with sufficient entry into the brain [90]. Several other scaffolds (e.g., bis(arylvinyl)pyrazines, -pyridazines, and -pyrimidines) have been proposed as potential tau and Aβ imaging agents [91].

4.1. ^{18}F-FDDNP

The first reported human amyloid imaging tracer with nanomolar affinity to Aβ fibrils [92] was ^{18}F-FDDNP (Fig. 1), a radiofluorinated 6-dialkylamino-2-naphthy ethylidene derivative developed, synthesized, and characterized by Barrio et al. at University of California, Los Angeles [93]. ^{18}F-FDDNP was reported to bind to both the extracellular Aβ plaques and the intracellular NFT in AD [94,95] ^{18}F-FDDNP was used to obtain the first human PET images of Aβ in an 82-year-old woman with AD, in whom it showed a differential tracer clearance in different areas of the brain, being slower in areas of Aβ and tau deposition, as pathologically confirmed later at autopsy [92,95]. In a follow-up study, AD patients again demonstrated higher accumulation and slower clearance of ^{18}F-FDDNP than controls in brain areas such as the hippocampus [94]. Retention time of ^{18}F-FDDNP in these brain regions was correlated with lower memory performance scores in patients with AD [96]. These findings were further confirmed in a larger series in which AD and mild cognitive impairment (MCI) participants were successfully differentiated from those with no cognitive impairment [97]. ^{18}F-FDDNP was also used in the assessment of adult Down syndrome patients [98] and football players suspected of CTE [99]. In a non-AD tauopathy such as PSP [99], the retention pattern of ^{18}F-FDDNP in subcortical and midbrain regions followed the known distribution of tau pathology in PSP [100]. It has been shown that ^{18}F-FDDNP also binds prion plaques in Creutzfeldt-Jakob disease [101] and Gerstmann-Straussler-Scheinker disease [102]. Independent direct comparison of ^{18}F-FDDNP with ^{11}C-PIB in monkeys [103] and human subjects highlighted the very limited dynamic range of ^{18}F-FDDNP [104,105]. ^{18}F-FDDNP still remains the only amyloid tracer showing retention in the medial temporal cortex of AD patients, suggesting higher binding affinity of FDDNP to NFT than to Aβ [105]. However, in vitro evaluation of FDDNP in concentrations similar to those achieved

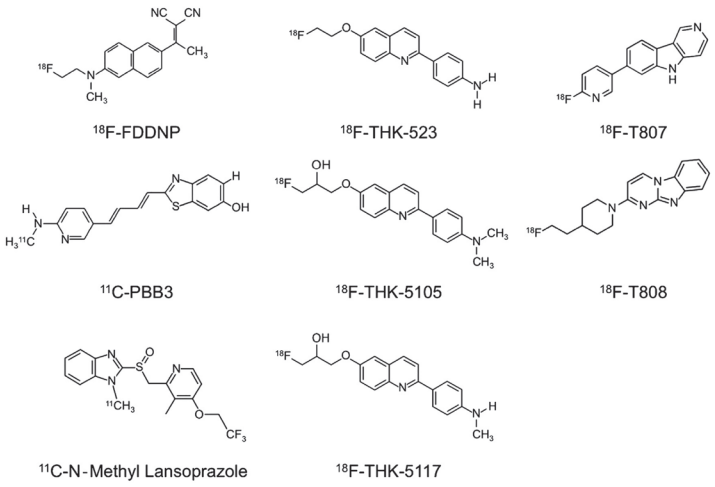

Fig. 1. Chemical structure of currently available tau radiotracers. Most of them have been evaluated in clinical studies.

during a PET scan showed limited binding to both NFT and Aβ plaques [106]. The lack of selectivity of FDDNP for tau might preclude its use in most cases requiring the identification of the misfolded protein responsible of a specific phenotype.

4.2. ^{11}C-lansoprazole

The benzimidazole derivatives lansoprazole and astemizole, based on their in vitro ability to bind Aβ and recombinant tau fibrils, as well as PHF tau isolated from AD brains, were also proposed as potential PHF tau imaging agents [107]. A derivative of lansoprazole, N-methyl-lansoprazole (Fig. 1), with a low nanomolar affinity for tau fibrils was radiolabeled with ^{11}C [108] and tested in mice and nonhuman primates [77]. The initial studies in mice showed no entry of the tracer into the brain, an effect that was reversed by inhibiting the permeability-glycoprotein 1 transporter with cyclosporine. [77] Although studies with rhesus monkeys showed unencumbered entry into the brain [77], no human studies have been reported to date.

