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What Happens in the Brain After a Concussion

By GRETCHEN REYNOLDS

A remarkable recent experiment allowed scientists to see inside the skull and brain of animals that had just experienced a concussion, providing sobering new evidence of how damaging even minor brain impacts can be. While the results, which were published in Nature, are worrisome, they also hint at the possibility of treating concussions and lessening their harm.

Concussions occur when the brain bounces against the skull after someone's head is bumped or jolted. Such injuries are fairly common in contact sports, like football and hockey, and there is growing concern that repeated concussions might contribute to lingering problems with thinking or memory. This concern was heightened this week by reports that the brain of the late major league baseball player Ryan Freel showed symptoms of chronic traumatic encephalopathy, a degenerative condition. He reportedly had been hit in the head multiple times during his career.

But scientists did not know exactly what happens at a molecular level inside the brain during and after a concussion. The living brain is notoriously difficult to study, since it shelters behind the thick, bony skull and other protective barriers. In some earlier studies, scientists had removed portions of lab animals' skulls to view what happened to their brains during subsequent impacts. But removing part of the skull causes its own tissue damage and physiological response, muddying any findings about how the brain is affected by concussions.

So scientists at the National Institute of Neurological Disorders and Stroke, a division of the National Institutes of Health, decided to develop a less destructive means of seeing inside skulls and came up with the deceptively simple method of shaving away microscopic layers of a lab mouse's skull, thinning it to the point that powerful microscopic lenses could see through it, even as the skull remained essentially intact.

They then gently compressed a portion of the skull toward the brain, imitating (in reverse) the thumping that the brain endures when it strikes the skull during a concussive head injury, such as might occur after a jarring football tackle or if your head slams against the slope when you fall while skiing. Meanwhile, microscopic lenses positioned atop the animals' thinned skulls documented in real-time everything that subsequently occurred around and within the brain as a result of the concussion.

The brain is, in many ways, the body's best-protected organ. Besides the skull, it is shielded by multiple layers of membranes located just beneath the skull that block out harmful molecules. But, as the N.I.H. researchers saw, these membranes became

slightly ripped and frayed by the force of the concussion, leaving them leaky and the brain potentially vulnerable to the influx of molecules.

And such molecules soon appeared. “We saw a very quick build-up of reactive oxygen species” in the space between the skull and the brain after the concussion, said Dorian B. McGavern, a senior N.I.H. investigator who oversaw the study. Reactive oxygen species, which are also called free radicals, are known to play a role in various normal tissue processes, including the inflammatory response to any injury, but in excess they can contribute to cell death and tissue damage.

In the case of concussion, the body mounted a brave repair campaign, sending specialized immune cells from the blood and the brain to patch and fill in the frayed membranes. But the process was too slow, allowing an excess of free radicals to pass through the weakened membranes and migrate into the brain tissue, where they soon caused the death of brain cells far from the original impact site.

While concerning, this development also suggested to the scientists the possibility of treatment. If they could reduce the number of free radicals clustering near the brain, they reasoned, they could lessen the subsequent damage. So, in follow-up experiments, they inserted large amounts of a powerful antioxidant into the space between the animals’ skull and brain. Antioxidants soak up free radicals and, it turned out, dramatically blunted the trauma associated with impacts to the brain. In animals that received the treatment immediately after a concussion, almost 70 percent fewer brain cells died than in untreated mice.

These findings are “promising and intriguing,” Dr. McGavern said, although they are extremely preliminary and, for now, applicable only to mouse brains, not those of humans. But he and his N.I.H. colleagues are mounting a number of follow-up experiments to learn more about what precisely happens inside a concussed brain and how potentially to treat the injury. They are, for instance, looking at whether antioxidant patches applied to the scalp might be as effective at reducing concussion-related brain-cell death as more invasive approaches. Results should start rolling in next year.