The Race Is on for a 'Concussion Pill' as New NFL Season Begins

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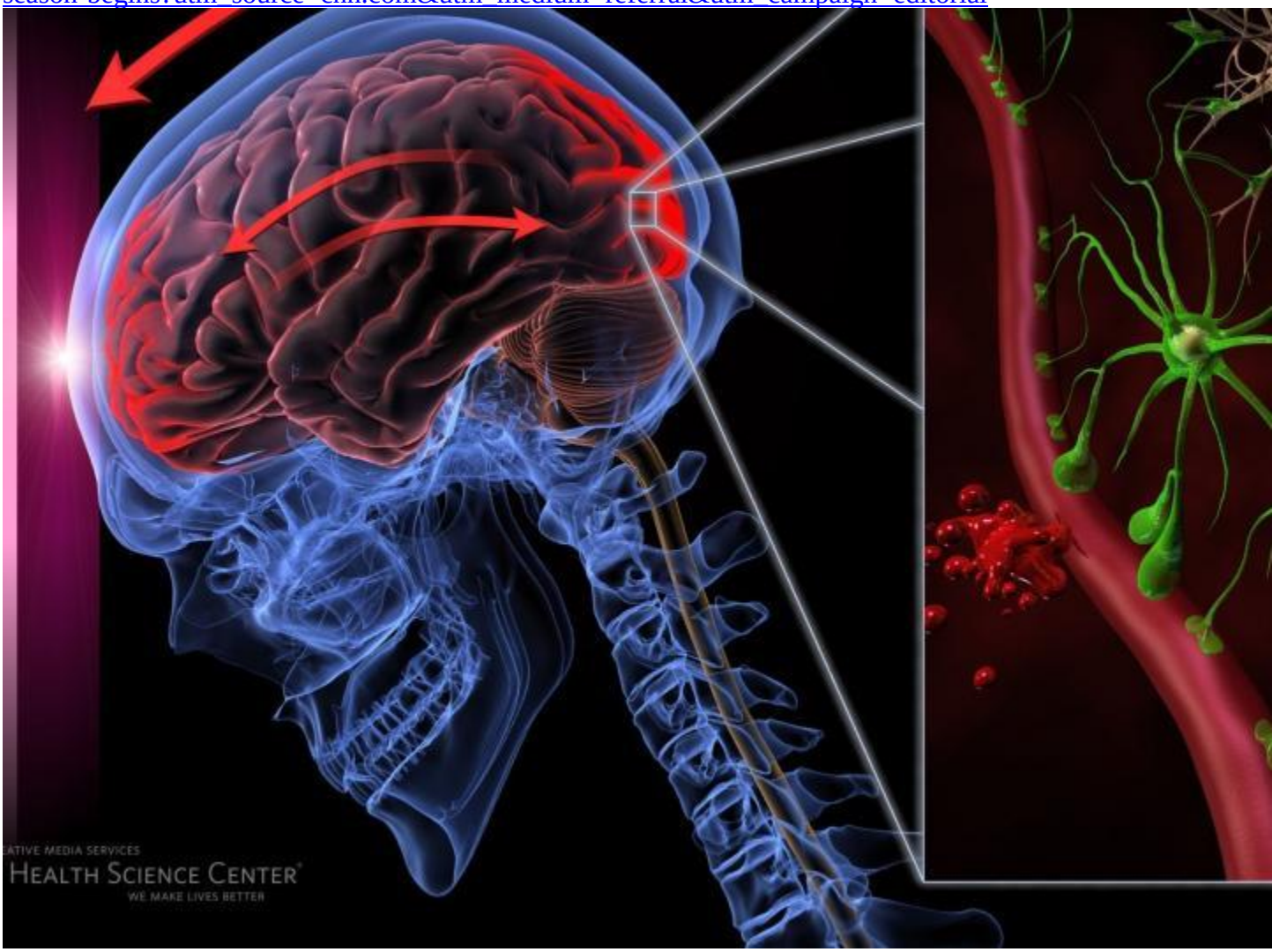


Courtesy of Astrocyte Pharmaceuticals

Imagine a pill that could make all the NFL's concussion problems go away.

Imagine a treatment—or a battery of treatments, therapies and tools—that eradicates CTE and makes concussions only slightly more mysterious and threatening than sprained ankles.

Imagine equipment that provides swift, precise diagnoses, pills that provide immediate relief and speedy recovery and medications that can actually repair the damage that causes long-term brain damage.

Imagine wonder drugs that improve (and sometimes save) the lives of not only football players, but also of military veterans, crash victims, stroke victims, opioid addicts and perhaps even those with Alzheimer's disease.

