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Research finds that zinc binding is vital for regulating pH levels in the brain

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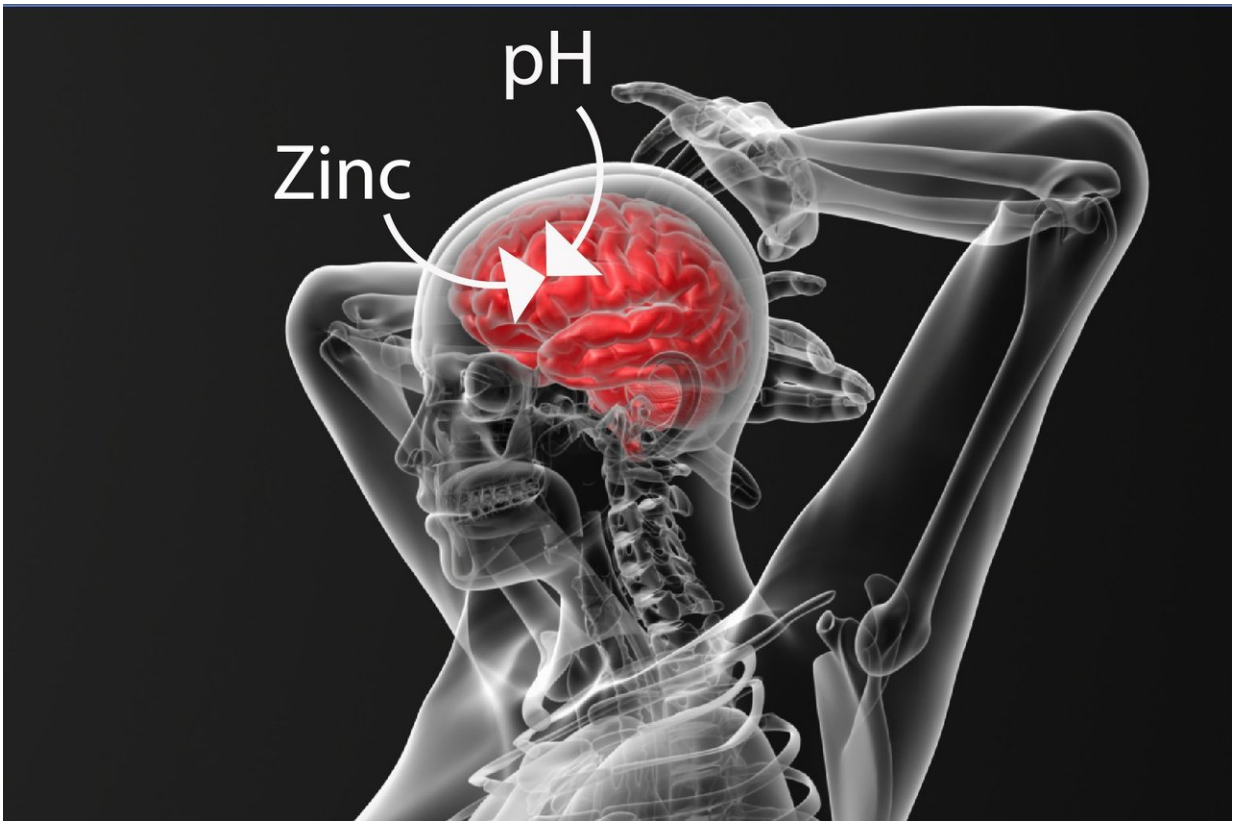

Zinc and regulation of pH is linked at the atomic level through specific bicarbonate transporters. Credit: Colourbox.com/JP Morth

Researchers in Oslo, Norway, have discovered that zinc binding plays an important role in the sensing and regulation of pH in the human brain.

The findings come as one of the first studies that directly link zinc binding with bicarbonate transporters.

The Morth Group, led by J. Preben Morth, recently published the findings in *Scientific Reports*. The group is based at the Centre for Molecular Medicine Norway, and studies the structure and function of membrane proteins, and their interaction with lipids in the biological membrane.

When we inhale, oxygen is distributed via our red blood cells to every living cell of our body. Human cells use oxygen to produce Adenosine triphosphate (ATP) - the molecule that fuels vital processes in the cells, such as maintaining the electrical potential across the membranes of the cells that allow us to think and feel.

ATP generation is directly linked to the citric acid cycle, which leads to the complete breakdown of nutrients. This process ultimately generates carbon dioxide (CO2) as the final waste product, which is expelled when we exhale.

However, before we can exhale the excess CO2, this vital molecule is involved in one of the most important biological functions on our body: it regulates pH in our cells. This process is incredibly important; if the pH in and around our cells is lower than 6.8 or higher than 7.8, then we are in danger of dying due to cell death and tissue damage.

An example of how important pH levels are to our health is demonstrated by the fact that pH levels in blood from the umbilical cord are always tested in newborn babies. A low pH value is correlated with a low oxygen supply during birth, which can lead to severe brain damage.

When in water, CO2 forms bicarbonate (HCO3-) and is transported by specific transport proteins across the cell membrane. How these

transport molecules sense what the pH value is inside the cell is still an open question. However, the work performed by Alvadia et al.describes that the transition metal, zinc, likely interacts with the proteins that facilitate the transport of HCO3- through the membrane.

This zinc binding therefore plays an important role in the sensing and regulation of cellular pH, in particular in the transporters found in neurons of the human brain. This is one of the first studies that directly associates zinc binding with a bicarbonate transporters.

Preben Morth, Group Leader at NCMM comments, "This is a basic research project and at this stage it is difficult to predict what the medical consequences will be. However, it is likely that zinc may play a key role in the regulation of pH in the brain and therefore has implications for brain function and health."

The results have recently been published in *Scientific Reports* from the Nature publishing group.

More information: Carolina M. Alvadia et al. The crystal structure of the regulatory domain of the human sodium-driven chloride/bicarbonate exchanger, *Scientific Reports* (2017). DOI: 10.1038/s41598-017-12409-0

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