Key mechanism discovered which prevents memory loss in Alzheimer's disease

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Neurons communicate with one another by synaptic connections, where information is exchanged from one neuron to its neighbor. These connections are not static, but are continuously modulated in response to the ongoing activity (or experience) of the neuron. This process, known as synaptic plasticity, is a fundamental mechanism for learning and memory in humans as in all animals. In fact, we now know that alterations in synaptic plasticity are responsible for memory impairment in cognitive disorders such as Alzheimer's disease. Nevertheless, the mechanisms by which these alterations take place are still starting to be uncovered.

This new research work, published in *Nature Neuroscience*, has been led by Dr. Shira Knafo (Ikerbasque, Biophysics Unit: CSIC/The University of the Basque Country), Dr. Jose A. Esteban (Severo Ochoa Center for Molecular Biology, National Research Council/ Autonomous University of Madrid), and Dr. César Venero (Univ. Nacional de Educación a Distancia). These investigators have discovered that in Alzheimer's disease, synaptic plasticity is altered by a protein originally described as a tumor suppressor: PTEN. In 2010, the research group of Dr. Esteban discovered that PTEN is recruited to synapses during normal (physiological) synaptic plasticity. This new investigation by Drs. Knafo, Venero and Esteban, now indicates that this mechanism runs uncontrolled during Alzheimer's disease. One of the pathological agents of the disease, the beta-amyloid, drives PTEN into synapses excessively, unbalancing the mechanisms for synaptic plasticity and impairing memory formation.

An important aspect of this study is that it also describes how PTEN is recruited to synapses in response to beta-amyloid, and proposes a strategy to prevent it. Using a mouse model of Alzheimer's disease, the investigators developed a molecular tool to shield synapses from the recruitment of PTEN. With this tool, neurons are rendered resistant to beta-amyloid, and Alzheimer's mice preserve their memory.

Although this is basic research using animal models, these studies contribute to dissect the mechanisms that control our cognitive function, and orient us towards potential therapeutic avenues for mental diseases where these mechanisms are deficient.

More information: Shira Knafo et al. PTEN recruitment controls synaptic and cognitive function in Alzheimer's models, *Nature Neuroscience* (2016). DOI: 10.1038/nn.4225

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