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Scientists identify critical new protein complex involved in learning and memory

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Scientists from the Florida campus of The Scripps Research Institute (TSRI) have identified a protein complex that plays a critical but previously unknown role in learning and memory formation.

The study, which showed a novel role for a protein known as RGS7, was published April 22, 2014 in the journal *eLife*, a publisher supported by the Howard Hughes Medical Institute, the Max Planck Society and the Wellcome Trust.

"This is a critical building block that regulates a fundamental process—memory," said Kirill Martemyanov, a TSRI associate professor who led the study. "Now that we know about this important new player, it offers a unique therapeutic window if we can find a way to enhance its function."

The team looked at RGS7 in the hippocampus, a small part of the brain that helps turn short-term memory in long-term memory.

The scientists found the RGS7 protein works in concert with another protein, R7BP, to regulate a key signaling cascade that is increasingly seen as a critical to cognitive development. The cascade involves the neurotransmitter GABA, which binds to the $GABA_b$ receptor and opens inhibitory channels known as GIRKs in the cell membrane. This process ultimately makes it more difficult for a nerve cell to fire.

This process turned out to be critical to normal functioning, as the

research showed mice lacking RGS7 exhibited deficits in learning and memory.

Martemyanov believes the findings could ultimately have broad therapeutic application. "GIRK channels are implicated in a range of neuropsychiatric conditions, including drug addiction and Down's syndrome, that result from a disproportionate increase in neuronal inhibition as a result of greater mobilization of these channels," he said. "Now that we know the identity of the critical modulator of GIRK channels we can try to find a way to increase its power with the hopes of reducing the inhibitory overdrive, and that might potentially alleviate some of the disruptions seen in Down's syndrome. It is possible that similar strategies might apply for dealing with addiction, where adaptations in the $GABA_b$-GIRK pathway play a significant role."

Targeting the RGS7 protein could allow for better therapeutic outcomes with fewer side effects because it allows for fine tuning of the signaling, according to Olga Ostrovskaya, the first author of the study and a member of Martemyanov's lab, who sees many ways to follow up on the findings.

"We're looking into how RGS7 is involved in neural circuitry and functions tied to the striatum, another part of the brain responsible for procedural memory, mood disorders, motivation and addiction," Ostrovskaya said. "We may uncover the RGS7 regulation of other signaling complexes that may be very different from those in hippocampus."

More information: "RGS7/Gβ5/R7BP Complex Regulates Synaptic Plasticity and Memory by Modulating Hippocampal Gababr-Girk Signaling," *eLife*, www.elifesciences.org/lookup/d … /10.7554/elife.02053

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