Press release

Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP)
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Slow version of the glutamate receptor AMPA discovered

The glutamate receptor AMPA was previously known for its lightning-fast transmission of excitation. All the more surprising, therefore, are the results that researchers from the Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP) in Berlin have now made: AMPA-receptors can also be extraordinarily slow. The discovery of the new type of receptor puts synaptic signaling in a whole new light. The groundbreaking findings were recently published in the journal Cell Reports.

The glutamate receptor AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) ensures that neurotransmitter signals are transferred from brain cell to brain cell at enormous speed. The fact that the receptor performs this vital task in a few milliseconds and is thus faster than all other glutamate receptors was considered certain.

Now it looks like the textbooks will have to be rewritten. Scientists from the Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP) in Berlin have discovered in mouse brains that there are also extraordinarily slow AMPA-receptors. These remain active for 500 milliseconds after stimulation - in other words, they are about 100 times slower than the "original". These are not isolated cases: About two-thirds of all hippocampal pyramidal cells express slow AMPA-receptors.

Two new AMPA-receptors identified

"Our results are a small revolution in biophysics and neuroscience," says Heisenberg Professor Dr. Andrew Plested, head of the Molecular Neuroscience and Biophysics group at the FMP and member of the Cluster of Excellence "NeuroCure". "This is because, for the first time, we were able to demonstrate that, in addition to the lightning-fast AMPA-receptors, there are at least two other types that operate in a much slower mode." This had already been suspected, he said, but had never been shown in such detail in brain tissue.

AMPA-receptors are vital for our brain function. It is still unclear what significance the now discovered slow AMPA-receptors with their synaptic potential of more than 100 milliseconds have for cognitive processes such as thinking, speaking, calculating or remembering. This exciting question will have to be explored further. Researchers are still not entirely sure whether AMPA-receptors take on different properties by being able to switch between fast and slow modes - or whether they are fundamentally different types. The researchers suspect that there are fast, slow and multifunctional AMPA-receptors.

"Based on our data, we are currently assuming multiple receptor types, which offers some really interesting new functions for this type of glutamate receptor," said Niccolò Pampaloni, Ph.D., first author of the study published in Cell Reports.

Unstable process with dangerous aspects

In this context, the research team has made another spectacular discovery: According to current doctrine, the response of the AMPA-receptor is exclusively determined by the signaling from the pre-synaptic cell, and the post-synaptic cell is merely a passive receptor. However, the researchers found robust evidence that slow AMPA-receptors in the postsynaptic cell control the duration and strength of synaptic signal transmission. For this purpose, they apparently
use auxiliary proteins.

But this could also have dangerous aspects, says Niccolò Pampaloni, who is funded by an EMBO stipend. "We're dealing with a very unstable feedback process. If somehow acts in the wrong way, this could lead a runaway excitation that could be linked to epilepsy, for example. We also don't know what happens once this process gets out of control - for example, due to an accident, a stroke or some other event in which a lot of glutamate is released."

New chapter opened in neuroscience
The impact of the slow AMPA current regarding brain function and pathologies can only be answered in the next step. First of all, it must be clarified whether humans actually possess these newly-discovered AMPA receptors. The researchers plan to investigate this crucial question shortly using human tissue samples. A cooperation with the Charité –Universitätsmedizin via the Cluster of Excellence "NeuroCure" has already been initiated.

Based on the current data, the Berlin research team assumes that slow AMPA-receptors are widely distributed in the mammalian brain, beyond the hippocampus. Biophysicist Plested: "We hope we've opened a new chapter with our discovery, which both basic researchers and neuroscientists will be able to exploit."

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