It sounds like science fiction. Or a Roger Goodell daydream. But the race to find just such treatments is already underway, and significant progress has already been made.

The "concussion pill" may be coming soon.

"This is coming in 2025 if all goes well," Dr. William Korinek, the CEO of Astrocyte Pharmaceuticals, said of a drug that turbocharges the brain's ability to heal its own damage.

Dr. Kun Ping Lu, who's working on a medication that destroys the compounds that cause brain damage, isn't quite that optimistic but said, "I hope it should be here in 10 years."

From the sound of it, there appears to be hope for concussion victims and CTE sufferers on the not-too-distant horizon.

But right now, that hope spends most of its time running through laboratory mazes.

Of Mice and Men

If you give a mouse enough concussions, it becomes antisocial, reckless...or even suicidal.

The search for a concussion pill is largely in the "mouse model" phase right now. Researchers expose rodents to tiny (for us) pressure blasts which cause major (for them) damage, then study the results, either anatomically through autopsies or behaviorally through experiments.

Ravens offensive lineman John Urschel retired after only three seasons this summer, reportedly after the release of a new study that linked CTE with playing football.George Gojkovich/Getty Images

It turns out that mice with traumatic brain injuries (TBIs) suffer many of the same symptoms which now plague former football players.

Dr. Korinek described one such test. A so-called "teenage" mouse is given five concussions within a week. The mouse is then allowed to

grow to its equivalent of middle age. Then the "Three Chamber Social Interaction Test" is applied. A "stranger" mouse is placed in one section of a three-chambered apparatus, behind a glass plate. The afflicted mouse then has its run of the other two chambers.

"Mice are social creatures," Dr. Korinek explained. "The mouse is going to see that stranger mouse and check it out."

A healthy mouse will spend twice as much time in the chamber next to the stranger as in the third, isolated chamber. But the mouse who suffered multiple concussions in its youth behaves differently.

"They may check out the other mouse, but they end up spending equal amounts of time between the two chambers," Dr. Korinek explained. "They don't have the same curiosity or interaction that you see in a normal mouse who has not been injured."

The human analog is both obvious and chilling. Former football players with CTE symptoms, most notably Junior Seau, are known to isolate themselves socially, which only compounds their physical and emotional struggles.

Dr. Lu, a professor of medicine at Harvard University, described an even more revealing experiment, one in which mice with TBI are placed in mazes that contain high-elevation, exposed "arms."

"Mice are afraid of heights and afraid of open space," Dr. Lu explained. "Because in nature, mice in the open are going to get eaten by eagles."

Healthy mice instinctively avoid the high, open portions of the maze, just as they avoid scurrying across the middle of your kitchen floor in broad daylight. But the afflicted mice behave very differently.

"After traumatic injury, it doesn't matter. Open arm? Closed arm? They just do it, because they don't sense that by going out into the open arm there's a risk."

Normal mice are afraid of heights. But mice with brain injuries are much more reckless.Courtesy of Astrocyte Pharmaceuticals

Again, the human analog is clear and frightening. Individuals who suffer CTE symptoms often engage in compulsive, sometimes dangerous behavior, throw themselves through glass doors, even attempt or commit suicide: all signs of the brain's risk-assessment software going haywire.

But these lab mice are not suffering in vain.

Dr. Korinek's research has resulted in a medication that prevents the onset of anti-social mouse behavior. "If we treat these mice within a half-hour of their concussions, then look at them again when they are "40 year olds," they don't have those symptoms," he explained.

Dr. Lu and researchers at Harvard have created a different treatment: an antibody that keeps mice from running blithely beneath the potential path of a hungry raptor. "After the antibody treatment, they're back to normal. When they see the open arm, they don't go out there."

These drugs aren't just anesthetizing the mice or masking symptoms. While the drugs work differently, they each perform a similar function: they make the brain better at healing itself.

Good Guys, Bad Guys, Helpers and Pruners

Most of the breakthroughs that led to the current race for a concussion drug occurred in the last decade or so. Neurologists still grapple with misunderstandings and emerging research. Luckily, they have come up with some analogies and metaphors to keep the rest of us from becoming hopelessly lost.

