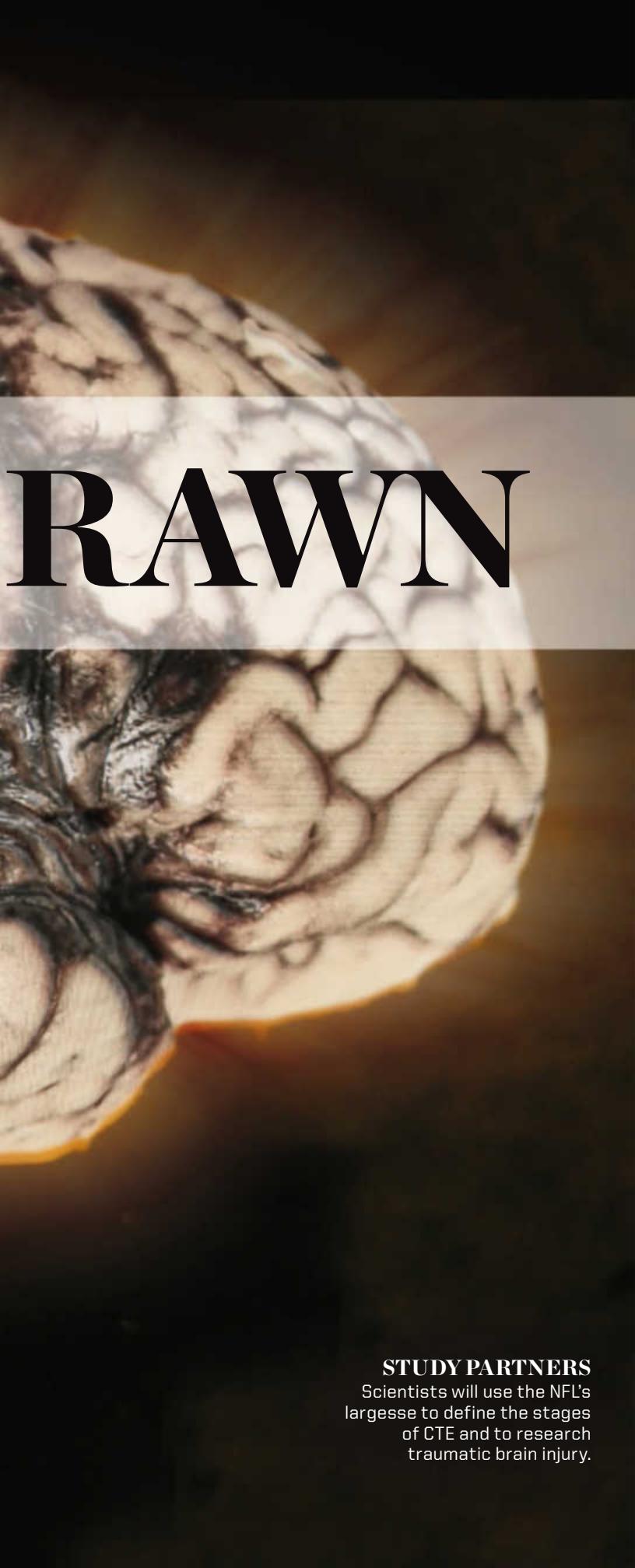


**SPECIAL REPORT**

# **BRAIN AND B**

**TO ADDRESS THE PERCEPTION THAT BRAIN INJURIES ARE EPIDEMIC  
IN THE NFL, THE LEAGUE DONATED MILLIONS TO FUND  
RESEARCH ON THE SUBJECT. SCIENTISTS HAVE LEARNED  
A LOT SINCE, BUT WE STILL CAN'T DIAGNOSE  
CHRONIC TRAUMATIC ENCEPHALOPATHY IN LIVING PEOPLE,  
AND SOME PLAYERS ARE GIVING UP THE GAME IN FEAR  
OF A DISORDER THAT MIGHT NEVER AFFECT THEM**

**BY TOM TAYLOR**



# RAWN

**STUDY PARTNERS**  
Scientists will use the NFL's largesse to define the stages of CTE and to research traumatic brain injury.

