The phosphodiesterase 5 inhibitor tadalafil, for enhancing cognition

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Therapeutic approaches based on agents that regulate signalling pathways involved in processes of memory formation could be good options to treat cognitive decline that occurs not only in different pathological conditions such as Alzheimer’s disease (AD), but also in normal aging. Phosphodiesterases (PDE) are enzymes that catalyze the hydrolysis of adenosine and/or guanosine 3’, 5’ cyclic monophosphate (cAMP or cGMP). cAMP/cGMP regulate signalling cascades that lead to the phosphorylation and activation of the transcription factors cAMP responsive element binding protein (CREB), one of the most important molecules in neuronal plasticity processes including learning and memory. PDE5 inhibitors have been shown to effectively restore memory function in animals in both physiological and different pathological conditions. Among them, Tadalafil, by its longer half-life and its safety profile could be a reliable good option for enhancing cognition. In the present study, the effect of tadalafil on PDE5 by measuring cGMP levels in the CSF of non-human primates was primarily analysed. Furthermore, the effect of a chronic treatment with tadalafil on cognitive function and on hippocampal spine density was studied in aged-mice. Two hours after tadalafil administration, cGMP levels in CSF of non-human primates were significant higher than the basal levels. A chronic treatment of 5 weeks with tadalafil produced a cognitive enhancement effect in both the Morris water maze and the fear conditioning test. This effect was accompanied by an increase in spine density of apical dendrites of CA1 pyramidal neurons and with a significant increase in the hippocampal brain derived neurotrophic factor (BDNF).

Biography

Garcia Osta A received her Bachelor Degree and her PhD in Pharmacy from the University of Navarra, Spain. Her postdoctoral training was obtained in the Alberini’s laboratory, in the Neuroscience Department at the Mount Sinai School of Medicine in New York. She joined the Neuroscience Department of CIMA in 2007. She is Investigator in the laboratory of Neurobiology of Alzheimer’s disease and she interested in the investigation of molecular basis of dementia in Alzheimer Disease. As an independent group, she leads several projects related to the search for new therapeutic targets to reverse the dementia associated with the pathology of Alzheimer’s disease.

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