

Basic Research Emergency Medicine Studies Brain

Many problems cause the brain to swell. The causes can be as varied as head trauma or chronic liver disease. The effects can be diffuse swelling throughout the brain, as with Reye's syndrome, or it can be localized in a specific region, as in a stroke. Whatever its origin, brain edema is a function of the same basic ingredient—water.

"In all of these conditions there is an increase in the total water content of the brain," explains James Olson, Ph.D., professor of emergency medicine and physiology and biophysics at Wright State. He recently received a three-year, \$750,000 grant from the National Institutes of Health (NIH) to study how the brain adapts at the cellular and tissue levels to changes in water volume.

Like tissue throughout the body, the brain is mostly water. The

brain is softer tissue than skin, muscle, and other internal organs. Evolution has encased the brain in a hard skull and cushioned it in its own hydraulic shock system of cerebral-spinal fluid. This protects the brain from external injury but leaves little room to accommodate changes in brain volume when the threat comes from within.

"If you get hit in the arm with a baseball, it swells. It may be painful, but the swelling itself doesn't restrict blood flow or impede the use of your arm," Dr. Olson says. "When tissue swells in the brain, it restricts blood flow. The result is ischemia, one of the worst consequences of brain edema."

As brain tissue swells, heart rate and blood pressure increase to maintain blood flow to the brain. With severe brain edema, however, swelling can exceed the body's

capacity to compensate. Current medical treatments tend to be generalized and short-lived, treating the edema's effect rather than its specific cause in the brain.

The brain itself has mechanisms, as yet little understood, that control water volume under normal conditions. Water moves freely across brain cell membranes through the process of osmosis, adjusting the concentration of a host of metabolic substances within cells by changing the cells' water volume. Water transport in the brain is a subtle yet powerful force.

"There is a normal physiologic range in which the brain is able to adapt to water volume changes," Dr. Olson says. His research is investigating how brain cells known as astrocytes increase and decrease water volume by transferring the amino acid taurine.

Astrocytes are so named because they resemble stars when stained in living brain tissue and viewed through a microscope. Astrocytes are glial cells, a brain cell type that is more numerous but less familiar than neurons, the cells that transmit nerve signals throughout the body. In the human brain glia outnumber neurons by a ratio of 10 to 1. In frogs, by comparison, the ratio is closer to 1 to 1.

"You might argue that we need to count the number of glial cells in Einstein's brain, rather than the number of neurons, to correlate brain cells with intelligence," Dr. Olson says with a laugh. After



James Olson, Ph.D., at work in his laboratory at the Cox Institute on Kettering Medical Center campus.

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studying glial cell biology for more than 20 years, he believes the glia play an instrumental role in regulating brain metabolism.

In earlier studies funded by a research challenge grant from the Ohio Board of Regents, Dr. Olson found that water volume in neurons remains constant while it fluctuates in glial cells tested under similar experimental conditions. This

suggests that neurons and glia interact to maintain neuronal water volume. The movement of taurine between the cells may trigger water transport. A major thrust of the new research will be to study the interaction of neurons and glia in living tissue removed from rat brains. Collaborators in the research include Ann Taylor, Ph.D., and Robert Fyffe, Ph.D., from

Wright State’s Department of Anatomy, and Norman Kreisman, Ph.D., from Tulane University.

“When we understand better how brain cells regulate water volume under normal conditions,” Dr. Olson says, “we may be able to devise better treatments for brain edema that treat the cause rather than the effect.”

— Mark Willis