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What a concussion looks like inside your brain

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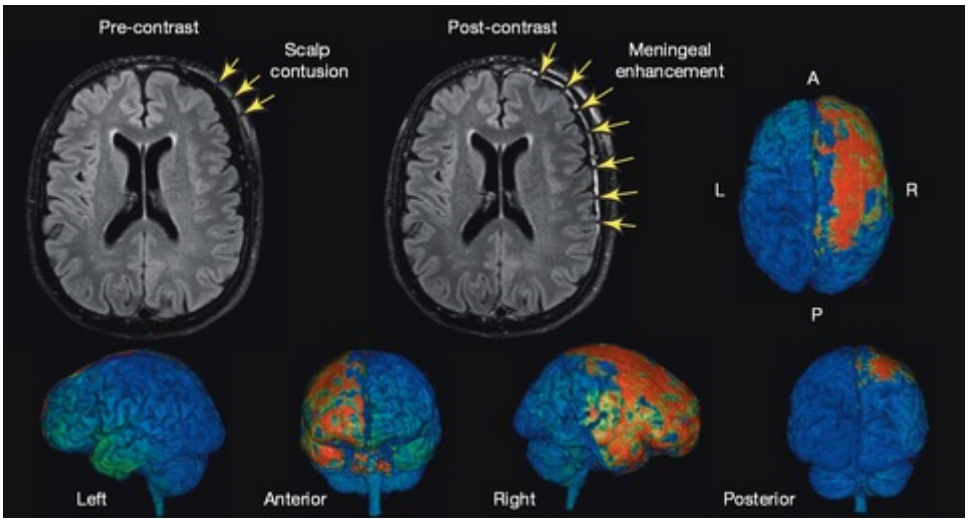

An MRI of a patient's brain 19 hours after a fall shows bleeding and damage to the meninges, the lining between the skull and the brain. Photo by the National Institute of Neurological Disorders and Stroke.

Concussions and traumatic brain injuries have been receiving national attention lately. Former football players reached a $765 million settlement against the NFL stemming from a lawsuit where they claimed to have memory loss, depression, headaches and dizziness after multiple head injuries during their careers. It's not just athletes; the U.S. Department of Defense estimates that 22 percent of all combat injuries are traumatic brain injuries.

But what happens to the brain right after a concussion? Researchers at the National Institute of Health peered into the brains of mice and watched how a traumatic brain injury progresses over a day. Their findings, published in the journal Nature this week, showed that a single concussion can cause cell death in the brain in a matter of hours.

On Sunday, Denver Broncos wide receiver Wes Welker reportedly received a concussion after a hit during a play against the Tennessee Titans. Though Welker will sit out for the Bronco's next game, doctors can do little to treat concussions. Photo by AAron Ontiveroz/The Denver Post via Getty Images

Concussions are difficult to diagnose, said Larry LaTour, a researcher who has been studying traumatic brain injuries at the National Institute of Health. The symptoms -- headaches, dizziness -- are vague, he said. Patients report different symptoms, often at different times after their accident. CAT scans and MRIs can show bleeding and swelling, but previously no one was sure how severe the damage following a bump to the head could be.

So researchers at NIH found a way to watch what happens to the brain when it collides with the skull. (If you're squeamish, you might want to jump ahead.)

Scientists already developed a technique to thin a mouse skull until it is see-through under the light from a two-photon microscope, which scientists use to observe the mouse's brain while it is under anesthesia. Thinning a skull takes a lot of skill and at least three months of practice, said Dorian McGavern, senior investigator at NIH and lead author on the study. He noticed that while trainees in his lab were learning how to do this, they often injured the mouse's brain by pressing on the thinned bone. That's when he realized this would make a good model to study traumatic brain injuries and see how the brain reacts.

To induce brain injury, McGavern's lab shaved the mice's skulls down with a special drill -- much like a dentist's drill -- then they scraped it further using a surgical scalpel until it was 30 microns thick. That's as thin as a human hair, he explained. They turned the scalpel over and using its round end gently pushed down, making contact with the brain. His group then filmed the injury response using light microscopy.

On camera, the minutes and hours after injury revealed how the damage spread and how the brain defends itself. Within minutes, blood vessels were obstructed and some leaked into the meninges, the lining between the skull and the brain. After 30 minutes, McGavern saw cell death in the meninges. That's to be expected, he said. MRIs of

patients admitted to emergency rooms immediately after a head injury showed similar damage to the meningeal blood vessels.

It's important that the border between the meninges and the brain stays intact, McGavern added. Leaking blood and fluids into the brain tissue kills neurons, the cells in your brain which send information. *After injury, the brain sends in its first responders to start patching the holes. Microglia, which McGavern calls the brain's "garbage men," arrive at the scene to keep the barrier between the meninges and the brain intact.* They swell to fill the gaps, making jellyfish-like shapes, creating inflammation to keep the fluids from flowing freely into the brain.

But after 10 hours, all of the mice had lesions in their brains -- big red spots on the images -- which indicated cell death, McGavern said. After 12 hours, those lesions could be as large as one cubic millimeter, about 1/500 of the mouse's brain, and they could get larger as time goes on, he said.

"Typically when you have something happen in your brain, regardless of the insult, you don't want the cells to die. You don't want the neurons to die," McGavern said. "As a consequence of this injury, brain tissue is not being preserved."

This damage was the result of a single injury, similar to what LaTour had observed in patients coming to the emergency room after car accidents or falling 6 feet from a ladder. The injury isn't fatal, but the concussion leaves a scar on your brain. **Our bodies don't replace dead neurons, McGavern said. Your brain can compensate for it, and work around it, but it will never be the same.**

And initially that inflammation is natural, and a good thing, LaTour said. A little initial inflammation can help protect the brain tissue from greater damage.

But if the microglia don't get turned off, then they "go haywire" and the inflammation continues, something seen in chronic encephalopathy, said Joseph Maroon, vice-chair of the department of neurosurgery at the University of Pittsburgh Medical Center. That's when the damage from concussions and multiple traumatic brain injuries becomes more serious, he said. As the inflammation rages and neurons die, the brain can't compensate for the lost tissue and patients experience a range of symptoms, from mood changes to vision distortion.

Right now, doctors can do little to treat concussions, Maroon said. They urge patients to rest as much as possible after a concussion to prevent further trauma, and they treat the symptoms -- pain, depression, vision problems -- as well as they can, he said.

"You get drugs to treat all of the symptoms ... without addressing the underlying problem of ongoing inflammation," he said.

But if the inflammation can be soothed, then the brain tissue and the neurons can be spared, something scientists like Maroon and McGavern are both investigating.

McGavern looked at transcranial options for delivering glutathione, an antioxidant that our cells produce naturally which reduces inflammation. They created a solution containing glutathione and applied it directly to the skull, where it seeped through to reach the tissue below.

When administered 30 minutes after injury, it saved 67 percent of the cell tissue. And when applied three hours later, it prevented 50 percent of the brain tissue from dying.

While that method worked, it's not a practical application yet for humans, Maroon said. No patient admitted to the emergency room with a concussion in the near future will have their scalp opened to apply an antioxidant to their surgically-thinned skull. But McGavern is hopeful that with further study this may lead to a new treatment for concussions, with medications that can pass directly through the skin and the skull bone to the heal the injured brain.

The most important lesson from this experiment, McGavern said, is that when it comes to dealing with a traumatic brain injury, every minute counts.

"The holy grail is finding compounds that can treat (traumatic brain injuries)," he said. "The key to dealing with TBI is speed. You have to get on this lightning fast."