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Better management of traumatic brain injury

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New treatments to lessen the severity of the more than 21,000 Traumatic Brain Injury (TBI) cases that occur in Australia each year are on the horizon.

Published today in the leading neurology journal, *Brain*, a study led by researchers from Monash University's Australian Centre for Blood Diseases (ACBD) revealed how inhibiting certain enzymes decreased the severity of TBI, providing a target for future treatments.

Caused by a blow to the head, often suffered during falls or road crashes, severe TBI can result in long-term disability or death. Effects can include impairments to cognitive and motor function, vision, hearing and emotional regulation. Additionally, the post-injury disruption to blood flow, oxygen supply and nerve function around the brain has been linked to debilitating diseases including Alzheimer's disease and post-traumatic epilepsy.

The study was led by Professor Robert Medcalf and Dr Maithili Sashindranath of the ACBD, who collaborated for five years with scientists at the University of Geneva in Switzerland and the University of Michigan in the United States.

Professor Medcalf said the researchers identified two enzymes, known as t-PA and MMP-3, that act together to promote injury severity following TBI.

"The enzyme t-PA, well known for its ability to remove blood clots, also

has a healthy and very important role in supporting learning and memory functions in everyday life. However, previous research has shown that in TBI cases, its presence makes the injury much worse," Professor Medcalf said.

Initially, the researchers thought t-PA itself exacerbated the injury. However, a surprising finding of the study was that t-PA is not the culprit - its inhibition triggers the activation of MMP-3, the enzyme which does the damage.

"The activity of naturally occurring enyzmes is controlled by specific enzyme inhibitors," Professor Medcalf said.

"Unexpectedly, we found that the process of t-PA inactivation by one of its natural inhibitors actually contributed to brain injury, because it leads to the activation of MMP-3.

"Now we know that if we block MMP-3 with an inhibitor, we can protect the brain following TBI," Professor Medcalf said.

Co-author and international expert on TBI, Professor Jeffrey Rosenfeld, from Monash University's Department of Surgery said the results were exciting.

"We now have a new and promising therapeutic target for the treatment of human TBI, which has not, so far, been significantly improved by pharmacological intervention," Professor Rosenfeld said.

Research is continuing with the aim of bringing this finding to a point where clinical trials can evaluate this novel approach in patients with TBI.