SOUTHWESTERN NEWS

Media Contact: Amanda Siegfried
214-648-3404
amanda.siegfried@utsouthwestern.edu

EMBARGOED UNTIL 11 A.M. CST WEDNESDAY, FEB. 16, 2005

New research questions basic tenet of neuron function

DALLAS – Feb. 16, 2005 – New findings by researchers at UT Southwestern Medical Center challenge one of the established views of how nerve cells communicate with one another.

Every time we move, feel emotions, think or remember, the nerve cells, or neurons, in our body transmit messages to one another via chemical signals called neurotransmitters. Within neurons are tiny organelles called synaptic vesicles that sequester neurotransmitters and release them when needed into the synapse, or space between nerve cells, where the chemical signal is transmitted to other neurons.

It is known that synaptic vesicles release their neurotransmitters in two different "modes" – one when the neuron is stimulated and actively relaying a message, and the other through spontaneous release when the neuron is "at rest," or inactive. Until now it was believed that the same synaptic vesicles were responsible for releasing neurotransmitters in both modes.

However, new research by UT Southwestern scientists appearing in the Feb. 17 issue of the journal *Neuron* suggests that two distinct types of synaptic vesicles are responsible for the two different modes of neurotransmitter release – one type of vesicle for spontaneous release, another vesicle associated with activity-dependent release.

"These findings question one of the core tenets of synaptic function and reveal significant complexity in organization of synaptic vesicles within individual synapses," said Dr. Ege Kavalali, assistant professor in the Center for Basic Neuroscience and of physiology at UT Southwestern and senior author on the study.

Neurotransmitters regulate many different aspects of mood, cognition and behavior, such as emotional state, reactions to stress, pain, and the physical drives of sleep, appetite and sexuality.

A better understanding of such fundamental mechanisms of neurotransmitter release will aid researchers in their investigations of psychiatric disorders and neurological disorders such as mental retardation, autism, depression and epilepsy, all of which have been linked to abnormal

(MORE)

neurotransmitter function, said Dr. Kavalali.

In neuronal cell cultures, the researchers labeled synaptic vesicles with a fluorescent dye and observed how and when the vesicles released neurotransmitters, both when the neurons were at rest and when they were active. From these observations, as well as data gathered from electrophysiological techniques, the researchers found two distinct types of vesicles.

"The functional differences of these two sets of vesicles may be the result of differences in the protein and/or lipid composition of the vesicles," Dr. Kavalali said. "Higher-resolution analysis is needed to test whether the two sets of vesicles are indeed distinct."

Dr. Kavalali said that if the two types of vesicles have different molecular compositions, as their findings suggest, those differences may make it possible to independently regulate spontaneous and activity-dependent neurotransmitter release. Spontaneous release is thought to play a role in the development of the neural circuitry in the brain and body, while activity-dependent release is responsible for functions such as learning and memory.

Other researchers involved in the study were Dr. Yildirim Sara, now at Hacettepe University in Turkey, Dr. Xinran Liu, assistant professor of molecular genetics in the Center for Basic Neuroscience, Dr. Ferenc Deak, research associate with the Howard Hughes Medical Institute at UT Southwestern, and Medical Scientist Training Program student Tuhin Virmani.

###