Acid in the brain: Team develops new way to look at brain function

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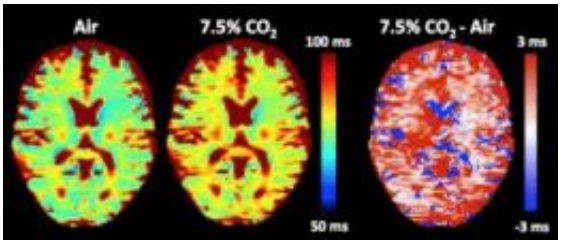

University of Iowa researchers have developed an MRI-based method to detect and monitor pH changes in living brains. The image shows MRI brain scans of human subject breathing air (left) or air containing 7.5 percent carbon dioxide (middle). The difference between the two scans (shown right) shows increased brain acidity in red caused by carbon dioxide inhalation as measured by the new MRI-based strategy. Credit: Vincent Magnotta, University of Iowa

University of Iowa neuroscientist John Wemmie, M.D., Ph.D., is interested in the effect of acid in the brain. His studies suggest that increased acidity or low pH, in the brain is linked to panic disorders, anxiety, and depression. But his work also suggests that changes in acidity are important for normal brain activity too.

"We are interested in the idea that pH might be changing in the functional brain because we've been hot on the trail of receptors that are activated by low pH," says Wemmie, a UI associate professor of psychiatry. "The presence of these receptors implies the possibility that low pH might be playing a signaling role in normal brain function."

Wemmie's studies have shown that these acid-sensing proteins are required for normal fear responses and for learning and memory in mice. However, while you can buy a kit to measure the pH (acidity) of your garden soil, there currently is no easy way to measure pH changes in the brain.

Wemmie teamed up with Vincent Magnotta, Ph.D., UI associate professor of radiology, psychiatry, and biomedical engineering, and using Magnotta's expertise in developing MRI (magnetic resonance imaging)-based brain imaging techniques, the researchers developed and tested a new, non-invasive method to detect and monitor pH changes in living brains.

According to Wemmie, the new imaging technique provides the best evidence so far that pH changes do occur with normal function in the intact human brain. The findings were published May 7 in the Proceedings of the National Academy of Sciences (*PNAS*) Early Edition.

Specifically, the study showed the MRI-based method was able to detect global changes in brain pH in mice. Breathing carbon dioxide, which lowers pH (makes the brain more acidic), increased the signal, while bicarbonate injections, which increases brain pH, decreased the MRI signal. The relationship between the signal and the pH was linear over the range that was tested.

Importantly, the method also seems able to detect localized brain activity. When human volunteers viewed a flashing checkerboard -- a classic experiment that activates a particular brain region involved in vision -- the MRI method detected a drop in pH in that region. The team also confirmed the pH drop using other methods.

"Our study tells us, first, we have a technique that we believe can measure pH changes in the brain, and second, this MRI-based technique

suggests that pH changes do occur with brain function," Magnotta says.

"The results support our original idea that brain activity can change local pH in human brains during normal activity, meaning that pH change in conjunction with the pH-sensitive receptors could be part of a signaling system that affects brain activity and cognitive function," Wemmie adds

A new way to view brain activity

Importantly, this technique may also provide a new way to image the brain

Currently, functional MRI (fMRI) measures brain activity by detecting a signal that's due to oxygen levels in the blood flowing to active brain regions. The UI team showed that their method responds to pH changes but is not influenced by changes in blood oxygenation. Conversely, fMRI does not respond to changes in pH.

"What we show is our method of detecting brain activity probably depends on pH changes and, more than that, it is distinct from the signal that fMRI measures," says Wemmie. "This gives us another tool to study brain activity."

pH and brain function

Wemmie's previous studies have suggested a role for pH changes in certain psychiatric diseases, including anxiety and depression. With the new method, he and his colleagues hope to explore how pH is involved in these conditions.

"Brain activity is likely different in people with brain disorders, such as bipolar or depression and that might be reflected in this measure,"

Wemmie says. "And perhaps most important, at the end of the day; could this signal be abnormal or perturbed in human psychiatric disease? And if so, it might be a target for manipulation and treatment?"

Provided by University of Iowa