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In females, childhood head injury could lead to alcohol abuse later in life

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Girls who suffer a concussive bump on the head in childhood could be at increased risk for abusing alcohol as adults, a new study suggests.

The research in mice found that females with a mild closed-head brain injury were more likely to misuse alcohol later in life and associate drinking with reward and pleasure. This effect was not seen in males.

The effect was reversible, however, for female mice living in an enriched environment - with more toys and exercise options - after the injury than for mice living in standard housing conditions. The environmental enrichment prevented increased drinking and reduced degeneration of axons, the long, slender extensions of the nerve cell body.

The enriched environment is intended to mimic sustained follow-up care after a human brain injury, said Zachary Weil, assistant professor of neuroscience at The Ohio State University and lead author of the study.

"We wanted to demonstrate that this effect is not set in stone at the time of injury," Weil said. "There are ways to intervene, but they're expensive in terms of effort and money. It requires sustained treatment and rehabilitation and educational support.

"The best therapy for a childhood brain injury is everybody getting great medical care and rehabilitation, regardless of socioeconomic status," he said. "People with juvenile head injuries are already at risk for memory

problems, difficulty concentrating, poor learning and reduced impulse control. If we can prevent alcohol misuse, chances for a good life are much better."

The study is published in the *Journal of Neurotrauma*.

Alcohol is already strongly linked to traumatic brain injuries. An estimated one-third to one-half of concussion patients are intoxicated at the time of the injury. The most common cause of nonmilitary brain injuries is a car accident.

"So what we hoped to determine was whether it's possible that if you had an injury as a juvenile, would you be more likely to drink heavily later on - which would put you at risk for having a more severe brain injury as an adult," Weil said. "There is some evidence that if you have a brain injury, you're more likely to drink. But nobody has looked at the time of the injury and nobody has looked at sex differences."

Mice received a concussive head injury at age 21 days - equal to between 6 and 12 years old in humans - and later were allowed to choose between two bottles containing water and escalating doses of ethanol diluted in water, which was adjusted over time because they don't like the taste. Female adult mice that had been injured at 21 days of age drank significantly more ethanol than uninjured mice. The juvenile head injury had no effect on drinking in male mice.

Physiological tests suggested the injury had nothing to do with how the animals processed alcohol, which led researchers to pursue the potential reward that young injured female mice linked to alcohol.

In this experiment, mice were placed in a box with visibly different patterns covering separate sections of the floor. Over 10 days, researchers injected them with alcohol in specific sections of the box

and with saline in other sections.

"Then we let them walk back and forth between boxes. If they liked alcohol, they would spend more time on the side of the box associated with alcohol. Again, we saw this effect only in females that had been injured. They spent about 65 percent of their time in the box linked to alcohol," Weil said. "We had proven to ourselves that there is something about the way reward and pleasure is processed in these animals with regard to alcohol."

In studying the effects of enrichment, Weil and colleagues put recently injured mice in bigger cages with running wheels, toys and tunnels, providing a new experience every week for six weeks. Control injured animals lived in standard housing conditions. When the mice were tested for alcohol intake, the enriched environment had completely blocked the females' increase in drinking. The enriched environment also reduced axon damage in their brains by about 40 percent.

The results for females are particularly concerning to researchers because two populations of traumatic brain injury patients are currently increasing: elderly adults and young women - "not just athletes, but athletics is driving it," Weil said. "But there isn't a lot of research on understanding how and why the injury effects are different between men and women."

Weil plans to follow up by studying whether hormones - not just which hormones, but when in life they're most active - drive this difference in alcoholism risk between males and females with juvenile head injuries.

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