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Treating traumatic brain injury

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After a traumatic brain injury (TBI), the brain produces an inflammatory response. This prolonged swelling is known as cerebral edema and can be fatal. Unfortunately, the only medications available just address symptoms and cannot directly treat the inflammation.

Some people can walk out okay after suffering from this injury, yet others can become comatose or may even die. This raises the intriguing question: why do people with similar injuries end up with vastly different outcomes? TBI affects nearly 2 million Americans every year and nearly 52,000 of these injuries are fatal.

"To a certain extent, the way the body responds to injury is probably genetically hardwired," said Dr. Daniel Laskowitz, a neurologist at Duke who has been working on the mysteries of traumatic brain injuries for two decades. He said in medical school, he preferred the approach of treating the whole body and not super specializing. He chose to work specifically with brain injury because he could treat patients with other conditions along with brain injury.

One of Dr. Laskowitz's first publications was about brain injury. As a fellow training in neurology in the mid-1990s, he looked at genetic factors that could make a difference in the outcome of a brain injury and found that genetic variation in a protein called apolipoprotein E (apoE) played a role. ApoE comes in three slightly different flavors, and one of the common forms of apoE (apoE4) was associated with bad outcomes after brain injury. This raised the question of what apoE was doing in the brain to affect outcome after injury.

In 1997, he published an article about the effect of apoE on mice suffering a stroke and found that mice with the apoE allele had a better recovery than mice with an apoE deficiency. These findings were later repeated in an article in 2001,which found that following traumatic brain injury, animals with apoE had better outcomes than animals without this protein.

Since it was found that apoE could improve an injured patient's neurologic outcomes, it became a model for medication to treat brain injuries. However, apoE does not easily cross the blood-brain-barrier, making it a challenging molecule to dispense as a drug.

Dr. Laskowitz's lab has spent almost a decade looking at how apoE works. They have recently developed a peptide made of 5 amino acids, CN-105, that is based off of this protein and is able to cross the blood-brain-barrier, giving it the potential to be distributed as a treatment. This has been tested in mice and shown to improve outcomes.

In July, CN-105 completed a first phase clinical trial and found that drug administration was safe and well tolerated. In the coming year, a phase 2 study will look at whether CN-105 improves outcomes in patients with brain hemorrhages.

The plan is to give the peptide through an IV every six hours for three days, the time period when most of the swelling happens after injury.

Dr. Laskowitz's research has already had a significant impact on the treatment of brain injury, and hopefully, this new medication could be another great contribution to this field.

More information: Beilei Lei et al. Neuroprotective pentapeptide CN-105 improves functional and histological outcomes in a murine model of intracerebral hemorrhage, *Scientific Reports* (2016). DOI:

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