Zinc regulates communication between brain cells

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Zinc has been found to play a critical role in regulating communication between cells in the brain, possibly governing the formation of memories and controlling the occurrence of epileptic seizures.

A collaborative project between Duke University Medical Center researchers and chemists at the Massachusetts Institute of Technology has been able to watch zinc in action as it regulates communication between neurons in the hippocampus, where learning and memory processes occur – and where disrupted communication may contribute to epilepsy.

"We discovered that zinc is essential to control the efficiency of communication between two critical populations of nerve cells in the hippocampus," said James McNamara, M.D., senior author and chair of the Department of Neurobiology at Duke. "This addresses a longstanding controversy in the field."

The study appeared in *Neuron* journal online on Sept. 21.

McNamara noted that zinc supplements are commonly sold over the counter to treat several different brain disorders, including depression. It isn't clear whether these supplements modify zinc content in the brain, or modify the efficiency of communication between these nerve cells. He emphasized that people taking zinc supplements should be cautious, pending needed information on the desired zinc concentrations and how oral supplements affect them.

More than 50 years ago scientists discovered that high concentrations of zinc are contained in a specialized compartment of nerve cells, called vesicles, that package the transmitters which enable nerve cells to communicate. The highest concentrations of brain zinc were found among the neurons of the hippocampus, the center of learning and memory.

Zinc's presence in these vesicles suggested that zinc played some role in communication between nerve cells, but whether it actually did so remained controversial.

To address this controversy, McNamara and his colleagues at Duke teamed up with Dr. Steve Lippard and colleagues in the Department of Chemistry at the Massachusetts Institute of Technology.

The Lippard team synthesized a novel chemical that bound zinc far more rapidly and selectively than previously available compounds. Use of this chemical let the Duke team rapidly bind the zinc released by nerve cells, taking it out of circulation and preventing enhanced communication.

The Duke team went on to confirm that eliminating zinc from the vesicles of mutant mice also prevented enhanced communication. They also found that increases in the transmitter glutamate seemed to increase zinc-mediated enhancement of communication.

Interestingly, the nerve cells in which the high concentrations of zinc reside are critical for a particular type of memory formation. Excessive enhancement of communication by the zinc-containing nerve cells occurs in epileptic animals and may worsen the severity of the epilepsy.

"Carefully controlling zinc's regulation of communication between these nerve cells is critical to both formation of memories and perhaps to occurrence of epileptic seizures," McNamara said.

McNamara also noted that the scientific collaboration between the Duke and MIT scientists was critical to the success of this work. The availability of the novel chemical provided a critical tool that allowed the neuroscientists to unravel the puzzle.

Provided by Duke University Medical Center