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A mechanism to improve learning and memory

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There are a number of drugs and experimental conditions that can block cognitive function and impair learning and memory. However, scientists have recently shown that some drugs can actually improve cognitive function, which may have implications for our understanding of cognitive disorders such as Alzheimer's disease. The new research is reported 21 February in the open-access journal *PLoS Biology*.

The study, led by Drs. Jose A. Esteban, Shira Knafo and Cesar Venero, is the result of collaboration between researchers from The Centro de Biología Molecular Severo Ochoa and UNED (Spain), the Brain Mind Institute (EPFL, Switzerland) and the Department of Neuroscience and Pharmacology (Faculty of Health Sciences, Denmark).

The human brain contains trillions of neuronal connections, called synapses, whose pattern of activity controls all our cognitive functions. These synaptic connections are dynamic and constantly changing in their strength and properties. This process, known as synaptic plasticity, has been proposed as the cellular basis for learning and memory. Indeed, alterations in synaptic plasticity mechanisms are thought to be responsible for multiple cognitive deficits, such as autism, Alzheimer's disease and several forms of mental retardation.

The study by Knafo et al. provides new information on the molecular mechanisms of synaptic plasticity, and how this process may be manipulated to improve cognitive performance. They find that synapses can be made more plastic by using a small protein fragment (peptide)

derived from a neuronal protein involved in cell-to-cell communication. This peptide (called FGL) initiates a cascade of events inside the neuron that results in the facilitation of synaptic plasticity. Specifically, the authors found that FGL triggers the insertion of new neurotransmitter receptors into synapses in a region of the brain called the hippocampus, which is known to be involved in multiple forms of learning and memory. Importantly, when this peptide was administered to rats, their ability to learn and retain spatial information was enhanced.

Dr. Esteban remarks: "We have known for three decades that synaptic connections are not fixed from birth, but they respond to neuronal activity modifying their strength. Thus, outside stimuli will lead to the potentiation of some synapses and the weakening of others. It is precisely this code of ups and downs what allows the brain to store information and form memories during learning".

Within this framework, these new findings demonstrate that synaptic plasticity mechanisms can be manipulated pharmacologically in adult animals, with the aim of enhancing cognitive ability. Dr. Knafo adds: "These are basic studies on the molecular and cellular processes that control our cognitive function. Nevertheless, they shed light into potential therapeutic avenues for mental disorders where these mechanisms go awry".

More information: Knafo S, Venero C, Sa´nchez-Puelles C, Pereda-Pere´z I, Franco A, et al. (2012) Facilitation of AMPA Receptor Synaptic Delivery as a Molecular Mechanism for Cognitive Enhancement. *PLoS Biol* 10(2): e1001262. doi:10.1371/journal.pbio.1001262

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