Non-concussion football head hits can cause brain changes, Cleveland Clinic-led study finds

By John Mangels, The Plain Dealer
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In practices and games, amateur and pro football players regularly experience head blows that don't cause obvious concussion symptoms. Depending on the position they play, and how often they're on the field, athletes may receive hundreds of such impacts during a season. Players call them "dings."

But those seemingly routine hits can lead to brain abnormalities that linger for at least six months, a Cleveland Clinic-led study involving local college players has found. The study, published online late Wednesday in the journal PLOS One, revealed that players with the most head blows showed evidence of damage to the brain's protective barrier, and changes in brain structure and function.

The research also suggests – though without ironclad proof – that repeated "sub-concussive" blows may trigger the body's immune system to inadvertently attack the brain. The Clinic and University of Rochester Medical Center scientists suspect that, if the heightened immune response persists, it may play a role in the mental decline and dementia that plague some football players years after they've left the game.

The findings are certain to further raise concerns about the toll from head impacts in sports, a lightning-rod topic that affects players, coaches, trainers, doctors, schools and colleges, and the athletes' families.

Thousands of former NFL players, including former Cleveland Browns running back Jamal Lewis, are suing the league, alleging that repeated concussions have permanently damaged their brains. Many parents of young athletes struggle with the risks of hard-contact sports.

"This raises a little bit the caution level that we should have for sub-concussive episodes," said Cleveland Clinic neuroscientist Damir Janigro, the study's lead author. "Further research obviously is needed, a lot of it. But I think what we have to start to understand is that perhaps it's not only the traditional concussion that is bad for you. We should look at the cumulative effect of lesser impacts."

"This is a very strong study to suggest that you don't have to have any recognized concussions to have brain dysfunction," said Boston University neurosurgeon Dr. Robert Cantu, a leading brain injury researcher who was not involved in the study but has reviewed its findings.

"The big message is that those [football players] who are taking 1,000, 1,500 hits over the course of a season, a significant number of them may be taking some brain abnormalities as a result of it," Cantu said.
"This is giving parents food for thought about the concept that no trauma is good for the brain."

Previous studies have documented some worrisome consequences of sub-concussive hits in football, hockey and soccer players. But the Clinic/Rochester research took a more comprehensive approach, attempting to relate sub-concussive brain dysfunction to what was happening with the brain's and body's protective systems.

The scientists' focus was a brain protein called S100B which is known to leak into the bloodstream after a head injury. Researchers aren't sure of S100B's precise purpose, though it may help nurture and regulate brain cells.

Normally, S100B isn't found elsewhere in the body in large amounts; it's confined by the "blood-brain barrier," a unique filtering system that keeps harmful stuff such as toxins away from the vulnerable organ, while retaining beneficial substances that keep the brain working properly.

If a blood test detects elevated levels of S100B outside the brain, it's a strong indicator that the blood-brain barrier has been disrupted somehow, like by a strong head jolt. Many European countries -- though not the United States -- have approved the use of S100B blood tests as a concussion screen in emergency rooms. Janigro and fellow Clinic neuroscientist Nicola Marchi have a U.S. patent on an S100B blood test.

Janigro, Marchi and their University of Rochester Medical Center colleague, emergency medicine specialist Dr. Jeffrey Bazarian, wanted to examine whether S100B leaked from the brain after lower-impact, sub-concussive head blows. A typical football player may sustain more than 1,000 such hits per season, according to one study. Linemen who butt heads while blocking are a prime example.

The Cleveland and Rochester scientists also wanted to study how the body and brain react to the protein's release. They suspected that repeated exposure, from multiple lower-impact head hits, might trigger a harmful over-reaction.

To test their hypotheses, the researchers sought volunteers from the football teams at Northeast Ohio's John Carroll and Baldwin Wallace universities, and the University of Rochester in New York. None of the participants had head blows while playing that were strong enough to produce concussion symptoms.

The scientists took blood samples from 57 of the Ohio players before and after games, and tracked their head impacts using game videos and interviews. Ten of the Rochester players gave blood and also underwent pre- and post-season cognitive tests, and brain scans using a sophisticated new type of MRI that can detect subtle changes in the brain's structure.