4.3. ^{18}F-THK523, ^{18}F-THK5105, and ^{18}F-THK5117

Quinoline and benzimidazole derivatives were identified as candidates for tau imaging tracer by screening small molecules binding to β sheets [74,109,110]. A quinoline derivative, THK523 (Fig. 1), was radiolabeled with ^{18}F and preclinically tested [73]. In vitro saturation binding studies demonstrated that this tracer bound with higher affinity to tau (K_d = 1.67 nM) than to Aβ fibrils (K_d = 20.7 nM). Although autoradiography analysis indicated that ^{18}F-THK523 bound selectively to PHF tau deposits at tracer concentrations [111], fluorescent studies showed that THK523 selectively binds to PHF tau and not Aβ in AD brains, while failing to bind to tau lesions in non-AD tauopathies or to α-synuclein deposits in Parkinson's disease brains [112]. Furthermore, ^{18}F-THK523 can cross the BBB and successfully labeled tau protein deposits in the brain of a tau transgenic mouse model [73]. First-in-human PET studies of ^{18}F-THK523 were performed in AD patients and healthy elderly controls [113]. To assess radiotracer selectivity to tau over Aβ, all participants also underwent a ^{11}C-PiB PET scans. Significantly higher ^{18}F-THK523 retention was observed in the lateral temporal, parietal, orbitofrontal, and hippocampi of AD patients compared with age-matched healthy controls, and ^{18}F-THK523 retention was not associated with the retention of ^{11}C-PiB, suggesting that in vivo ^{18}F-THK523 binds selectively to tau and not to Aβ. Furthermore, ^{18}F-THK523 retention was correlated with cognitive parameters, which is in agreement with postmortem studies showing a strong association of neurofibrillary pathology with dementia severity. Interestingly, in those healthy controls with high Aβ burden as assessed by ^{11}C-PiB, although cortical ^{18}F-THK523 retention was low, ^{18}F-THK523 retention in hippocampus and insula was at the levels observed in AD [113,114]. However, ^{18}F-THK523 retention in gray matter is relatively lower than that in white matter, which does not allow clear visualization of the distribution of tau pathology by visual inspection of PET images [113].

Through compound optimization process, novel ^{18}F-labeled 2-arylquinoline derivatives, ^{18}F-THK5105 and ^{18}F-THK5117 (Fig. 1), were further developed [110]. In vitro binding assays demonstrated higher binding affinity of ^{18}F-THK5105 to synthetic tau fibrils (K_d = 1.45 nM) than to $A\beta_{1-42}$ fibrils (K_d = 35.9 nM). In addition, both ^{18}F-THK5105 (K_d = 2.63 nM) and ^{18}F-THK5117 (K_d = 5.19 nM) showed higher binding affinity for tau-rich AD brain homogenates than ^{18}F-THK523. In an autoradiography analysis of AD brains, laminar distributions of ^{18}F-THK5105 and ^{18}F-THK5117 were observed in the deep layer of temporal gray matter and coincided with NFTs and neuropil threads [110]. Furthermore, the distribution of the binding of these tracers in AD brain sections was completely different from that of ^{11}C-PiB (Fig. 2). First-in-human PET studies of ^{18}F-THK5105 were performed in AD patients and healthy elderly controls [115]. PET images

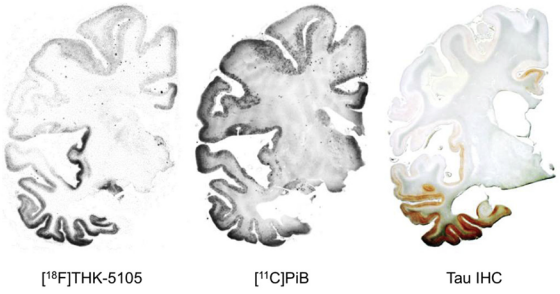

Fig. 2. Autoradiographic studies of contiguous AD hemibrain sections with ^{18}F-THK5105, ^{11}C-PiB, and tau immunostaining, showing the different binding pattern of ^{18}F-THK5105 and ^{11}C-PiB, where ^{18}F-THK5105 binding resembles tau immunostaining (modified from [110]).

