Secretions of the mind

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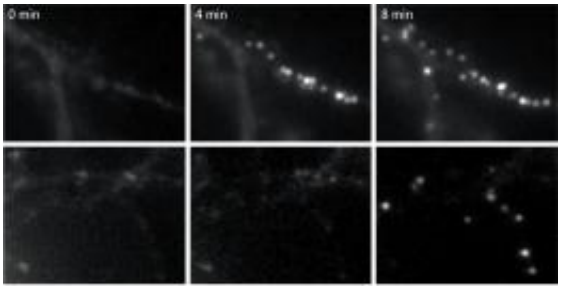

Enhanced BDNF secretion by overexpression of CAPS2 (top), photographed at four-minute intervals, in hippocampal neurons from mice lacking the CAPS2 gene (bottom: without CAPS2 expression). Credit: The National Academy of Sciences of the United States of America

A molecule called calcium-dependent activator protein for secretion 2 (CAPS2) promotes the secretion of a neurotrophic factor that is critical for the proper development and survival of networks of interneurons in the brain's hippocampus, researchers in Japan have shown.

Teiichi Furuichi of the RIKEN Brain Science Institute in Wako, and his colleagues showed previously that CAPS2 is involved in secretion of brain-derived neurotrophic factor (BDNF) from cerebellar granule cells and neurons in the cerebral cortex, but its exact role in secretion was unclear.

Yo Shinoda, a researcher of the Furuichi's group used antibody staining to examine the distribution of CAPS2 in cultured hippocampal neurons

of mice. He saw that most CAPS2 localized along the axons, but found some on secretory vesicles that contain and release BDNF.

To investigate the role of CAPS2 in BDNF secretion, the researchers visualized BDNF secretion in cells from mutant mice lacking the CAPS2 gene. They found that these cells secreted significantly less BDNF than normal cells, but the level returned to normal or became enhanced when they transfected the cells with CAPS2 (Fig. 1).

The researchers then examined hippocampal interneurons in the mutant mice and compared them with those in normal animals. These interneurons synthesize and secrete γ-aminobutyric acid (GABA), the main inhibitory neurotransmitter in the brain. The mutants had reduced numbers of these cells in hippocampus of the brain. Furthermore, analysis of inhibitory synapses under the electron microscope revealed that the mutants had fewer synaptic vesicles than the normal animals. The researchers also revealed that the vesicles were distributed over a smaller area within presynaptic boutons, the specialized area where loaded vesicles dock to release their contents.

Finally, the researchers used microelectrodes to examine the electrical activity of the cells from the mutants and discovered that there was a significant reduction in both the number and size of spontaneous inhibitory postsynaptic currents. Consequently, the mutant mice displayed anxiety-like behaviors that would be expected with a GABA signaling impairment.

The findings show that CAPS2 promotes BDNF secretion by affecting the kinetics of its release from dense-core vesicles, and that BDNF is essential for proper development and function of the networks of inhibitory interneurons in the hippocampus, the researchers conclude. “We are interested in the molecular mechanism underlying the enhanced BDNF secretion, and would like to analyze the kinetics of secretion

using state-of-the art cell imaging technology," Furuichi explains. "We also want to study relation of CAPS2-BDNF-GABA pathways in anxiety and depressive behavior."

More information: Shinoda, Y., et al. Calcium-dependent activator protein for secretion 2 (CAPS2) promotes BDNF secretion and is critical for the development of GABAergic interneuron network. *Proceedings of the National Academy of Sciences* USA 108, 373–378 (2011). www.pnas.org/content/early/201 … /1012220108.abstract

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