SOUTHWESTERN NEWS

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RESEACHERS CLOSER TO DEFINING FUNCTION OF TWO PROTEINS INVOLVED IN NEUROTRANSMITTER RELEASE

DALLAS – Jan. 16, 2002 – Researchers at UT Southwestern Medical Center at Dallas are a step closer to defining the function of two proteins involved in neurotransmitter release, which initiates communication between neurons in the brain.

Findings from the two-part study, published in today's issue of *Nature*, provides new insight in understanding how the brain functions, which ultimately has broad implications for the development of drug therapy to treat neurological diseases such as Alzheimer's and Parkinson's, as well as learning and memory disorders.

"This is pure, fundamental research," said Dr. Thomas Südhof, director of the Center for Basic Neuroscience at UT Southwestern and senior author of the first part of the study. "It is essential for understanding various diseases of the nervous system. The premise of our work is the understanding of neurotransmitter release, which is a necessity for understanding brain function and how the brain works."

The researchers bred mice that lacked the brain proteins RIM1α or Rab3A. In part one of the study, the researchers report a change in short-term plasticity in the mice lacking the RIM1α protein compared to other types of mutant mice. In part two of the study, the researchers report a correlation between the RIM1α protein and long-term plasticity. The terms short- and long-term plasticity refer to changes that occur during neurotransmitter release.

"We found that the mice lacking the protein were still viable, but there were some deficits in short-term plasticity – when changes occur at the synapses for a short period of time. The strength of synaptic transmission determines how we process information. It affects everything from memory to thinking and feeling," said Dr. Susanne Schoch, a postdoctoral research fellow and lead author of the two-part study.

(MORE)

"We also found that RIM1α has a central function in neurotransmitter release and is required for long-term plasticity, which is similar to short-term plasticity, but the changes are usually smaller and last longer. Long-term plasticity has been particularly well-studied in recent years, more so than short-term plasticity. It is thought to be important for long-term memory," Schoch said.

The RIM1 protein was identified in 1997 by Südhof and his research collaborators.

"I think once the whole process is better understood there definitely could be implications for drug development," Schoch said. "Right now we're trying to put together a huge puzzle, so the full picture is still very unclear. Once we learn more about the entire process, then it would be helpful for understanding more about learning and memory, but right now we are getting a basic understanding of how the process works."

Südhof's research focuses on nerve-cell interaction and neurotransmitter release. Through this research he hopes to gain a better understanding of brain function under normal and pathologic conditions. Südhof and his collaborators made an important discovery last year about how a harmful Alzheimer's disease protein functions in healthy brains. The findings, which put researchers one step closer to defining the pathogenesis of the disease, were published in *Science* in July 2000.

Other contributors to the *Nature* studies included researchers from Stanford University School of Medicine; Albert Einstein College of Medicine of Yeshiva University; the Leibniz Institute for Neurobiology in Magdeburg, Germany; and the Max-Plank Institute for Experimental Medicine in Göttingen, Germany. Dr. Konark Mukherjee and Dr. Yun Wang, both research fellows in the Center for Basic Neuroscience at UT Southwestern, also contributed to the first part of the study.

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