RICK FRIEDMAN FOR SPORTS ILLUSTRATED; PHOTO ILLUSTRATION BY SI PREMEDIA

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

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

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

In September 2012, NFL commissioner Roger Goodell announced that the league was donating \$30 million to the National Institutes of Health. It was the single largest donation the league had made in its 92-year history, and it was designed to support research on injuries affecting athletes, with a focus on brain trauma. The donation also offset some of the bad press the NFL was receiving about football's alleged toll on players' brains. The

## SPECIAL REPORT

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

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

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

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

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

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

But when Josh got his midterm report card, his father confronted him. He was struggling in AP math and history. George worried that his formerly straight-A kid had become a lazy teenager. "You don't understand: I can't sleep at night," Josh said. "My head still hurts every day."

Josh stayed home more and more. He holed up in his bedroom, playing video games and trying to sleep. He stopped exercising, stopped hanging out with friends and rarely ate dinner with his family. One day in late January he had a panic attack as his mom was dropping him off at school. Angie took him home. "I locked myself in the bathroom and just sat there,"



## CONCUSSION IS A TRAUMATIC BUT—IF TREATED CONDITION, WHILE CTE IS

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

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

Nothing seemed to work, so Josh's neurologist suggested he get a PET-CT scan of his brain. The family's medical insurance would not cover the procedure, but Angie and George felt they had no other choice. They paid the \$1,500 cost of the scan. On March 28, 2014, a small amount of radioactive tracer was injected into Josh's arm, and a radiation detector created an image of where the tracer collected, showing the structure of his brain. A preprocedure report listed his history as "chronic encephalopathy, traumatic brain injury."

SIMON BRUTY FOR SPORTS ILLUSTRATED



## BACK KICKING

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

**CORRECTLY—RECOVERABLE**

**AN INCURABLE DEGENERATIVE DISEASE.**

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

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

**HARRISON MARTLAND**, a forensic pathologist and the chief medical examiner of Essex County, N.J., called CTE "punch drunk" when he first identified it in boxers during autopsies in 1928. *Dementia pugilistica*, linked almost exclusively with boxing throughout the 20th century, made the leap to football in 2002 when Bennet Omalu, a neuropathologist at the University of Pittsburgh, identified CTE in the brain of Steelers Hall of Fame center Mike Webster, who had died at age 50 and suffered from dementia. Omalu then found CTE in the brains of two more deceased Steelers, Justin Strzelczyk (who died in 2004) and Terry Long (2005).

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

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

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

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

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

Even cutting-edge science cannot yet definitively diagnose Alzheimer's disease in living patients, let alone the far less common CTE. The only way to do that is at autopsy, when the brain can be examined under a microscope. And CTE takes years to develop. At age 16, Josh was almost certainly too young to have the disease.

"We don't have a true handle," says Julian Bailes, chairman of the department of neurosurgery and codirector of the NorthShore Neurological Institute near Chicago. "We don't have the knowledge of how prevalent [CTE] is, of what the incidence is in former players. We just don't know because everybody is sort of self-selected." Because the majority of the brains studied so far have come from players who were exhibiting

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

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

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

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

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

Last March, 49ers star linebacker Chris Borland quit football after his rookie season, citing fears of the long-term risk of brain damage. But did he jump ship too early or too late? He might have hit a genetic jackpot and not be susceptible to CTE at all.

Or the accumulation of hits from youth, college and his single year of pro football might already be causing rogue tau protein to clump inside his brain.

Several NFL veterans have come forward saying that they have been clinically diagnosed with CTE based on symptoms of dementia, including Brent Boyd, a guard with the Vikings, who claims to be the first person alive to have been diagnosed with the disease, and former Vikings linebacker Fred McNeill. McNeill was originally diagnosed with dementia in 2009, then CTE by Omalu in 2010, and finally with amyotrophic lateral sclerosis (ALS), a degenerative disease of the motor neurons, in 2014. Last month he died from complications of ALS.

