Investigating a sometimes-faulty protein's role in brain links

May 5 2009, by Deborah Halber

(PhysOrg.com) -- Researchers at MIT's Picower Institute for Learning and Memory have shed light on how a protein implicated in cognitive disorders maintains and regulates brain cell structures that are key to learning and memory.

The work could lead to new treatments for autism, mental retardation and Fragile X syndrome, which researchers believe are tied to abnormalities in synapses, the junctures through which neurons communicate.

"Increase in the size of synapses and memory formation are closely linked," said Mariko Hayashi, a Picower Institute research affiliate and co-author a new study about the work that appeared in a recent issue of the journal Cell. "Synapses get larger when we learn something and smaller when we forget something or unused connections are pruned. This happens in infants' growing brains and in learning and memory during adulthood. "

The study shows how two proteins -- named Shank and Homer -- work together to form a structural platform that allows other critical proteins to link to it like Legos, changing the active neurons' synapses.

Getting the message

When one neuron sends a signal to another neuron through chemical

messages called neurotransmitters, receptors on the target membrane receive the signal. Shank and Homer help the receiving neuron get the message by interacting with a phalanx of receptors -- a kind of central switchboard for synaptic transmissions -- called the postsynaptic density (PSD).

Researchers hope that elucidating the little-understood structure and composition of the PSD will shed light on synaptic plasticity, the brain's ability to change, learn and remember.

Researchers are particularly interested in Shank because the protein is disrupted in a small proportion of autistic individuals.

"If a protein is missing or not working correctly, then the network structure is not formed the way it's supposed to be and cognitive problems occur. A striking example is in some cases of autism spectrum disorder, Shank has a mutation," Hayashi said. "Potentially, we may be able to manipulate the function of Shank in the brain and cure the disease."

Homer and Shank, the MIT researchers found, latch onto each other to form a solid structure other proteins can bind to. This helps explain how PSDs and spines get bigger when learning and memory occur, and could lead to new therapies that boost the size and integrity of these tiny complexes.

Specifically, Hayashi and colleagues from RIKEN Brain Science Institute, Brookhaven National Laboratory, University of Milano and New York University found that Homer forms a dumbbell-shaped structure that binds to two Shank molecules at each end. "We showed through electron microscope analysis that these two proteins form a mesh-like matrix structure," Hayashi said.

During brain development and learning and memory, "it is highly likely that Homer and Shank assemble or disassemble to change the shape of the PSD," Hayashi said.

This helps explain how the size of synapses and the number of receptors increase when learning and memory occur, and could lead to new therapies that control the size and integrity of the PSD.

Provided by Massachusetts Institute of Technology (news : web)