Press Release

Cornichon Proteins Are Key to Improved Brain Signaling

Neurobiologists show how cornichon proteins dictate the course of excitatory transmission between nerve cells

Prof. Dr. **Bernd Fakler** and Dr. **Sami Boudkkazi** and their research team at the Institute of Physiology and the Cluster of Excellence BIOSS 'Centre for Biological Signalling Studies' of the University of Freiburg have succeeded in clarifying the function of the so-called cornichon proteins in the brain: They improve the communication between neurons and the reliability of signal transmission. The biologists published their findings in the journal *Neuron*.

In 2009, Fakler's research group has already demonstrated that the cornichon proteins are part of the AMPA-type glutamate receptors in the membranes of neurons in the brain. These receptors are composed of a pool of up to 35 proteins, and 70-80 percent of them contain cornichon proteins. The AMPA receptors are located at synapses – the junctions between two neurons where signals are transmitted. Upon its release from one cell, the neurotransmitter glutamate binds to the AMPA receptors of a neighboring cell and thus excites it. As a general rule, however, neurons in the brain do not pass on information upon single excitations, but rather integrate excitations over time. Thus, the more excitatory stimuli a neuron receives from different synapses, the more likely it will transmit the information.. AMPA receptors have a special function for cellular learning, explains Fakler: "After 'learning', a neuron transmits signals more quickly and reliably upon stimulation. As far as we can tell, neurons achieve this primarily by increasing the amount of AMPA receptors in their synapses, which leads to stronger excitation." By elucidating the structure of the AMPA receptors, researchers hope to improve their understanding of learning processes in the brain.

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Freiburg, 21.05.2014

The biologists have now discovered that “Cornichon-containing AMPA receptors keep their pores open for a longer period of time after activation by glutamate, thus promoting a longer-lasting excitatory current,” says Fakler. As a consequence of the increased synaptic excitation, the threshold for transmission of information is reached more quickly and reliably. It was previously unclear why some neurons, such as interneurons, show short excitatory currents, while others, like mossy cells or pyramidal cells, exhibit longer-lasting excitations. The Freiburg researchers demonstrated the key role of the cornichon proteins by studying the electrical signals at individual synapses in the rat brain: They stimulated the synapses of mossy cells and interneurons and compared the ionic currents through the respective AMPA receptors. By labelling the cornichon proteins, they demonstrated that mossy cells with cornichon-containing AMPA receptors maintain their excitation for longer periods. In addition, the biologists shortened the periods of excitation by removing cornichon proteins from the mossy cells via virus-mediated protein knockdown. When they added cornichon proteins to interneurons via virus-driven protein expression – these neurons were excited for longer periods of time.

Original publication:
Cornichon2 dictates the time course of excitatory transmission in individual hippocampal synapses. Boudkkazi S, Brechet A, Schwenk J and Fakler B (2014). Neuron 82 (in press)

Caption:
Experimental situation at a synapse: The “upper” pipette triggers an action potential (upper white trace) in the presynaptic ending (violet), while the “lower” pipette records the ionic currents through the AMPA receptors (lower white trace) in the postsynaptic mossy cell (red). Illustration: Bernd Fakler

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