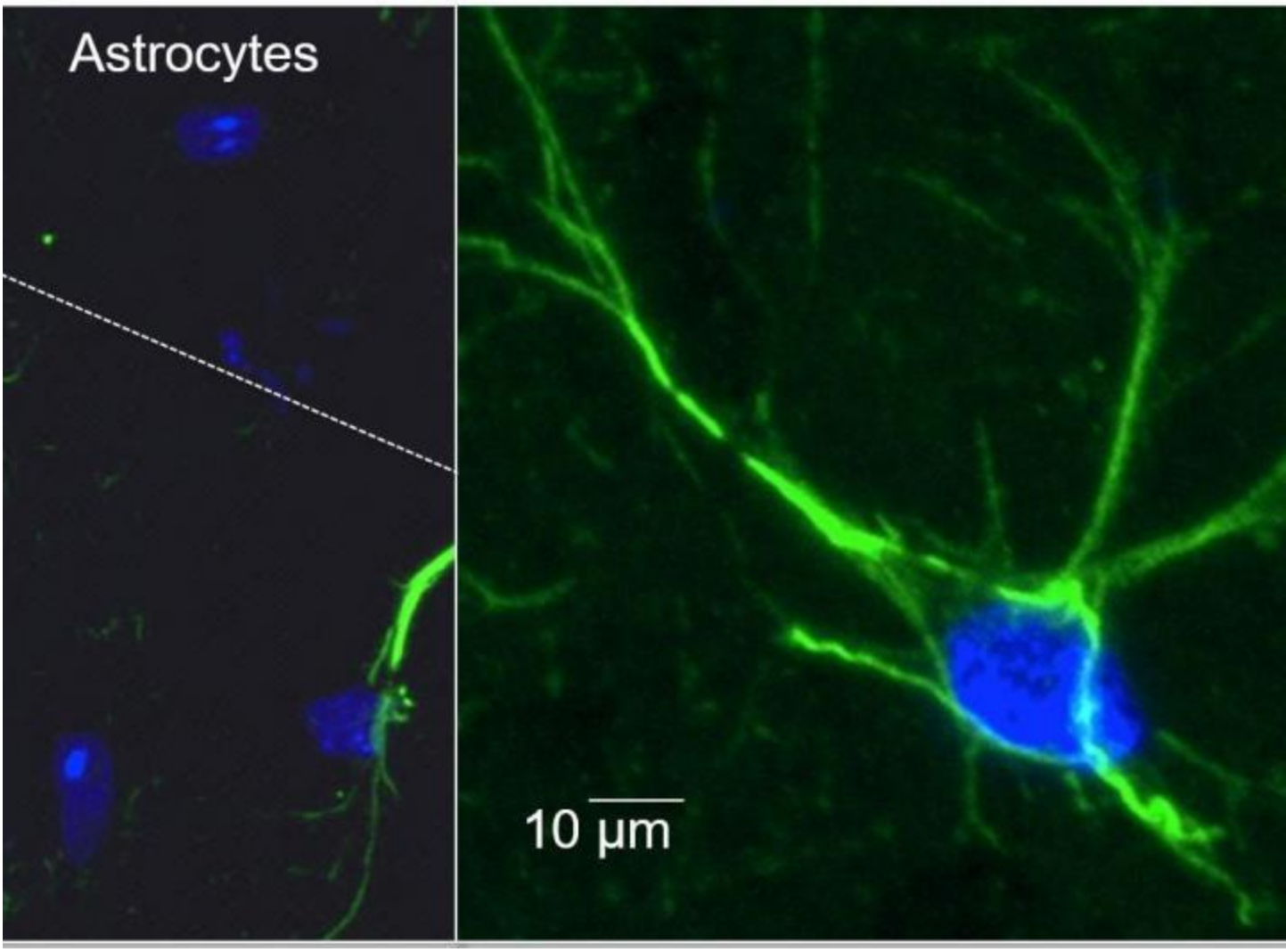
"Think of it like the police," Dr. Lu explained of his research. "The toxic proteins are the bad guys. The antibody can arrest them and not allow them to do damage to the brain."

Dr. Lu was studying the telltale "tangles" in the brains of Alzheimer's patients, the same evidence of severe damage found in the brains of CTE sufferers, and in his research discovered a toxic form of the P-tau protein labeled cis P-tau which becomes prevalent in the brain before the tangles develop. Regular P-tau is helpful to brain function. The toxic cis P-tau is devastating.

If, as Dr. Lu suggested, you think of the brain as a highway, the cis P-tau "basically makes the highway lane collapse, jams the traffic," Dr. Lu said. "Cars cannot move, the signal cannot transmit and neurons die."

So Dr. Lu developed an antibody that keeps mice from wanting to become eagle food. It's similar in principle to a vaccine, "arresting" the "bad guy" without damaging anything else. Because cis P-tau may be one of the agents which cause Alzheimer's disease, the antibody may

have applications that range far beyond treating ex-football players or sufferers of TBI.



