

# Faulty development of immature brain cells causes hydrocephalus

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Researchers at the University of Iowa have discovered a new cause of hydrocephalus, a devastating neurological disorder that affects between one and three of every 1,000 babies born. Working in mice, the researchers identified a cell signaling defect, which disrupts immature brain cells involved in normal brain development. By bypassing the defect with a drug treatment, the team was able to correct one aspect of the cells' development and reduce the severity of the hydrocephalus. The findings were published online Nov. 18 in the journal *Nature Medicine*.

"Our findings identify a new [molecular mechanism](#) underlying the development of neonatal hydrocephalus," says Calvin Carter, a student in the UI Graduate Program in Neuroscience and first author on the study. "By targeting this defective signaling pathway in mice using an FDA-approved drug, we were able to successfully treat this disease non-invasively."

Hydrocephalus, sometimes called water on the [brain](#), involves build-up of fluid inside brain spaces known as ventricles. If the excess fluid is not removed, the ventricles expand, which can cause serious [brain damage](#) or death. Although hydrocephalus is one of the most common types of brain abnormality in [newborn infants](#), treatment has not changed much over the last half century and involves invasive brain surgery to drain the fluid. Complications are common and the procedure often fails, meaning that children often need repeated surgeries.

"This disease is devastating and costly (almost \$2 billion annually), and

current treatment options are extremely limited," says Carter, who also is a National Science Foundation graduate research fellow. "Development of non-invasive therapies would revolutionize treatment of this condition."

Carter notes that reducing the size of the ventricles in mice is a clinically significant accomplishment because reducing ventricular size in humans is associated with better patient outcome.

Working in a mouse model of hydrocephalus, the research team honed in on a specific group of immature cells called neural precursor cells (NPCs) that give rise to most types of [brain cells](#), including neurons and glia cells. One particular subgroup of NPCs, which has only recently been identified and is involved in the development of normal ventricles, became the focus of the team's study.

During brain development, this population of immature cells proliferates and dies off in a precisely coordinated process to produce normal [ventricles](#).

The team discovered an imbalance in the proliferation and survival of these cells, which leads to hydrocephalus in the experimental mouse model.

The imbalance is caused by problems in signaling pathways that prompts these NPCs to die or to proliferate. Both processes are abnormal in the [mouse model](#) – the cells died at twice the rate seen in normal mouse brains and proliferated at only half the normal rate.

Having identified the problem, the researcher then showed that treatment with lithium bypasses one aspect of the abnormal signaling and restores normal proliferation of the precursor cells, which in turn reduces the hydrocephalus in the mice.

"Our findings demonstrate for the first time that neural progenitor cells are involved in the development of neonatal hydrocephalus," Carter says. "We are also the first to manipulate the development of these progenitor cells and successfully treat neonatal hydrocephalus, a feat which opens the door to novel treatment strategies in treating this disease and other neurological diseases."

Because the study identifies cell signaling defects as a cause of hydrocephalus, the findings pave the way for identification of additional signaling pathways involved in the development of this disease, and lay the groundwork for developing non-invasive therapies to treat this disease.

The finding also suggests that successful treatment of hydrocephalus will rely on individualized treatment strategies based on the particular type of hydrocephalus a patient has rather than using a single approach for treating [hydrocephalus](#) regardless of its molecule or genetic causes.

**More information:** [www.nature.com/nm/journal/vaop...ent/abs/nm.2996.html](http://www.nature.com/nm/journal/vaop...ent/abs/nm.2996.html)

Provided by University of Iowa

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