

# **Mechanisms of harmful overhydration and brain swelling**

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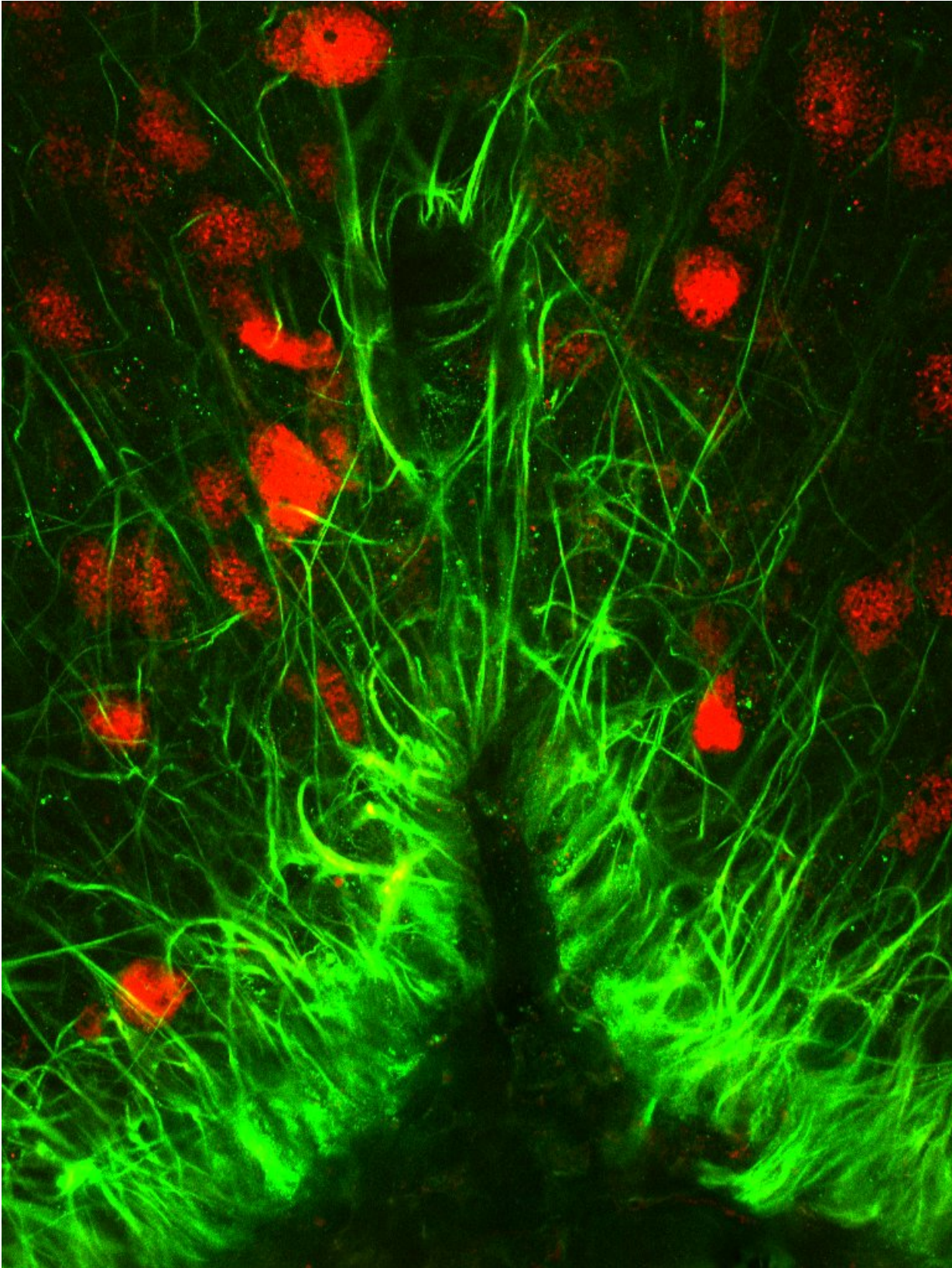


Image shows the hydration sensing neurons (red) and the glial cells (green) in a mouse brain. Credit: Charles Bourque's lab

We are all familiar with the drawbacks of dehydration, but we rarely hear about the harmful effects of overhydration. For one, excess fluid accumulation can lead to dangerously low sodium levels in the blood or hyponatremia—a life-threatening condition that can result in brain swelling. Similarly, more is known about the mechanisms in the body that detect and drive thirst while little is known about how the brain detects a state of overhydration.

