Timing is key for traumatic brain injury treatment

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Researchers at the University of Adelaide have discovered two potential treatments for traumatic brain injury that are most effective when given at different stages after the injury has occurred.

Laboratory studies conducted in the University's School of Medical Sciences have confirmed that changes in brain water channels over time play a critical role in traumatic brain injury.

For his PhD at the University, researcher Dr Joshua Burton tested two compounds that alter the natural flow of water activity in and out of the brain. He found that recovery from brain injury can be greatly assisted when these compounds are given at the right times.

Dr Burton's work could point to the potential development of new drugs as well as new approaches to preventing brain damage and death. The research also has implications for treatment of brain swelling after stroke.

"One of the serious consequences of traumatic brain injury is an increase in brain moisture content and associated brain swelling, which significantly impacts patients' neurological outcomes. This swelling can occur for days after the initial injury and is frequently life-threatening," Dr Burton says.

"The water channels normally function to protect the brain, but in the case of traumatic injury or stroke they become a pathway of

vulnerability that allows swelling. Unfortunately, the swelling creates pressure within the skull – there's nowhere for the brain to expand to – decreasing oxygen levels and blood to the brain."

Dr Burton has found that applying a drug that closes the water channels can inhibit initial water entry, helping to close the window of vulnerability. A second drug used later in the progression of the injury acts to enhance the water channel activity, letting superfluous moisture out when needed. "By using both of these compounds – a blocker at the early stage of injury, and an activator at the later stage – we're able to complement the brain's natural healing processes and maintain a reduced level of swelling," he says.

This work builds on more than a decade of research conducted by the University of Adelaide's Professor Andrea Yool on the water channel proteins known as "aquaporins".

"Dr Burton's work is groundbreaking because it clarifies the roles of aquaporins in the brain during the short and long-term responses to traumatic head injury. This work also demonstrates for the first time that recently discovered drug-like compounds can be used in series to initially reduce water entry and then enhance water exit over time," Professor Yool says.

"Most current therapeutic approaches are limited in their ability to reduce injury-induced brain swelling, and no treatments are available to resolve excess fluid at a later stage. While much more research is needed, there is exciting potential here for new interventions in clinical situations. New approaches that can improve the outlook for patients, especially in the later stages of injury development, would be of great benefit," she says.