Study finds concussions alter connectivity among brain regions

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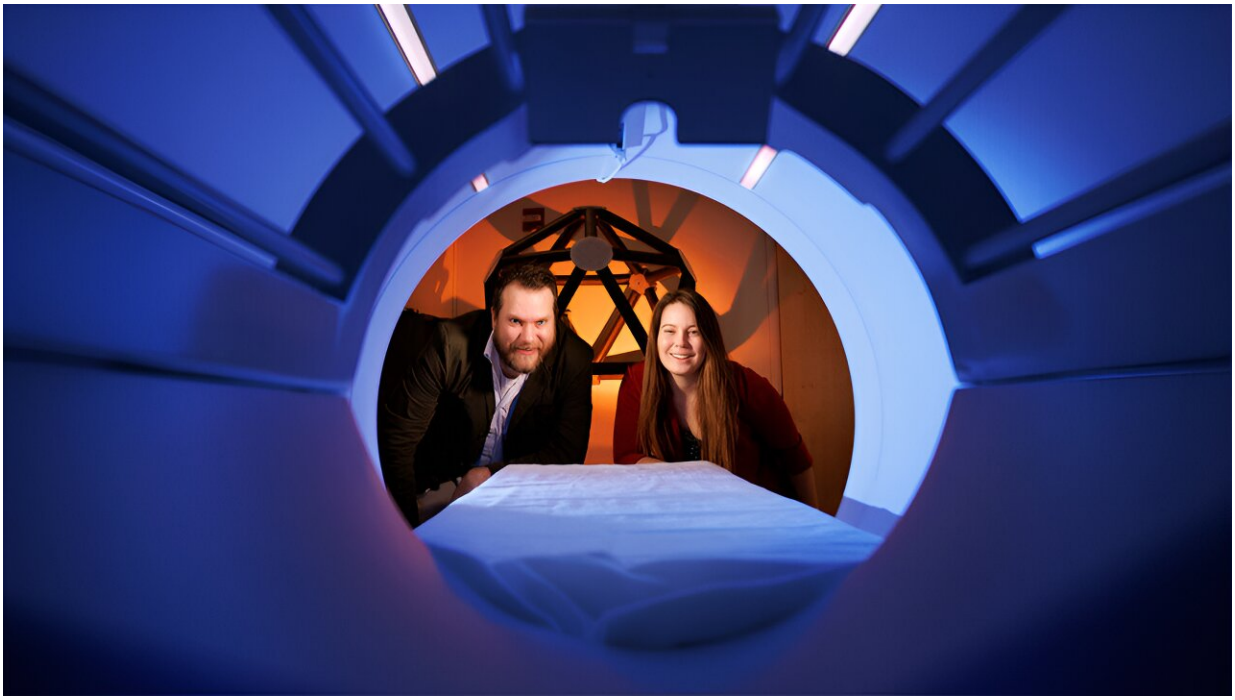

Doug Schultz (left) and Heather Bouchard peer into the chamber of an MRI machine at the Center for Brain, Biology and Behavior, located within Memorial Stadium. Credit: Craig Chandler | University Communication and Marketing

The University of Nebraska–Lincoln's Heather Bouchard and Doug Schultz are speaking of airports and blizzards, missed flights and reroutes. Surprising subjects, maybe, for a couple of researchers who study not the logistics of air travel but the effects of concussion on the

brain.

After a minute, though, their metaphor crystallizes and clarifies: The airports represent brain regions, some of them busy hubs like O'Hare, connecting to dozens of counterparts, with others semi-remote outposts like Lincoln's, catering mostly to locals.

As with flights, missed connections in the brain might bring headaches, or worse. But the still-young research into mild traumatic brain injury has yielded conflicting data on exactly how concussion can cloud that air traffic control, whose complexity makes even the holiday flight schedules of LAX and DFW look simple by comparison. One source of the confusion, the Husker researchers figured, was that so many studies have lacked baseline data on how individual brains were functioning prior to concussion, not just after.

With the help of functional MRI and athlete participation, Bouchard, Schultz and their colleagues have now authored a study published in the *Journal of Neurotrauma* comparing brain connectivity before concussion, in the immediate wake of it, and during recovery from it. Contrary to expectations, they found that the connections among certain brain regions actually strengthened in the aftermath of concussion, even as others weakened—and that some of those changes correlated with symptoms often accompanying concussion.

The findings could help reveal how brain networks recalibrate their balance of cooperation and specialization following a concussion, the team said.

"A lot of sports-related concussion literature really just looks at what's going on with the brain after somebody gets injured," said Schultz, a research assistant professor with Nebraska's Center for Brain, Biology and Behavior. "And we do know that, even at baseline, there are

differences in the way our brains are organized. So if you don't have an idea of what those differences are before somebody gets an injury, it's difficult to disentangle those potential differences from what actually might be caused by the injury.

"And that's one of the big advantages of our study, is that we have that baseline data to say, How does this person's brain change, specifically?"

U.S. athletes are diagnosed with an estimated 300,000 sports-related concussions per year. In their efforts to better understand concussion-related consequences, Bouchard and Schultz turned to 44 of those athletes—in this case, Husker football and soccer players.

