Study identifies a potential new approach to PTSD treatment

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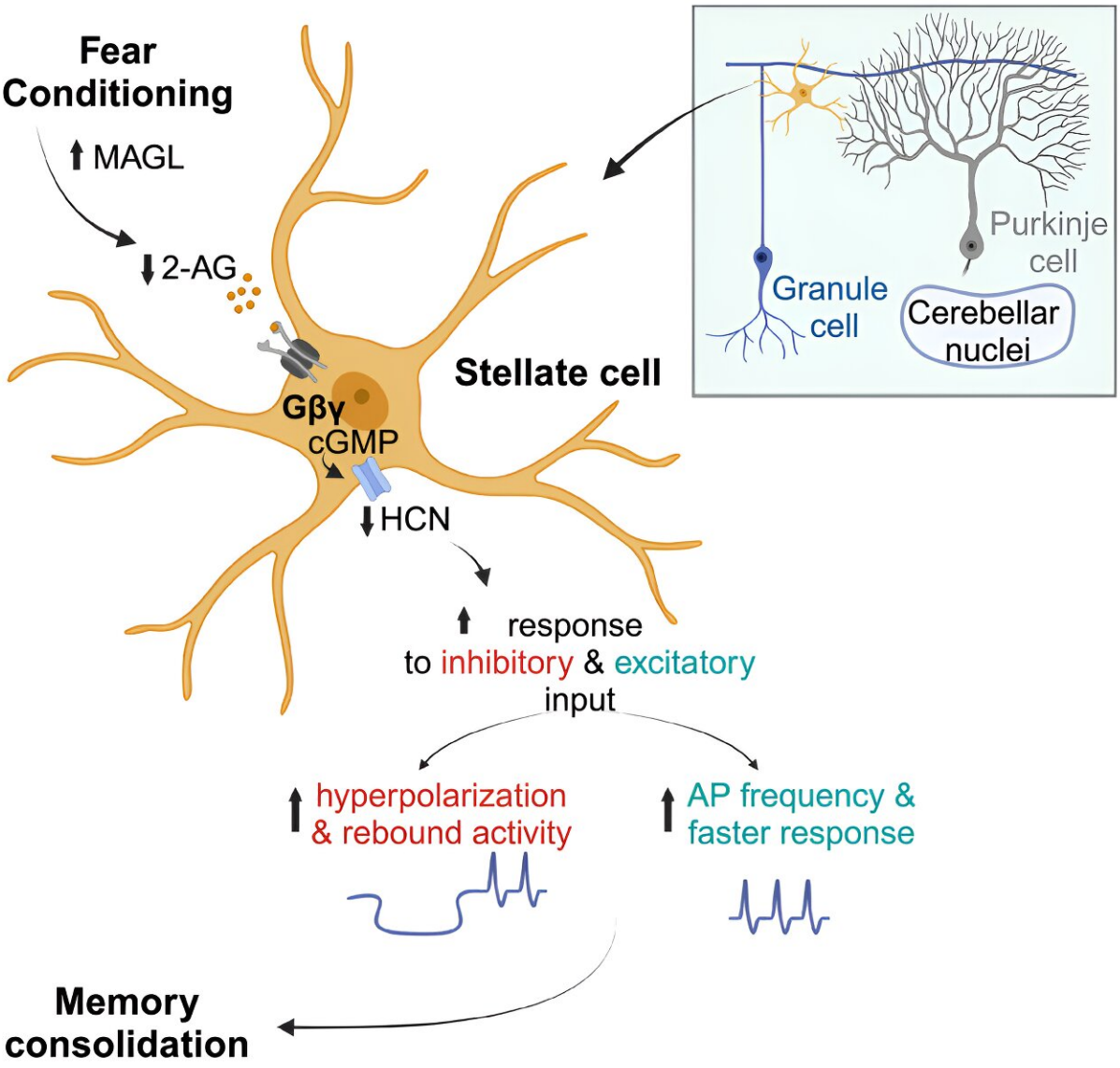

Graphical Abstract. Credit: *Cell Reports* (2023). DOI: 10.1016/j.celrep.2023.113057

An LSU Health New Orleans research study led by Siqiong June Liu, Ph.D., Professor of Cell Biology and Anatomy, has found that cerebellar inhibitory interneurons are essential for fear memory, a type of emotional memory formation. Inhibitory interneurons within the cerebellar circuitry act as gatekeepers and control the output of the cerebellar cortex.

The formation of fear memory requires the activity of these interneurons. The findings, which may lead to a novel treatment approach for post-traumatic stress disorder, are published in *Cell Reports*.

"While synaptic plasticity is considered the basis of learning and memory, modifications of the intrinsic excitability of neurons can amplify the output of neuronal circuits and consequently change behavior," notes Dr. Liu. "In the cerebellum, we find that silencing molecular layer interneurons completely abolishes fear memory, revealing their critical role in memory consolidation."

The cerebellum is a brain region that is known to control motor coordination. Recent work has shown that it is also critical for the formation of memory, but not how the cerebellar circuitry accomplishes this function.

The research team found that fear conditioning suppresses hyperpolarization-activated cyclic nucleotide-gated (HCN) channels and enhances cerebellar interneuron excitability. HCN currents are similar to pacemakers in the brain because they help regulate rhythmic activity and

communication between brain cells. HCN loss is driven by a learning-induced decrease in endocannabinoid levels. When the activity of these neurons is suppressed, experimental animals do not remember the experience a few hours after learning.

"Our study reveals that activity in cerebellar interneurons drives fear memory formation via a learning-specific increase in intrinsic excitability," Liu concludes. "This highlights the importance of moving beyond traditional synaptic plasticity-focused investigations of memory formation and suggests a novel therapeutic approach for the treatment of PTSD."

More information: Kathryn Lynn Carzoli et al, Cerebellar interneurons control fear memory consolidation via learning-induced HCN plasticity, *Cell Reports* (2023). DOI: 10.1016/j.celrep.2023.113057

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