

# Newly discovered link between traumatic brain injury in children and epigenetic changes could help personalize treatment for recovering kids

Lacey W. Heinsberg, Assistant Professor of Nursing and Human Genetics, University of Pittsburgh

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The effects of traumatic brain injuries go beyond what meets the eye.

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A newly discovered biological signal in the blood could help health care teams and researchers better understand how children respond to brain injuries at the cellular level, according to our research in the *Journal of Neurotrauma*.

In the future, this information could help clinicians identify children who need more tailored follow-up care after a traumatic brain injury.

## Basics of epigenetics

As part of our work as a nurse scientist and neuropsychologist studying traumatic brain injury, we wanted to look for biological markers inside cells that might help explain why some children recover smoothly after brain injury while others struggle.

To do this, we focused on DNA, the instruction manual of cells. DNA is organized into regions called genes, each of which codes for proteins that carry out different functions like repairing tissues.

While your DNA generally stays the same throughout your life, it can sometimes collect small chemical changes called epigenetic modifications. These changes act like dimmer switches, turning genes up or down without changing the underlying code. In general, dialing up the activity of a gene increases production of the protein it codes for, while dialing down the gene decreases production of that protein.

One common type of epigenetic modification is called DNA methylation. DNA methylation is not fixed but can instead change in response to what you eat, how you move your body or even how stressed you are. We wondered if these epigenetic changes might also change in response to brain injury in children.

## Epigenetic changes in traumatic brain injury

To explore this idea, we enrolled nearly 300 children at UPMC Children's Hospital of Pittsburgh in our study. Of these children, 189 had a traumatic brain injury serious enough to require at least one night in the hospital, while the others had broken bones but no head injury.

We collected blood samples while they were in the hospital, and again at six and 12 months after their injury. We then measured DNA methylation in a gene called brain-derived neurotrophic factor (BDNF), which plays a role in how the brain develops and repairs.

Within approximately 30 hours of injury, children with traumatic brain injury had lower levels DNA methylation than children without brain injury. Interestingly, these differences were not connected to how severe the child's injury appeared based on tests that health care teams use in the clinic, such as brain scans or evaluations of consciousness. This suggests that two children who look very similar to the eye may be responding to their injury differently at the cellular and epigenetic level.

Our findings also suggest that DNA methylation could help researchers understand something completely new about the brain's response to injury that existing clinical tools cannot detect.



Brain scans don't show what's happening at the cellular and genetic level.

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## Improving recovery after traumatic brain injury

When a child comes to the hospital with a traumatic brain injury, health care teams can assess the injury based on what it looks like and how the child is currently handling symptoms. But they cannot necessarily determine how a child's body is responding to their injury, or what other factors put them at risk for poor recovery. That gap makes it difficult to predict which children may later experience problems with thinking, attention or behavior. Because the brains of children are still developing, early injuries can disrupt development and lead to long-term cognitive or behavioral issues.

Our findings indicate that epigenetic signals like DNA methylation might help clinicians and researchers develop more effective treatment strategies. While it's still unclear whether these epigenetic changes influence children's cognitive function after injury, further research could enable DNA methylation to offer a more precise guide to rehabilitation. In fact, our team is currently examining how DNA methylation patterns across all genes affect long-term outcomes in children with traumatic brain injury.

Pairing what clinicians can observe at the bedside with information at the cellular and epigenetic level can bring medicine one step closer to individualized care plans matching children with treatments that can most effectively help them heal.

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