Astrocyte cells, depicted here, are the focus of Dr. William Korinek's research into combatting the effects of brain trauma. Courtesy of Astrocyte Pharmaceuticals

Dr. Korinek, meanwhile, focused his research on astrocyte cells, which for decades were assumed to be gap-fillers or insulators for the brain's message-carrying neurons. As it turns out, astrocytes are more than just the rubber around the wires. "The astrocyte has really emerged as the caretaker cell in the brain," he explained.

"It's the astrocytes that are helping clear away the signal to make sure it keeps functioning well. It's turning over or pruning 20 percent of the synapses at all times."

Given plenty of time, astrocytes can prune away the damage suffered during a concussion. But repeated concussions overtax the astrocytes at the cellular level. Dr. Korinek's treatment that makes mice sociable again "helps energize the caretaker cells, recharging their batteries so they are able to function again."

Both treatments show exceptional promise so far. But mouse tau protein is not human tau protein, and the human brain is so much more complex than a rodent brain that there is no guarantee that what works in a laboratory maze will automatically work for a football player coping with CTE. Dr. Korinek's team will soon ramp up experiments to larger mammals, while Dr. Lu synthesizes a human version of the protein that's suitable for human pilot studies.

But while two teams of researchers perform miracles with mice, others are developing treatments which have gotten results…for some well-known former players.

Infusion Cocktails

Jamie Dukes, former NFL lineman and NFL Network personality turned founder and CEO of Pro-IV, rattles off a laundry list of retired football players and other athletes currently using his treatment. It's a collection of Hall of Famers and Mt. Rushmore types, as well as more recent retirees like Michael Vick, who has gone on record endorsing the Pro-IV DripFusion therapy.

"When I got my first infusion, it was great," Vick said in a radio interview on behalf of Pro-IV. "I played a flag football game that night. No stretching or anything. And I felt like I was 22 again."

Former NFL Network personality Jamie Dukes is now CEO and co-founder of Pro-IV.Courtesy of Jamie Dukes

Dukes isn't shy about boasting what he believes his treatment could do. "This is the lone solution to the opioid epidemic as it stands today," he said.

According to Dukes and his chief neurological surgeon, Dr. Kevin Jackson, a version of the same treatment that makes Vick feel rejuvenated can be used to mitigate the effects of concussions. And this treatment is not 10 years away or trapped in the rat race of mouse mazes. "Before the end of the year, we should have three FDA drug indications for some of our therapies: two for chronic pain and one for our acute concussion protocol," Dukes said.

Dr. Jackson based the treatment on studies which showed that concussions have an impact on micronutrient levels in the brain.

"Magnesium levels fall in the brain after a head injury, regardless of the severity," he explained. "Urinary zinc increases fourteenfold. We know that there are minerals associated with brain function that change after a head injury."

The Pro-IV treatment is essentially a "cocktail" of substances that aim to rebalance those micronutrients, with some anti-inflammatories and non-opioid pain relievers mixed in to treat immediate symptoms. All of the individual ingredients are FDA approved; hence, retired players like Vick can already receive the treatment.

Because Pro-IV reached the market before undergoing full clinical testing, both Dukes and Dr. Jackson are quick to point out that endorsements like Vick's are purely anecdotal evidence of the treatment's efficacy.

There's one clinical study underway with retired football players, another with the Veterans Administration.

Right now, Pro-IV is an intravenous treatment: patients are infused with the substance via a saline bag. It's inconvenient, not covered by insurance and involves needles. Dr. Jackson hopes to reconfigure the treatment into a pill, patch or nasal spray. He also acknowledges the need to determine ideal dosages and do all of the other nitty-gritty medical work that stands between making Michael Vick feel young again and creating a medicine that insurance carriers will cover and can be safely administered to a high school athlete who suffers a concussion.

But Dukes said that there is no shortage of former NFL players willing to take an IV full of substances that haven't officially cleared all of the clinical and governmental hurdles. Such is the fear and urgency among ex-players, due both to the ailments so many of them face and the studies which increasingly link those ailments to CTE.

Of course, there's another substance with well-known mood-altering effects which is also in the midst of a broad but not-quite clinical trial among both NFL players and the public at large.

The Whole Entire Plant

Nate Jackson played six NFL seasons filled with major and minor injuries, yet he needs no traditional medications to get through his days.

"I use cannabis when I am in pain but otherwise lead a medication-free lifestyle," he said.

Nate Jackson is outspoken about the potential benefits of medical cannabis. Courtesy of Athletes For Care

To be clear: when Jackson says "cannabis," he is not referring to some specialized strain of marijuana biologically engineered to treat pain symptoms without the other lava-lamp-and-cookie-binge effects.

"When I say cannabis, I mean the whole entire plant," he said. "Cannabis, marijuana, weed: It's all the same plant."

