Newsweek

Tau Could Be the Key to Monitoring Brain Damage From Concussions

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On October 24, 1896, the Maroon of Lafayette College trotted onto Philadelphia's Franklin Field as the visitors for a football game against the mighty University of Pennsylvania. It was a hard-fought contest, the kind of scrimmage-line grind common before the legalization of the forward pass. Lafayette won, 6–4, upsetting a Penn team that went on to win the national championship, but the biggest news that day concerns what was strapped to the head of Lafayette's halfback.

Known as "the Rose," according to an alumni newsletter, for his "concern with his looks and his eye for the ladies," George Barclay stood 5-foot-9 and weighed less than 160 pounds, and he'd apparently grown tired of banging heads with bigger players. Strapping three pieces of leather over his ears for the Penn game, he launched an arms race—players creating their own protective headgear—that led to mandatory helmets in both college and professional football by 1941.

But it took another 70 years for coaches, players, fans and even doctors to realize that the problem with football collisions isn't the immediate dizziness after a hit but the concussions that can cause lasting and irreparable damage. The Centers for Disease Control and Prevention counts more than 1.6 million sports-related traumatic brain injuries a year, and there is a huge market for preventative products. Brain Pads—"impact-protective" sweatbands—are sold to soccer teams for $10.95 a pop. Then there are dietary supplements that claim to lower concussion risk. These products, which do not require approval from the Food and Drug Administration because they are not pharmaceuticals, have names like Klean Cognitive and Brain Armor.

Football helmets have become a symbol for both the promises and failures of concussion management. In a federal courtroom in New Jersey, a high school football coach is now seeking national class-action status for a lawsuit against helmet makers. Douglas Aronson claims helmet makers used the surge of negative publicity about concussions over the past decade to hype their products beyond scientifically defensible fact. "In their thirst for profits," says the lawsuit, companies "target their concussion reduction marketing to youth football leagues and high school teams, often offering their Riddell Football Helmets at a discount to high-profile high school teams to increase exposure and profits."

Riddell, which has yet to respond in court, declined to comment to *Newsweek*. But no matter the outcome of Aronson's lawsuit, the stage is set for a stampede in what is now the big business of concussion management. Now, almost 120 years after the debut of the football helmet, concussion management is finally on the verge of the next big step forward. Scientists are getting smarter about our brains, and about the role of a mysterious substance called tau.

FINDING THE TAU

Not so long ago, the detection of concussions involved rubbing two fingers over the head to feel for bumps. Today, the process is a little more complex, involving a cadre of cognitive and physical response assessments. And, of course, there's an app for that. For $4.50 per student-athlete, a company called Concussion Vital Signs offers athletic directors a diagnostic system complete with a "Mobile-Enabled Pocket SCAT2 Sideline Assessment Tool." Like several other similar products on the market, the tool functions as a highly evolved version of your doctor's knee hammer, comparing cognitive responses to a preseason baseline.

Tau, though, promises much more accurate diagnoses—and much bigger profits for companies that can harness its potential. One business research firm predicts the cognitive assessment market, which includes concussion screening, will grow from $1.7 billion in 2012 to $5.7 billion in 2018.

Scientists know this much about tau: It's a kind of protein, and it should not be floating around loose in your head. In a complex neurological system often likened to a railroad, tau proteins serve as the "ties" between the "tracks." Essentially, when everything's as it should be, tau proteins are what keep the nerve cells in your brain together, helping various areas of the brain communicate. The more tau knocked loose in the first 12 hours after a head injury, researchers have reported, the more likely something called the Extended Glasgow Outcome Scale may eventually veer away from a score of 8 (good recovery) and toward a score of 2 (vegetative state) or perhaps even 1 (death).

After enough hits or time, or both—and perhaps in conjunction with some other factor (scientists are not sure)—tau proteins can undergo a chemical change and no longer hold nerve cells together. They can become damaged and all tangled up, and they no longer help different parts of the brain communicate. Instead, they seem to get in the way. Damaged tau may play a role in some of the symptoms associated with Parkinsonism and Alzheimer's disease. Some research suggests tangled tau may also indicate the onset of chronic traumatic encephalopathy (CTE), the degenerative disorder associated with dementia, depression and memory loss among an expanding number of former football players.

