New clues into how the circadian clock helps the brain recover after injury

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A type of brain cell that can renew itself is regulated by circadian rhythms, providing significant insights into how the body's internal clock may promote healing after traumatic brain injuries (TBI), according to new research from Children's National Hospital.

Released in the latest issue of *eNeuro*, the findings open new avenues of investigation for future TBI therapies. These injuries are currently managed only with supportive care and rehabilitation, rather than targeted drug treatment options. The findings also underscore the importance of addressing circadian disturbances to help injured brains heal.

Many of the body's cells follow a 24-hour rhythm driven by their genes known as the circadian clock. The Children's National research team found that a relatively newly discovered type of brain cell—known as NG2-glia, or oligodendrocyte precursor cells—also follow a circadian rhythm. This cell type is one of the few that continually self-renews throughout adulthood and is notably proliferative in the first week after brain injuries.

"We have found evidence for the role of this well-known molecular pathway—the molecular circadian clock—in regulating the ability for these NG2-glia to proliferate, both at rest and after injury," said Terry Dean, M.D., Ph.D., critical care specialist at Children's National and the lead author of the paper. "This will serve as a starting point to further investigate the pathways to controlling cellular regeneration and optimize recovery after injury."

Sometimes called "the silent epidemic," TBI afflicts an estimated 69 million people worldwide each year, with injuries ranging from mild concussions to severe injuries that cause mortality or lifelong disability. In the United States alone, approximately 2.8 million people sustain TBI annually, including 630,000 children. TBI is the leading cause of death in people under age 45, and those who survive are often left with persistent physical, cognitive and psychological disabilities.

Yet no targeted therapies exist for TBI, creating a critical need to uncover the mechanisms that could unlock the regeneration of these NG2-glia cells, which are the most common type of brain cell known to proliferate and self-renew in adult brains.

"It is essential for researchers to know that cell renewal is coordinated with the time of day," said Vittorio Gallo, Ph.D., interim chief academic officer and interim director of the Children's National Research Institute. "With this knowledge, we can dig deeper into the body's genetic healing process to understand how cells regulate and regenerate themselves."

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