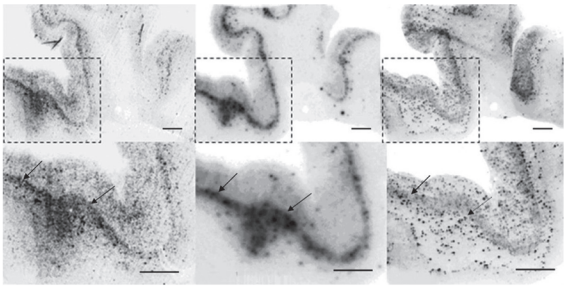

Fig. 3. ^{18}F-T807 autoradiography on brain sections from different groups and its comparison with paired helical filament (PHF) tau and amyloid-β (Aβ) double immunohistochemistry (IHC). ^{18}F-T807 colocalized with PHF tau but not with Aβ plaques. Low (top row) and high magnification from the framed areas (bottom row). Images of PHF tau (left) and Aβ (right) IHC double immunostaining and autoradiogram image (middle) from two adjacent sections (10 mm) from a PHF tau–rich brain (frontal lobe). Positive ^{18}F-T807 labeling colocalized with immunostaining of PHF tau but not with Aβ plaques, as indicated by arrows. Fluorescent and autoradiographic images were obtained using a Fujifilm FLA-7000 imaging instrument (Fuji Photo Film Co., Ltd. Tokyo, Japan). Scale bars, 5 2 mm (Reproduced with permission from *Alzheimer Dement* [116]).

clearly distinguished AD patients from healthy control subjects. In AD patients, ^{18}F-THK5105 retention was observed in those brain areas, such as the mesial and lateral temporal lobes, known to have high tau deposition. Similar to ^{18}F-THK523, ^{18}F-THK5105 retention in AD patients was not associated with ^{11}C-PiB retention but was correlated with dementia severity and brain atrophy [115]. First-in-human PET studies with ^{18}F-THK5117 are currently ongoing. Preliminary data indicate a better pharmacokinetics and better signal-to-noise ratios for ^{18}F-THK5117 than ^{18}F-THK5105.

4.4. *^{18}F-T807 and ^{18}F-T808*

Using in vitro autoradiography to screen and characterize several novel benzimidazole pyrimidines derivatives [84], two novel tracers were identified, ^{18}F-T807 [116] and ^{18}F-T808 (Fig. 1), that bind with nanomolar affinity to PHF tau, displaying more than a 25-fold selectivity for PHF tau over Aβ. (Fig. 3) First-in-human ^{18}F-T807 PET studies in AD patients, MCI, and healthy participants have shown that cortical ^{18}F-T807 retention follows the known distribution of PHF tau in the brain [76] where higher ^{18}F-T807 cortical retention was significantly associated with increasing disease severity, consistent with postmortem studies showing the strong association of tau pathology with severity of dementia [117]. In contrast to ^{18}F-T807, human studies with ^{18}F-T808 in three healthy controls and eight AD patients showed better tracer kinetics than with ^{18}F-T807, but substantial deflurination was observed in some cases [118]. A PET-neuropathology correlation in one of the AD patients who died 5 months after undergoing a ^{18}F-T808 PET scan showed that the postmortem fluorescent PHF tau staining was largely in agreement with the observed in vivo ^{18}F-T808 cortical retention in several brain regions [119].

4.5. *^{11}C-PBB3*

The latest entry in the roster of tau imaging agents is a ^{11}C tracer: ^{11}C-PBB3 (Fig. 1) [120] based on a phenyl/pyridinyl-butadienyl-benzothiazoles/benzothiazolium (PBB) scaffold. These compounds are characterized by a π-electron conjugated backbone with a specific extent ranging from 13 to 19 Å that apparently allows binding to a broad range of AD and non-AD tau aggregates [120]. Several PBB candidates underwent a thorough preclinical evaluation. Although in vitro autoradiographic studies in AD brain sections showed substantial nonselective binding to plaques and tangles, two-photon laser scanning fluorescence microscopy studies in a tau transgenic mouse model showed rapid clearance of the tracer with selective binding to tau tangles. Similar results were observed in micro-PET studies, showing higher PBB3 binding in the spinal cord of the same transgenic tau mouse model [120]. Preliminary clinical studies in three healthy control volunteers and three AD patients assessed with both ^{11}C-PBB3 and ^{11}C-PiB showed a different pattern of brain retention between the two tracers suggesting that at high specific activities, ^{11}C-PBB3 binds selectively to tau, although marked retention of ^{11}C-PBB3 in the venous sinuses was also observed [120]. A ^{11}C-PBB3 PET study in a patient diagnosed with CBD showed tracer retention in the basal ganglia region, suggesting ^{11}C-PBB3 might bind other non-AD tau conformations.