A study by Peter Nelson, a professor of pathology at the University of Kentucky, published in the *Journal of Neuropathology & Experimental Neurology* in May 2010, found that about 18% of patients with a postmortem diagnosis of dementia did not fit within the National Institute on Aging and Reagan Institute recommendations for the diagnosis of Alzheimer’s disease. ALS, Parkinson’s disease and Alzheimer’s disease are “all characterized by very slow, progressive, steady dysfunction of various parts of the brain,” says Robert Pascuzzi, director of the ALS clinic at Indiana University. “The

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

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

### RACKED BRAINS

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



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

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

lary tangles and by using PET scans to depict the distribution of the marker. McNeill was one of the former players who took part in that research, and results showed evidence of tau protein buildup. If Omalu now finds definitive proof in McNeill’s brain, then PET scans may be a way to diagnose CTE in living patients.

Kun Ping Lu, a professor at Harvard Medical School, and his team have developed an antibody that binds to a form of tau that is suspected of forming tangles and triggering both CTE and Alzheimer’s. This antibody could be used to look for early signs of the disease through a blood test, or as an

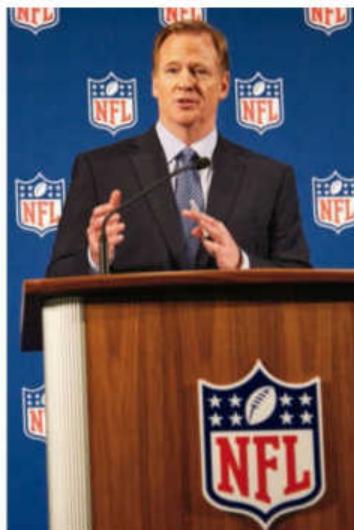
intervention to halt CTE's progress. But the results of these studies might take decades to reach patients, in part because of the long gestation period of the illness, and also because proof still requires an autopsy.

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

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

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

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



## WHY DO SOME ATHLETES DEVELOP THIS PEOPLE MORE SUSCEPTIBLE TO INJURY THAN OTHERS?

to play football or soccer or any other sport in which the head could suffer a blow. "America's problem is not that it plays football," says Uzma Samadani, an associate professor of neurosurgery at the University of Minnesota and a neurotrauma consultant to the NFL, "but that it watches football." According to the NIH, the age-adjusted leading cause of death in the U.S. in 2010 was coronary heart disease, which is strongly linked to obesity. A 2012 paper in *Neurology* concluded that the mortality from cardiovascular disease in a cohort of 3,439 NFL players was 32% less than that in their peers in the general population. The consequences of obesity remain significantly worse than the consequences of playing sports, including collision sports.

As much as Webster's and Seau's stories may illustrate the dangers of underestimating the consequences of head impacts, Josh Plesce's story highlights the danger of overestimating them. □

## ON THE LOOKOUT

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

**NFL** | League-employed spotters sit in a sky box monitoring the action. When they suspect a concussion, they are now authorized to call a medical timeout, stopping the game so medical personnel can attend to a player. The spotters relay any concerns to the team physician, an unaffiliated "neurotrauma consultant" and a trainer, who then evaluate the player. There have been three medical timeouts so far this season.

**NHL** | It too uses spotters. Before this season each club had its own trained concussion spotter. Now teams can use a spotter supplied by the league, who takes mandated online seminars and studies written materials but cannot stop games.

**MLB** | When a concussion is suspected, the athletic trainer is the first responder. The home-team physician then

takes over further evaluation.

### NCAA FOOTBALL

The NCAA's process is similar to the NFL's: Spotters stationed in the replay booth can stop a game when they suspect a concussion and relay information to trainers and physicians.

**NBA** | If a potential concussion occurs, the player is removed from the game by trainers to undergo evaluation by team doctors.

**NASCAR** | When a driver is involved in a crash and his car can no longer roll, he must be taken to the infield, where doctors evaluate him. If his car is not immobilized, the infield doctors can decide whether to evaluate him.

**MLS** | After a concussion is believed to have occurred, the player is removed from the game and evaluated by his team's medical staff, led by the club's neuropsychologist.

—Jeremy Fuchs