In 2011, researchers from Milan University and Washington University in St. Louis collaborated on a study correlating high tau levels with "adverse clinical outcomes after severe traumatic brain injury." The researchers argued that tau measurement promised

more easily quantifiable results than, say, tests for memory, reaction speed and fine motor control. But their technique for testing was not exactly convenient: It required inserting a catheter into the brain fluid. For the next few years, the only place where one could make a diagnosis of degenerative CTE was the morgue, which is why it was pathologists who found elevated levels of tau in the autopsies of several recently deceased former NFL players, including David Duerson and Junior Seau.

Researchers around the world raced to find a way to use tau levels in the diagnosis of living patients. Japanese researchers at the National Institute of Radiological Sciences developed a chemical that would attach to tau proteins and show up in brain scans. A Swedish group (in close affiliation with a business called Quanterix) started working on a blood test to measure the tau levels of hockey players.

A groundbreaking moment in tau research came in November 2013, when a medical team affiliated with UCLA diagnosed Tony Dorsett, the then-59-year-old former Dallas Cowboys All-Pro running back, with CTE. This was based on brain scans showing high concentrations of tau. It was the first time a living person was diagnosed with degenerative CTE. "Don't ask me what tau protein is because I don't know exactly what it all is," Dorsett told *The Dallas Morning News*. "All I know is that before, [doctors] could only be able to find tau if you die first and they open up your brains."

Dorsett had suffered from depression and memory loss for many years, and was one of approximately 4,500 ex-NFL players who in 2011 filed a yet-to-be-settled class-action lawsuit against the league for damages related to on-field concussions. He went to UCLA seeking answers: What was the connection between the skull-rattling hits he'd endured in the 1970s and 1980s and the debilitating symptoms he suffered from today?

After examining Dorsett, the UCLA group claimed for the first time to have linked multiple concussions to tau buildup, then to CTE and all the life-sucking symptoms that come with it. The doctor who made the diagnosis, Gary Small, announced the findings to ESPN, capturing the attention of nearly every football player, parent, caretaker and fan.

Small, who declined to speak to *Newsweek*, is a psychiatry professor at UCLA, the founding director of the UCLA Memory Clinic and the director of the UCLA Center on Aging. He also has a stake in a business called TauMark, according to records on file with the secretary of state of West Virginia. In promotional materials posted online, the

company claims that a "TauMark brain PET scan is the only available noninvasive method to measure the distribution and level of brain tau (your 'T-number') so doctors can detect problems early and monitor treatments."

On November 5, the same day as his announcement on ESPN, Small filed notice of a new clinical trial with the U.S. National Institutes of Health. Building on his research with athletes, his new study proposes to "detect tau deposits in the brain of living subjects at risk for CTE.... This project aims to expand these findings to the population at large," he wrote.

In other words, your kid's Pee-Wee football team could get the same treatment made available to the likes of Tony Dorsett.

Small's proposal does not mention the potential market for TauMark, but in publicity materials, the firm says it can "help athletes make informed decisions about treatment options and lifestyle habits so they can optimize their brain health as they age."

RUSHING IT?

"Tau Test Can Save Your Brain," declared a headline last month in a syndicated column by America's doctor (and TV megastar) Mehmet Oz.

Maybe. In April, Bristol-Myers Squibb quietly acquired San Francisco–based biotech firm iPierian in a deal worth up to $725 million, primarily to tap into its pipeline of antibodies to treat tau-related diseases. It is one of many efforts to create the first blockbuster tau drug. NeuroPhage Pharmaceuticals of Cambridge, Massachusetts, just announced that it has engineered molecules to treat neurological disorders by attacking tangled tau as well as other "misfolded proteins."

The arrival of a locker room tau kit seems imminent. And why not? If you could quickly diagnose tau-related problems, you could, in theory, make more informed decisions about whether or not to send a player back onto the field or court. But many experts feel the marketing is outpacing the science. "We have a long way to go to understand the causal link," says Jacob Resch, a kinesiologist at the University of Texas-Arlington. "Parents, athletes and coaches still need to be wary of a lot of these claims being made. There're a lot of things we don't know."

And there are concerns even if the link is established. Dr. Michael Collins, of the highly regarded University of Pittsburgh Medical Center Sports Medicine Concussion Program, fears that coaches will see a big hit on the field, grab their scanners and get a quick tau reading on the sideline. If it comes back negative, the player will be sent back into the game. But right now, he says, the science isn't there to justify that decision.

And it could be a momentous decision. Each of us gets only one brain, housed in a shell so disappointingly fragile as to suggest some purposeful design in that fragility, and evidently dependent to some extent on this substance called tau. We would be smart, some experts say, to proceed with humility, and caution, and awe.