A specific neurotransmitter receptor supports optimal information processing in the brain

March 30 2015

Researchers have been fascinated for a long time by learning and memory formation, and many questions are still open. Bochum-based neuroscientists Prof Dr Denise Manahan-Vaughan and Dr Hardy Hagena have discovered a key building block for this complex process. A particular neurotransmitter receptor, namely the metabotropic glutamate receptor 5, is a switch for activating opposing forms of plasticity in the hippocampus, a brain region vital for memory forming. They reported in the current edition of the *Journal of Neuroscience*.

Synapses between neurons process different information

The brain region surrounding the hippocampus is crucial for memory forming and for processing of spatial information. The hippocampus itself can be subdivided into different regions: dentate gyrus, Cornu Ammonis (CA) 3 and CA1. The information that has to be processed passes these three regions successively like a traffic route with each region processing different spatial information of the environment. CA3 plays a significant role here. It receives information via the so-called mossy fibres (MF), which originate in dentate gyrus neurons and, together with pyramidal neurons, form synapses in CA3; in this case MF-CA3-synapses. "These synapses are likely to participate in the encoding of a new memory trace" says Prof Manahan-Vaughan. In addition, the neurons in the CA3 region of the same as well as the neighbouring brain

hemisphere communicate via certain fibres – i.e. associative/commissural (AC) fibres via the AC-CA3 synapses, and are likely to support retrieval of established memories, a process that is called "pattern retrieval". "We have already demonstrated that these two synapses process different types of information that in turn is likely to comprise the cellular mechanisms for memory encoding and retrieval at these synapses" explains Hardy Hagena.

Adapting to requirements: synaptic plasticity

But how is information at MF-CA3 synapses and AC-CA3 synapses processed differently? On the neural level, information processing triggers an adaptation to the requirements, i.e. essentially a memory effect. Researchers call this synaptic plasticity. It manifests itself in two forms: as long-term potentiation, LTP, a strengthening of synaptic efficacy, and as long-term depression, LTD, a weakening of synaptic efficacy. Both LTP and LTD encode different types of spatial information. Previous studies have shown for different brain regions that the metabotropic glutamate receptor 5 (mGlu5 receptor) plays a crucial role in this long-term form of synaptic plasticity.

How a receptor affects memory formation

"Based on these findings, it was particularly interesting to find out if and to what extent the mGlu5 receptor affects synaptic plasticity and, consequently, memory formation in the CA3 region," explains Hagena. The researchers switched off the receptor pharmacologically at MF-CA3 synapses and then stimulated the respective information-transmitting fibres. Subsequently, they did not detect any LTP anymore, but they continued to observe LTD. As opposed to this, after switching off the mGlu5 receptor at AC-CA3 synapses, LTD got blocked, but LTP did not. "These results show that once the mGlu5 receptor is activated, LTP is primarily triggered in the MF-CA3 synapses and LTD in the AC-CA3

synapses," conclude the researchers.

Fascinating insight into the mode of operation of the hippocampus region

"These results have granted us a fascinating insight into the mode of operation and regulation of synaptic plasticity in the CA3 region of the hippocampus," as the researchers sum up their findings. "The impact of the mGlu5 receptor is particularly interesting, which determines the direction of synaptic plasticity on activation, e.g. for learning processes, for processing of new information regarding the environment and during memory retrieval processes such as 'pattern completion', by triggering LTP primarily in MF-CA3 synapses and LTD in AC-CA3 synapses." This opposing regulation of synaptic plasticity supports optimal information processing and storage and highlights the unique role this region plays in learning processes and memory formation.

More information: "mGlu5 acts as a switch for opposing forms of synaptic plasticity at mossy fiber-CA3 and commissural associational-CA3 Synapses," The *Journal of Neuroscience*, DOI: 10.1523/JNEUROSCI.3417-14.2015

Provided by Ruhr-Universitaet-Bochum