Study reveals fatty acids hold clue to creating memories

February 6 2024

L to R: Dr. Isaac Akefe and Professor Fred Meunier in the lab. Credit: Queensland Brain Institute

Researchers at the University of Queensland have revealed the crucial role of saturated fatty acids in the brain's consolidation of memories.

Dr. Isaac Akefe from UQ's Queensland Brain Institute has uncovered the molecular mechanism and identifies the genes underlying the memory creation process, opening the door to a potential treatment for neurodegenerative disorders. The research paper is published in the EMBO Journal.

"We've shown previously that levels of saturated fatty acids increase in the brain during neuronal communication, but we didn't know what was causing these changes," Dr. Akefe said.

"Now for the first time, we've identified alterations in the brain's fatty acid landscape when the neurons encode a memory.

"An enzyme called phospholipase A1 (PLA1) interacts with another protein at the synapse called STXBP1 to form saturated fatty acids."

The brain is the body's fattiest organ, with fatty compounds called lipids making up 60% of its weight. Fatty acids are the building blocks of a class of lipids called phospholipids.

The work done in Professor Frederic Meunier's laboratory has shown that STXBP1 controls the targeting of the PLA1 enzyme, coordinating the release of fatty acids and directing communication at the synapses in the brain.

"Human mutations in the PLA1 and the STXBP1 genes reduce free fatty acid levels and promote neurological disorders," Professor Meunier said.

"To determine the importance of free fatty acids in memory formation, we used mouse models where the PLA1 gene is removed.

"We tracked the onset and progression of neurological and cognitive decline throughout their lives.

"We saw that even before their memories became impaired, their saturated free fatty acid levels were significantly lower than control mice.

"This indicates that this PLA1 enzyme, and the fatty acids it releases, play a key role in memory acquisition."

The research has important implications for understanding of how memories are formed.

"Our findings indicate that manipulating this memory acquisition pathway has exciting potential as a treatment for neurodegenerative diseases, such as Alzheimer's," Professor Meunier said.

The research team acknowledges the contributions of Ph.D. candidates Saber Abd Elkader from the Australian Institute for Bioengineering and Nanotechnology, and Benjamin Matthews from the Queensland Brain Institute.

This is a collaborative study with the University of New South Wales, University of Strasbourg, University of Bordeaux, The Scripp Research Institute and the Baylor College of Medicine.

More information: Isaac O Akefe et al, The DDHD2-STXBP1 interaction mediates long-term memory via generation of saturated free fatty acids, *The EMBO Journal* (2024). DOI: 10.1038/s44318-024-00030-7

Provided by University of Queensland