The analysis found that the players who had the most sub-concussive head hits during the season also had significantly raised levels of the S100B brain protein in their blood. That was a clear indication the repetitive impacts had disrupted the protective blood-brain barrier, allowing S100B to seep into the athletes' bodies.
Players with the heightened S100B levels also showed evidence their immune system had reacted to the wayward brain protein by unleashing defensive antibodies. Because S100B doesn't normally circulate in the body in large amounts, the immune systems' sentry cells don't recognize it. If the immune system encounters the strange protein often enough, it misjudges S100B as a foreign invader, and produce antibodies to attack it – a so-called auto-immune response.

The study showed that those players with the most S100B in their blood – the ones who'd had the most sub-concussive hits – also had correspondingly high levels of S100B auto-antibodies in their blood.

The Clinic and Rochester researchers suspect the marauding auto-antibodies or other immune system components can harm the brain if they get past its protective barrier, which is possible when repeated head hits have damaged it. The scientists couldn't take samples of the players' brains to determine whether the auto-antibodies were present, and what effects they might be having.

But the researchers did special brain scans on some of the Rochester players, using a special MRI tool called diffusion tensor imaging, or DTI. And they measured how well the athletes did on brain function tests.

The results showed that the players with the most sub-concussive head hits and a hyped-up immune reaction to the leaking brain protein had abnormalities on their DTI scans. Bazarian said the scans indicate swelling, and possibly loss, of white matter, the support and signal-processing part of the brain. It's unknown whether the changes seen on DTI as long as six months after the football season represent permanent damage.

On behavioral tests, the players with lots of head hits and an over-reactive immune response showed a decreased ability to control impulses, the study found.

The connections the researchers discovered between sub-concussive head hits, the auto-immune reaction and the brain changes are statistically strong, but they don't necessarily prove cause-and-effect. It's possible that something besides immune system over-activity – maybe the stretching and tearing of nerve fibers when an impact jostles the brain – is to blame for the changes the scientists saw in the players DTI scans and behavioral tests.

But blood-brain barrier disruption and brain-attacking auto-immune reaction have been implicated in multiple sclerosis, so there's a basis for the Clinic and Rochester scientists' suspicions about the consequences of repeated football impacts.

"This study kind of points out the possibility that what may be happening is an auto-immune phenomenon," Bazarian said. "I think we were careful to point out we were speculating about this. We couldn't actually prove it. Now you're looking for subsequent studies . . . to try to nail this down."

It's too early to know if, or how, the findings will affect sports policies regarding head blows. Athletic officials at John Carroll and Baldwin Wallace said Tuesday they had not yet been briefed on the research results.
"We participated in [the study] because we want to do what's best for our kids, to make sure we're protecting them as much as we can," said Baldwin Wallace football coach John Snell.

"Anything that deals with the head or the brain is going to be a little bit concerning, obviously," said John Carroll head athletic trainer Don McPhillips. But conveying to young, motivated football players the potential long-term harm of a "ding" they're used to shrugging off is difficult. "They want to play," he said. "An 18- or 19-year-old is not thinking even two years down the road, let alone 30 years."

Though critics contend the NFL has been slow to respond to the head-injury issue, the league has made some substantial rule and policy changes aimed at reducing the incidence of head hits. The 2011 collective bargaining agreement with the players' union limits full-contact practices to 14 times during the regular season, with no more than one per week. And the league forbids full-contact drills in the off-season.

The NCAA has no such restrictions on full-contact practices during the collegiate season, though individual schools, including Baldwin Wallace and John Carroll, do, limiting such drills to twice weekly. The Sports Legacy Institute and a group of current and former football players are lobbying states to adopt similar curbs on high school practices.

Cantu, who co-founded the Sports Legacy Institute and is a senior advisor to the NFL's Head, Neck and Spine Committee, said the new findings about the consequences of sub-concussive hits bolsters the argument in his 2012 book, "Concussions and Our Kids," that children younger than 14 shouldn't play tackle football because of the vulnerability of their still-developing brains.

Cantu said the study findings also should add urgency to efforts to develop sensors that track the number and magnitude of head hits. Several helmet-, headband- or mouthguard-mounted sensor systems already are on the market, though their accuracy hasn't been confirmed by independent testing, Cantu said. The NFL has tested two of the systems but has not yet released its findings or put the sensors in regular use.

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