5. Conclusions

Imaging of tau pathology will allow a more profound insight into tau deposition in vivo, facilitating research into the causes, diagnosis, and treatment of major neurodegenerative conditions such as AD, CTE or some variants of FTLD, in which tau plays a role. Although the underlying mechanism remains unknown, CTE and traumatic brain

injury (TBI) have been postulated as risk factors for the development of AD [16,121]. Does TBI accelerate the development of Aβ pathology, of misfolded tau, or of both? [17,121,122] TBI is a growing problem in both military and civilian populations, and the availability of selective tau tracers to measure tau pathology in humans will help to provide insights concerning the pathophysiology of TBI and CTE. The development of selective tau tracers will allow not only the in vivo assessment of regional tau burden in the brain of AD patients but also a means to evaluate its relation to Aβ deposition [73,76,123–125]. By allowing assessment of the time course of tau accumulation to be correlated with current cognitive impairment and predict cognitive decline, it will assist in the evaluation of the neurobiology of AD and non-AD tauopathies. In conjunction with Aβ imaging, it will improve the specificity of diagnosis and allow for early detection of tau pathology in those individuals deemed at risk of developing AD or CTE.

The development of selective tau radiotracers is faced with several challenges [59]. From a tracer development perspective, a candidate radiotracer should be amenable for high specific activity labeling with ^{18}F or other long-lived radioisotopes to allow a more cost-effective and wider application of the technique. These tracers should be lipophilic, nontoxic, small molecules with a high selectivity for tau, preferably with no radiolabeled metabolites that enter the brain. The current research indicates that the design of tau radioligands with nanomolar or subnanomolar affinity for tau with an appropriate lipophilicity is feasible [73,74,77,116,120]. Although nanomolar or subnanomolar affinity for tau is desirable for selectivity and to provide an adequate signal-to-noise ratio, it might also delay reaching steady state, therefore requiring prolonged scanning times. By the same token, although lipophilicity is necessary for the tracer to penetrate the BBB, high lipophilicity might lead to high nonspecific binding and a reduction of the signal-to-noise ratio [68,69].

There are also challenges associated with the idiosyncrasies of tau deposition [59]. For example, in AD, a tau radiotracer needs to be highly selective to overcome higher Aβ concentrations. Even more relevant, different conformations of the tau aggregates, either due to specific tau isoforms or different posttranslational modifications, might prevent the development of a "universal" tau radiotracer that will recognize all types of tau pathologies. As with Aβ [126], the polymorphism of tau aggregates might affect tracer binding, where a radiotracer that is able to identify PHF tau might not be able to bind, or bind with the same affinity, to other known ultrastructural conformations of tau. This is evident in some Aβ imaging reports in which in some cases of familial autosomal dominant forms of AD [127,128] or early stages of Aβ deposition [129], lacking the typical fibrillar Aβ conformation seen in sporadic AD, there was little PiB retention. Moreover, although Aβ's amino acid sequence in human and nonhuman primates is identical, nonhuman primates do not develop the full AD phenotype, and most importantly, the Aβ plaques do not bind PiB [130]. This illustrates the critical role of fibril polymorphism in regards to tracer binding.

Therapies targeting irreversible neurodegenerative process have a better chance to succeed if applied early. Therefore, early detection of the underlying pathologic process is likely to be critical for therapeutic trials aimed at modulating PHF tau [87,131,132]. Tau imaging, by quantifying tau burden in living patients will allow improved selection of those individuals most likely to benefit from disease-modifying therapy, as well as longitudinal patient monitoring and assessment of efficacy, to properly evaluate whether the treatment response is related to a slowdown or reduction in tau deposition.

There is an increasing body of research focused on the development of tau radiotracers that is allowing to establish which radiotracer characteristics are relevant for selective and specific binding to tau deposits in the brain. There is still much to be done. Development of new leads and new and improved radiotracers will be decisive for further progress in the field. The inception of new tau imaging tracers will make possible a more precise characterization of the role of tau deposits in TBI and neurodegenerative conditions, potentially allowing development and assessment of disease-specific therapeutics that will delay or prevent the onset of cognitive impairment among the civilian population and injured military personnel returning from the battlefield.

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