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IMBECU

## New mechanisms that promote neuronal plasticity have been discovered

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CONICET researchers have discovered new tracts by which the progesterone fosters the formation of dendritic spines, essential structures for knowledge, memory and learning.

At the Institute of Experimental Medicine and Biology of Cuyo (IMBECU-CONICET), in Mendoza, Argentina, Matias Sánchez and Marina Flamini investigate the fast signaling mechanisms that control the neuronal plasticity through sex hormones. These mechanisms modulate cells' movement through the control of the protein filament network that forms the cellular skeleton called actinic cytoskeleton.

In a recent study published in *Molecular Endocrinology* (April 2013), the investigators issued the finding of new tracts by which progesterone promotes the formation of dendritic spines. "These structures are fundamental for knowledge, memory and learning. The spines are neuron branches devoted to the reception and transmission of nerve stimuli and impulses", Sánchez, CONICET assistant investigator at the IMBECU.

### Sex hormones and the brain

For a long time the brain has been studied as an important sex hormones target, the ones that play multiple regulatory roles like proliferation, survival and cell differentiation. "Sex hormones, particularly in the estrogen and the progesterone, control neuronal plasticity, that is to say, the cellular property that allows neuron to establish interconnections that modulate the stimuli perception", Flamini, CONICET assistant investigator at the IMBECU, affirms.

Sex hormones control the neuronal plasticity through modifications in the spine density present in the neuron. These alterations are related to the cyclic changes of sex hormones levels such as estrogen and progesterone, which are relevant to explain the differences between men and women in neural functions and dysfunctions.

Recent clinical studies suggest that the lack or decrease of sex hormones levels, as in the case of menopausal women, could be correlated with the development of new neurodegenerative diseases such as Alzheimer, Parkinson or Dementia. Furthermore, it is stated that Hormone Replacement Treatments in menopausal women could diminish the progression in this type of pathologies. This suggests that the estrogens and progestogens could have a key role in plasticity control and the transmission of information between the neurons and a protective effect against neurodegenerative disease-derived damages.

### The importance of new findings and perspectives

It is known that the progesterone influences the neuronal embryonic development and it continues acting over mature neurons through the dynamic control of the actin filaments which form

part of the cell 'skeleton'. The results obtained by Sánchez and Flamini allow to understand how the progesterone fosters changes in neuronal plasticity and transmission, what promises biologic and medical implications.

"Our study showed that the progesterone uses various regulatory proteins of the actin skeleton to induce changes in the neuronal morphology and this is accomplished through at least two regulatory mechanisms that depend on the progesterone receptor", Sánchez, explains and adds that the interaction between the progesterone and its receptor allow the hormone to recruit/ take different proteins that are involved in the regulation of the actin cell cytoskeleton remodeling. Once these changes take place at the cell membrane level, focal adhesion complexes are formed and they allow cells to adhere and induce/provoke the formation of specialized structures such as the dendrites. These series of events are necessary to complete the delicate mechanism that controls the dendritic formation regulated by the progesterone.

Recent research proved that the function loss of the protein that controls this type of process results in a decline in the dendrites formation, which is related to knowledge, memory and learning deficit. "These facts suggest that some degenerative disorders associated to the decrease or loss of estrogen and progestogens could be produced, in some extent, by the lack of activation and control of proteins such as the one called WAVE1, which helps to 'anchor' filaments," Flamini comments.

According to the investigators, future research could lead to a better understanding of the sex steroids role over the dynamic control of the brain physiology. "At the same time, this could encourage the development of new drugs for endocrine therapies against relevant neurological diseases", they conclude.

### **The working group in Argentina and its international collaborators**

Sánchez and Flamini work along with national and international colleagues like Tommaso Simoncini and Andrea Riccardo Genazzani from Molecular and Cellular Gynecological Endocrinology Laboratory (MCGEL-University of Pisa, Italy), and Xiao Dong Fu from the Department of Physiology (Sun Yat-sen University, People's Republic of China). The group also includes undergraduate students and other collaborators. The investigations are subsidized by the Italian University, Scientific Research Ministry (MIUR) and the National Cancer Institute (INC-Argentina).

### **About the CONICET**

The National Scientific and Technical Research Council (CONICET) is the main organization in charge of the promotion of Science and Technology in Argentina. The principal objective of this agency is to boost and implement scientific and technical activities in the country and in all different fields of knowledge.

This institution has its own researchers and professionals. Thus, CONICET offers different grants and finances projects, institutions and national research centres in all parts of the country.

CONICET comprises general areas so as to enable comprehensive development of scientific and technological research. Thus, it is in charge of all social interest and productive areas of Argentina. Apart from that, this organization promotes different exchanges and stimulates national and international cooperative processes.

Areas of knowledge of CONICET:

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-Biological and Health Sciences.

-Exact and Natural Sciences.

-Social Science and humanities.

Technology is present in all the areas and it promotes the implementation of knowledge.

Founded in 1958, CONICET is a national institution under the Ministry of Science, Technology and Productive Innovation of Argentina. Besides, this agency is considered as one of the principal assets for the national fund in terms of science and technology.

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