Dynamic molecular mechanism to keep brain activity stable

July 13 2009

In the brain, many types of synaptic proteins are spatio-temporally regulated to maintain synaptic activity at a constant level. Here, the Japanese research group led by Professor Masaki Fukata, Drs. Yuko Fukata and Jun Noritake in National Institute for Physiological Sciences, Japan, found that two types of palmitoylating enzymes finely-tune the location and function of a major synaptic protein, PSD-95, in different ways. They also found that this mechanism contributes to keeping synaptic activity stable when synaptic activity dynamically changes.

The Japan Science and Technology Agency (JST) supported this study. They report the finding in Journal of Cell Biology published on July 13, 2009.

The research group focused on two types of palmitoylating enzymes, DHHC2 and DHHC3. Protein palmitoylation, the most common lipid modification with the 16-carbon fatty acid palmitate, provides an important mechanism for regulating synaptic proteins in neurons. Here, the research group found that DHHC3 is located in the cell body of neurons to palmitoylate newly synthesized synaptic proteins such as PSD-95, and move out them into dendrites of neurons. In contrast, DHHC2 are located mainly in dendrites of neurons. Dendritically localized DHHC2 mediates dynamic palmitoylation of PSD-95 at synapses upon extracellular signals. When synaptic activity decreases, DHHC2 translocates to the synaptic site to facilitate palmitoylation of synaptic proteins to keep synaptic activity at a constant level.

"We have already found 23 types of palmitoylating enzymes. Our finding suggests that individual palmitoylating enzymes have distinct functions in neurons. Some of palmitoylating enzymes are known to be differently related to neurological disorders such as mental retardation, schizophrenia and Huntington's disease. Therefore, this palmitoylating enzyme family may represent exciting therapeutic targets", said Professor Fukata.

Source: National Institute for Physiological Sciences