Hope for stroke victims

February 8 2011

Two new studies from Spain provide conclusive evidence that an approach developed at the Weizmann Institute could speed recovery from stroke and head trauma.

Much of the devastation of stroke and head trauma is due to damage caused the overproduction of a substance in the brain called glutamate. Preventing this damage has been impossible, until now, as many drugs don't cross the so-called blood-brain barrier, and those that do often don't work as intended. But a method originally devised at the Weizmann Institute of Science may, in the future, offer a way to avert such glutamate-induced harm.

Prof. Vivian I. Teichberg of the Institute's Neurobiology Department first demonstrated a possible way around these problems in 2003. Glutamate – a short-lived neurotransmitter – is normally all but absent in brain fluids. After a stroke or injury, however, the glutamate levels in brain fluid become a flood that over-excites the cells in its path and kills them. Instead of attempting to get drugs into the brain, Teichberg had the idea that one might be able to transport glutamate from the brain to the blood using the tiny "pumps," or transporters, on the capillaries that work on differences in glutamate concentration between the two sides. Decreasing glutamate levels in blood would create a stronger impetus to pump the substance out of the brain. He thought that a naturally-occurring enzyme called glutamate-oxaloacetate transaminase (GOT, for short) could "scavenge" blood glutamate, significantly lowering its levels. By 2007, Teichberg and his colleagues had provided clear evidence of the very strong brain neuroprotection that oxolacetate (a chemical

similar to GOT) afforded rats exposed to a head trauma.

Two new studies – conducted by Fransisco Campos and others from the lab of Prof. Jose Castillo in theUniversity of Santiago de Compostela, Spain – now provide a definitive demonstration of Teichberg's results. In the first, the scientists conclusively showed that oxoloacetate injected into rats with stroke-like brain injuries reduces glutamate levels both in the blood and in the affected brain region, while significantly lessening both cell death and the swelling that can accompany stroke. In the second, a team of neurologists in two different hospitals checked the levels of glutamate and GOT in several hundred stroke victims who were admitted to their hospitals. They found that the most significant predictor of the prognosis – how well they would recover at three months and how much brain damage they would suffer – was the levels of these two substances. High glutamate levels correlated with a poor outcome, high GOT levels with a better one.

The overall implication of these two papers is that administering GOT might improve a patient's chances of recovering, as well as speeding up the process. In addition to stroke and head trauma, a number of diseases are characterized by an accumulation of glutamate in the brain, including Alzheimer's disease, Parkinson, multiple sclerosis, epilepsy, glaucoma, certain brain tumors and amyotrophic lateral sclerosis, and there is hope that, in the future, treatments to scavenge glutamate could relieve the symptoms and improve the outcomes for a number of neurological problems. Yeda, the technology transfer arm of the Weizmann Institute, holds a patent for this method.

Provided by Weizmann Institute of Science