The participating student-athletes received fMRI scans, which, by measuring blood-delivered oxygen in the brain, help identify the regions of it that are active at any given moment. Those scans took place in three stages: before the start of the student-athletes' respective seasons; within 48 hours of a diagnosed concussion; and after being cleared to play but before returning to full contact. Participants also rated their concussion-related symptoms and took a test that assessed reaction times, verbal and visual memory, and visual-motor speed at all three stages of the study.

In analyzing the fMRI scans, the research team sought to pinpoint and evaluate the connections of hubs: those O'Hare-equivalent brain regions that tend to activate at roughly the same time and magnitude as many others do. The researchers quantified those connections among brain regions within and across 13 networks, or groups of regions that simultaneously activate to handle tasks too daunting for any region alone.

Of special interest was the so-called default mode network, which is active when a person is at rest and, partly for that reason, has become the most-studied of all brain networks in concussion research. To the team's surprise, communication between hubs and non-hubs within the default

mode network increased in the two days following a concussion. As symptoms diminished, the communication among those brain regions did, too.

"And I think that's really interesting, because a lot of other research was showing that functional connectivity within the network decreased after injury," said Bouchard, a doctoral student at Nebraska. "But that was (likely) because they were comparing people with a concussion to people who hadn't had one, which makes these subtle differences harder to detect with less severe injuries."

By contrast, the connections between hubs of the default mode network and certain non-hubs outside that network, especially regions dedicated to visual processing, tended to decline immediately after a concussion. Collectively, the researchers said, the outcomes suggest that concussion may be distorting how the brain typically prefers to spend energy on the various tasks demanded of it. Whereas visual processing might be better managed by a single network, for instance, higher-order thinking relies on coordinating activity in regions that span multiple networks.

"We always think of (brain) segregation and integration almost as this seesaw," Schultz said. "You need some kind of balance. And it might be that the balance between those things is being disrupted in concussion."

Getting a better sense of that balance, and any imbalances that stem from brain injury, could ultimately help refine the diagnosis of concussion, Schultz said. Among the Husker athletes who participated in the study, the weakening connections across networks corresponded with cognitive issues, worse performance on visual memory tasks, and physical symptoms that included headaches, nausea and sensitivity to light.

"By looking at neuroimaging data, can we determine whether somebody has had a concussion? Not yet. I think this is especially relevant to some

of the cases that might reside in a gray area, where a person took a blow to the head, but we're not really sure if it's a concussion or not," Schultz said. "Obviously, we want to treat the athlete in such a way that you're maximizing their health and well-being, so we want to make sure that if somebody has a concussion, we catch it."

'We need to know more'

Bouchard chose to pursue her doctorate at Nebraska primarily because of the partnership between Nebraska Athletics and the Center for Brain, Biology and Behavior, or CB3. The recent study, she said, could not have happened without it.

"One big reason that having this collaboration is so important is the early diagnosis that athletic departments have for their (athletes') concussions," said Bouchard, who also receives clinical training under Nebraska's Kate Higgins. "They pretty much get diagnosed immediately after an injury, whereas if you think of emergency rooms or community clinics, there can be a lot more barriers to getting that access to care.

"In this study, we saw that athletes are recovering within about a week. Sometimes, in the community, people aren't seeing a clinician for a week after a concussion. So for us to get those scans so early on is just really, really huge."

That timeliness owes much to the fact that CB3, and its fMRI machine, reside within Memorial Stadium. Since 2018, that proximity has allowed CB3 to obtain baseline fMRI scans of all Husker football players—scans that clinicians with Nebraska Athletics can later access when assessing the health of a player who has experienced a concussion. Many of Nebraska's academic peers, even those with similar technology, must ask programs and student-athletes to go out of their way for the sake of getting scanned.

"I've talked to other researchers, primarily at other Big Ten schools, who have had an interest in getting a project like this started," Schultz said, "and there are just a lot of hurdles."

"Our unique position, being located in the stadium, near the athletic department—and our relationship with Nebraska Athletics being so collaborative—is hugely helpful. I don't think that's the case everywhere."

Given the nature of the sport and the number of athletes who play it, football is a natural starting point for the study of concussion, Bouchard said. The team's study reflects that reality, with the majority of participants plying their skills on the gridiron.

But in much the same way that concussions differ from person to person, some research indicates that symptoms and recovery may vary by gender, too. Even so, Bouchard said that more than 40% of concussion studies have analyzed male participants alone. Those analyzing only girls or women make up less than 5% of that research literature.

Bouchard is now focusing her attention, and her dissertation, on collecting concussion-related data that can narrow the chasm.

"My interest is in pushing research to really focus on women: whether there are differences in the brain, or there are differences in their access to health care, because that's a big piece, as well," she said.

"There just has not been enough research," Schultz said. "To continue raising the standard of care, we need to know more."

More information: Heather C. Bouchard et al, Concussion-Related Disruptions to Hub Connectivity in the Default Mode Network Are Related to Symptoms and Cognition, *Journal of Neurotrauma* (2024).

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