Jackson is abreast of the research which separates the cannabidiol (CBD) substance in hemp plants, which may have both anti-inflammatory and neuroprotective elements, from tetrahydrocannabinol (THC), the substance that gives marijuana its notorious kick. But in Jackson's estimation, both CBD and THC may have a role in healing the many ailments ex-football players suffer from. "But we're learning that feeling might be helping to heal your body."

The University of Miami received a $16 million grant last October to determine whether CBD mixed with an "NMDA antagonist" (a type of anesthetic) can be used as an effective treatment for concussion and traumatic brain injury.

The Miami study is expected to last five years. Researchers are not yet ready to report any significant results.

"We're doing some basic testing of the properties of the compound in model (i.e. mice) format, in preparation for designing something for human use," Miami researcher Dr. Michael Hoffer said.

Dr. Hoffer's team has had more immediate success with a concussion diagnostic tool: virtual reality goggles that monitor eye movement when a potentially concussed patient tracks a series of moving targets across a virtual field. The goggles have a 95 percent diagnostic rate, according to Dr. Hoffer, and can be used to gauge the severity of the injury and provide feedback during treatment/recuperation.

Diagnostic goggles don't sound like much of a consolation prize when pursuing a marijuana-based concussion cure. But the devices could help take the guesswork out of a medical diagnosis still fraught with subjective elements.

"The pill can't be effective for concussions if you can't diagnose one," Dr. Hoffer said.

While marijuana is regularly prescribed by physicians in some states, its federal status as a Schedule 1 narcotic has slowed study of its medical value..

But Jackson is among many who feel that "weed" could hold the key to a better quality of life for many ex-players.

"I played six years. Chances are that my brain has been altered by the game. But I am not feeling symptomatic. Why am I not? If I do, when will it happen? Did the cannabis I used when I was playing help protect my brain? Is it helping me now? A lot of us say it is helping, but that's just our hunches. We don't know for sure."

Linebacker Luke Kuechly is driven off the field after suffering a concussion in November 2016. Grant Halverson/Getty Images

"You have athletes who are hurting, who have pain and brain damage, and this plant seems to be something that can help them all."

Urgency and Skepticism

Astrocytes. Tau proteins. Micronutrients. CBD and THC. It can be a lot to sift through. Especially for someone who already fears or is starting to cope with the symptoms of traumatic brain injuries or CTE.

Some potential remedies sound too good to be true. Jackson said that former players aren't always equipped to tell the difference between a

treatment with real scientific merit and a patent medicine that is formulated solely to separate them from their remaining NFL dollars.

"Football players have fallen prey to all kinds of silly science," Jackson said. "Snake-oil salesmen, not just with medicine but with business practices, all of that stuff. We have a very bad real-world sense. We've been coddled. We tend to not look really skeptically at people when they offer to help us."

It's hard to be skeptical when you're desperate for a cure. Dr. Lu says that he receives calls and emails from people with TBI affliction who are ready to take his protein antibody. They don't care that it's not human protein; they'll take their chances with mouse protein. Naturally, they are turned down. "That's not ethical and probably will not be effective," Dr. Lu deadpanned.

"Right now, there are no treatments," Dukes said. "What they consider a treatment is: Go in a room, turn the lights off, have everybody whisper to you. That's treatment by definition."

Most current CTE research (as well as the money that fuels it) still focuses on prevention and diagnostic tools like the University of Miami goggles. But "we're going to quickly be at the point where we know concussions are very bad and we can diagnose them accurately, but you can't do anything about it," according to Dr. Korinek.

Soliciting NFL dollars to conduct research, meanwhile, can be a double-edged sword. "They just don't have the credibility in the area," Dukes said, "because when they do anything, it's always viewed as being tainted."

The most encouraging component of concussion "pill" research right now is not any particular breakthrough; it's the fact that so many researchers are making so much progress along so many vectors.

Not all of the treatments will ultimately prove to be safe and effective. But more potential solutions increase the chances of success. "You need a lot of shots on goal in this space," Dr. Korinek said.

Players will be waiting, even if it takes years for those shots to reach the net. "Whenever that comes, it will be helpful," Nate Jackson said. "Guys will hold on. They are all very tough, very stoic."

"We will lose some guys, but we will have some guys who will really benefit from it."

Researchers, meanwhile, are well aware that while their first priority is saving lives, they may also be saving a sport.

"I have two sons who are eight and 10," said Dr. Korinek. "I told them they can't play football until dad's medicine's on the market."

Mike Tanier covers the NFL for Bleacher Report. Follow him on Twitter: @MikeTanier.

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