Medical Xpress

Molecular basis of age-related memory loss explained

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As we are getting older, our ability to learn and remember new things declines. Credit: Fotolia

From telephone numbers to foreign vocabulary, our brains hold a seemingly endless supply of information. However, as we are getting older, our ability to learn and remember new things declines. A team of scientists around Associate Prof Dr Antonio Del Sol Mesa from the Luxembourg Centre for Systems Biomedicine of the University of

Luxembourg and Dr Ronald van Kesteren of the VU University Amsterdam have identified the molecular mechanisms of this cognitive decline using latest high-throughput proteomics and statistical methods.

The results were published this week in the prestigious scientific journal *Molecular and Cellular Proteomics*.

Brain cells undergo chemical and structural changes, when information is written into our memory or recalled afterwards. Particularly, the number and the strength of connections between nerve cells, the so-called synapses, changes. To investigate why learning becomes more difficult even during healthy ageing, the scientists looked at the molecular composition of brain connections in healthy mice of 20 to 100 weeks of age. This corresponds to a period from puberty until retirement in humans. "Amazingly, there was only one group of four proteins of the so-called extracellular matrix which increased strongly with age. The rest stayed more or less the same," says Prof Dr Antonio del Sol Mesa from the Luxembourg Centre for Systems Biomedicine.

The extracellular matrix is a mesh right at the connections between brain cells. A healthy amount of these proteins ensures a balance between stability and flexibility of synapses and is vital for learning and memory. "An increase of these proteins with age makes the connections between brain cells more rigid which lowers their ability to adapt to new situations. Learning gets difficult, memory slows down," Dr Ronald van Kesteren of the VU University Amsterdam elaborates.

In addition, the researchers not only looked at the individual molecules but also analysed the whole picture using a systems biology approach. Here they described the interplay between molecules as networks that together tightly control the amount of individual molecules and their interactions. "A healthy network keeps all molecules in the right level for proper functioning. In older mice we found, however, that the overall

molecular composition is more variable compared to younger animals. This shows that the network is losing its control and can be more easily disturbed when we age," Prof Dr Antonio del Sol Mesa explains. According to the researchers this makes the brain more susceptible to diseases.

Hence, this insight into the normal aging process could also help in the future to better understand complex neurodegenerative diseases such as Alzheimer's and Parkinson's disease. Chemical compounds that modulate the extracellular matrix might be promising new treatments for learning disorders and memory loss.

More information: Vegh MJ, Rausell A, Loos M, Heldring CM, Jurkowski W, van Nierop P, Paliukovich I, Li KW, Del Sol A, Smit AB, Spijker S, van Kesteren RE. "Hippocampal extracellular matrix levels and stochasticity in synaptic protein expression increase with age and are associated with age-dependent cognitive decline." *Mol Cell Proteomics*. 2014 Jul 20. DOI: 10.1074/mcp.M113.032086

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