

Special protein helps maintain an efficient brain

May 18 2009, by Dian Land

(PhysOrg.com) -- The instruction manual for maintaining an efficient brain may soon include a section on synaptotagmin-IV (Syt-IV), a protein known to influence learning and memory, thanks to a study by UW-Madison researchers.

The study showed that Syt-IV keeps the strength of synapses — connections between <u>nerve cells</u> where communication occurs — within a useful range of neither too strong nor too weak.

Synapses' ability to adjust over time by becoming bigger and stronger or smaller and weaker — their plasticity — is at the heart of remembering, forgetting and learning. A delicate balance is required for this optimal <u>brain plasticity</u>.

The study appears in *Nature Neuroscience's* advanced online publication on May 17.

The findings may be useful in the future for treating neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease as well as epileptic seizures. Early stages of these disorders may stem from synaptic deficits.

"If a drug or genetic treatment could be designed to control Syt-IV expression and modify its effect on other key players involved in synaptic function, synapses might work better," says senior author Edwin R. Chapman, a Howard Hughes Medical Institute professor at the UW-



Madison School of Medicine and Public Health (SMPH).

Camin Dean, a postdoctoral fellow in Chapman's physiology department laboratory at the SMPH, did most of the work on the study.

The scientists have been studying synaptotagmins for several years, making great strides in understanding their role in releasing neurotransmitters and neuropeptides at both the sending and receiving sides of the synapse. The team is particularly interested in the way neurotransmitter-filled sacs, or vesicles, work at the nerve terminals.

In exploring Syt-IV, known for fluctuating up and down during the course of a typical day, the researchers first studied it in a cell culture and then in mice in which the protein had been knocked out. These animals usually show learning deficits.

"We quickly found that Syt-IV strongly affects multiple aspects of signal transmission, both pre- and post-synaptically," says Chapman, adding that the protein was not located where it was expected to be.

The researchers also performed standard experiments on the mice to test a phenomenon called long-term potentiation (LTP), the primary synapsestrengthening mechanism that promotes learning and <u>memory</u>.

"When we stimulate brain pathways heavily with this experiment, we see that synapses are reinforced and produce bigger responses," says Chapman. "The synapses remember the stimulation, they learn something from it and we can see evidence of that."

Despite having <u>learning</u> disabilities, the Syt-IV-free mice produced improved LTP. In fact, it was too high.

"If synapses are tweaked to the max, as they were in this case, they lose



plasticity and don't work well," says Chapman. "The overload also can lead to seizures."

The researchers believe that Syt-IV serves as a way to maintain synaptic homeostasis — or internal equilibrium — by reigning in LTP to a normal level.

The protein does its work indirectly by regulating brain-derived neurotrophic factor (BDNF), a growth factor essential for long-term nerve cell well-being. In recent years, BDNF also has been shown to affect synapses.

In the experiments, Syt-IV pulled down elevated LTP by restricting the release of BDNF on the receiving side of the synapse, gearing down synaptic activity.

"Syt-IV dynamically regulates LTP as it goes up and down, holding the activity in balance," he says. "For plasticity, you need a good dynamic range of synaptic activity — from low to high."

Meyer B. Jackson, Huisheng Liu, F. Mark Dunning and Payne Y. Chang were co-authors on the paper.

Provided by UW-Madison

Citation: Special protein helps maintain an efficient brain (2009, May 18) retrieved 4 May 2024 from <u>https://medicalxpress.com/news/2009-05-special-protein-efficient-brain.html</u>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.