Molecular mechanism of long-term memory discovered

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Caenorhabditis elegans. Credit: Wikipedia

Researchers at the University of Basel have discovered a molecular mechanism that plays a central role in intact long-term memory. This mechanism is also involved in physiological memory loss in old age.

Many life forms, from worms to humans, have differentiated memory functions, such as short-term and long-term memory. Interestingly, at the cell and molecule level, many of these functions are nearly identical from life form to life form. Detecting the molecules involved in memory processes is of great importance to both basic and clinical research, since it can point the way to the development of drugs for memory disorders.

By studying roundworms (*Caenorhabditis elegans*), scientists at the Transfaculty Research Platform for Molecular and Cognitive Neurosciences (MCN) at the University of Basel have now discovered a molecular mechanism of long-term memory that is also involved in memory loss in old age. They report on their findings in the journal *Current Biology*.

The team led by Dr. Attila Stetak, Professor Andreas Papassotiropoulos and Professor Dominique de Quervain used sensory stimuli to first examine the learning and memory ability of genetically modified roundworms lacking a certain gene, mps-2. This gene contains the blueprint for part of a voltage-dependent ion channel in the nerve cell membrane and is suspected of playing a role in memory functions.

It was found that modified worms had equally good short-term memory as unmodified specimens. However, as the length of the experiment increased, the researchers found that the genetically modified worms were less able to retain what they learned. Without mps-2, they had a reduced long-term memory.

Age-related memory loss

In roundworms, as in humans, a loss of memory can be observed with increasing age. However, the molecular basis for this process is largely unclear. In further experiments, the researchers were able to prove that unmodified worms with the mps-2 gene exhibit a strong reduction of the

MPS-2 protein, the product of the gene, in old age. This was related to reduced memory performance.

This lack of MPS-2 protein proved not to be a passive but an actively regulated process. The research team was able to identify another protein, NHR-66, as responsible for regulating this deficiency. NHR-66 actively curbs the reading of the mps-2 gene and thus production of the MPS-2 protein in old age. If in older worms MPS-2 protein level was artificially induced or their NHR-66 was turned off, they had a similarly good memory as younger worms. Both molecules, MPS-2 and NHR-66, therefore make for interesting targets for drugs that could mitigate age-related memory loss. In further studies, the researchers want to examine therapeutic options based on their discovery.

More information: Bank G. Fenyves et al, Dual Role of an mps-2/KCNE-Dependent Pathway in Long-Term Memory and Age-Dependent Memory Decline, *Current Biology* (2020). DOI: 10.1016/j.cub.2020.10.069

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