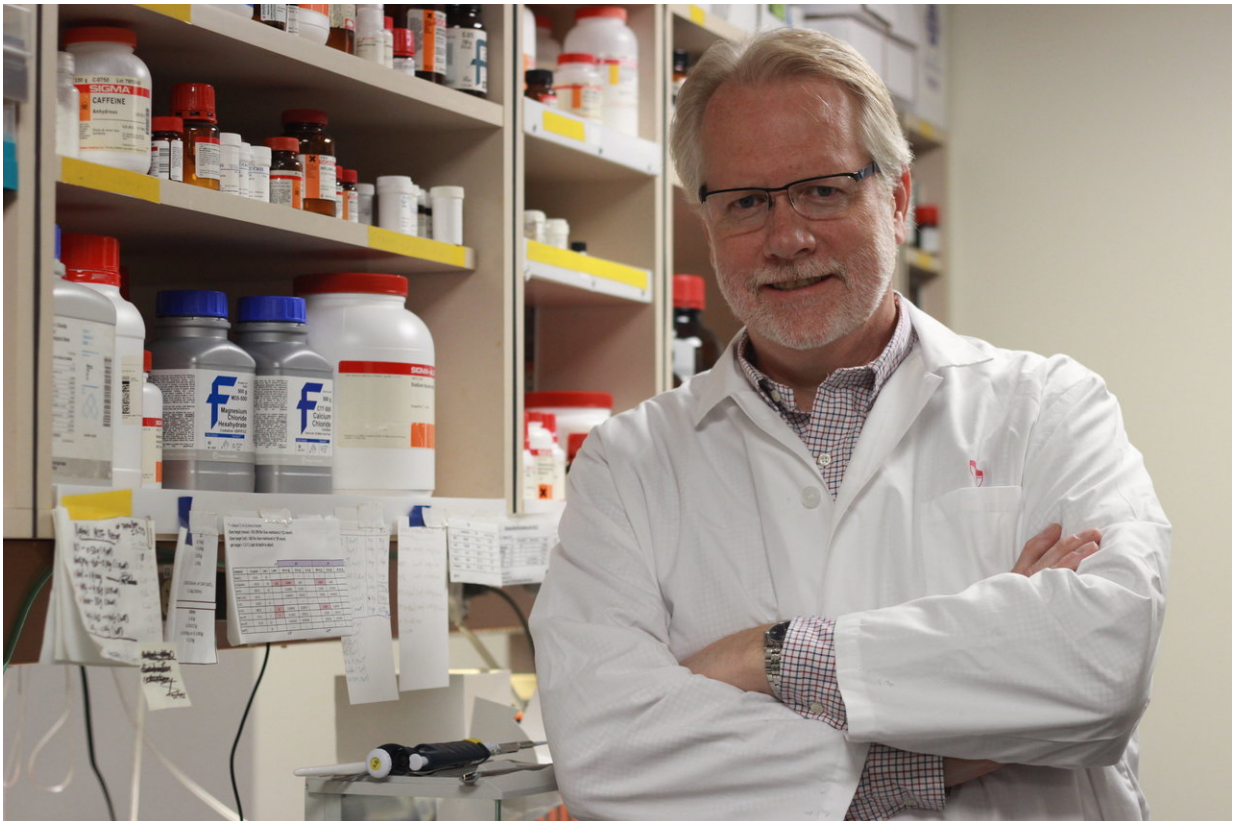
"[Hyponatremia] occurs in common pathological conditions, including [brain](#) injury, sepsis, cardiac failure and in the use of drugs, such as MDMA (ecstasy)," says Dr. Charles Bourque, whose team from the Centre for Research in Neuroscience at the Research Institute of the McGill University Health Centre (RI-MUHC) uncovered a key piece to the puzzle of how our brains detect hyponatremia and regulate overhydration. The new study featured in *Cell Reports* unearths the fundamental mechanism of how hyponatremia is detected in the brain.

"Our specific data will be important for people studying hydromineral and fluid electrolyte homeostasis, and clinicians who treat patients faced with hyponatremia," reports Dr. Bourque, who is a scientist in the Brain Repair and Integrative Neuroscience Program (BRAIN) at the RI-MUHC and a professor in McGill's Department of Neurology. This condition is more common in elderly patients and can cause cognitive problems and seizures in this vulnerable group. While it remains uncertain how hyponatremia develops, a defect in the hydration sensing mechanism of the brain could be the culprit.

No strangers to studying the mechanisms of hydration in the body, Dr.



Bourque's team, located at the Montreal General Hospital, has also made several key discoveries in the past on how the brain detects and prevents dehydration; how salt intake increases blood pressure; and how the brain's biological clock stimulates thirst prior to sleep. In this instance, experiments by Sorana Ciura, a Ph.D. student in Dr. Bourque's laboratory, who is now at the Institut Imagine, Hôpital Necker-Enfants Malades in Paris, revealed that the brain's hydration sensing neurons don't detect overhydration in the same way that they detect dehydration.



Dr. Bourque is a scientist in the Brain Repair and Integrative Neuroscience Program (BRAIN) at the Research Institute of the McGill University Health Centre in Montreal and a professor in McGill's Department of Neurology. Credit: McGill University Health Centre

The new research shows that overhydration activates Trpv4, which is a cellular gatekeeper implicated in maintaining the balance of water in the body. Trpv4 is a calcium channel that can be found in glial cells, which are cells that act to surround hydration sensing neurons.

"Our study shows that it is in fact glial cells that first detect the overhydrated state and then transfer this information to turn off the electrical activity of the [hydration sensing] neurons," explains Dr. Bourque. The researchers also found that it is the release of the amino acid taurine that acts to inhibit hydration sensing neurons. Essentially, when overhydration is detected by [glial cells](#), the Trpv4 channel triggers the release of taurine, which acts as a trip wire to inhibit hydration sensing neurons.

The brain's ability to detect excess hydration is essential to maintaining fluid balance in the body and preventing conditions like hyponatremia.

"Preclinical models of hyponatremia will be used to examine if the mechanism we report is affected in this condition with the long-term objective of designing new treatments or diagnostic tools," concludes Dr. Bourque.

Dr. Bourque is collaborating with Dr. Julie Marcoux, neurosurgeon at the MUHC on a study that aims to define the basis for the emergence of hyponatremia in a subset of patients that suffer from a TBI.

**More information:** Sorana Ciura et al, Trpv4 Mediates Hypotonic Inhibition of Central Osmosensory Neurons via Taurine Gliotransmission, *Cell Reports* (2018). [DOI: 10.1016/j.celrep.2018.04.090](https://doi.org/10.1016/j.celrep.2018.04.090)

Provided by McGill University Health Centre

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