Female and male mice suffer, recover from TBI differently

June 13 2017

Credit: martha sexton/public domain

Male mice have much greater brain distress in the week following a traumatic brain injury (TBI) than female mice, including skyrocketing

inflammation and nerve cell death, say researchers at Georgetown University Medical Center.

The study, published in *GLIA*, is the first to specifically examine how sex alters the time-course of inflammation in the brain after TBI, and their findings suggest that sex is an important factor to consider when designing and testing new drugs to treat TBI.

Previous research has shown that male animals have worse outcome after TBI than female animals, and recent clinical trials have studied female sex hormones as a therapy for TBI.

Sex differences are understudied in preclinical research, and the National Institutes of Health has recently issued guidelines to ensure that sex and other biological variables are included in research design.

"It is really important to include both sexes in preclinical research in order to design better human clinical trials," says Mark Burns, Ph.D., associate professor of neuroscience at GUMC and senior author of the study.

"When we looked to see if female mice had been included in TBI studies, we were surprised at what a blank slate we found," Burns says. "Up to now, most preclinical studies of drugs to treat TBI have been conducted with young male mice—with variables such as age and sex being overlooked. You can't develop a future of personalized medicine if you don't include females in your research," he adds.

The researchers focused on how sex alters key neuroinflammatory responses that follow TBI. They specifically looked at microglial cells, which are the resident immune cells of the brain, and movement of macrophages from the blood into the injured brain. Macrophages, which are also immune cells, offer the first line of defense against infection.

They found that the sex response was "completely divergent" up to a week after injury—there was a rapid activation of immune cells, along with robust neuron cell death, in males, but female mice experienced a markedly reduced response.

"It appears that female mice have more protection against brain trauma in the first week after TBI, and if that is true in humans it provides us with a much larger time-period to treat female patients following TBI. It will also help us design new treatments for TBI in males," says Burns.

Burns also says that although the female mice have less of the negative effects of neuroinflammation such as neuron cell death, there are also positive aspects to neuroinflammation that are missing in female mice such as waste removal and wound healing. Understanding how to minimize the negative effects while maximizing the positive effects of inflammation is an important goal in TBI research.

"It is clear that further research is needed on sex differences in response to TBI—and now we have interesting leads to follow," Burns says.

In addition to Burns, other authors include Sonia Villapol, PhD, assistant professor of neuroscience at GUMC and an expert on brain injury and neurodegeneration, and David Loane, PhD, an associate professor at the University of Maryland and an expert on neuroinflammation after brain injury.

More information: Sonia Villapol et al, Sexual dimorphism in the inflammatory response to traumatic brain injury, *Glia* (2017). DOI: 10.1002/glia.23171

Provided by Georgetown University Medical Center